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TRIAL DESIGN PLATFORM

Abstract

A method for determining trial designs that includes obtaining simulation data for a set of trial designs that includes combinations of design options for a set of criteria. The simulation data includes performance parameters and performance parameter values associated with each design in the set of trial designs for the set of criteria. The method further includes determining an optimality criteria for evaluating the trial designs. The optimality criteria includes at least one of Pareto optimality or convex hull optimality for clinical trial design performance values. The method further includes: determining at least one of a cooling cycle, a parameter change, or a direction; and searching, within the set of trial designs, for a set of globally optimum designs based on the optimality criteria using simulated annealing. The simulated annealing is based at least in part on at least one of the cooling cycle, the parameter change, or the direction.

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Background/Summary

CROSS-REFERENCE TO RELATED APPLICATIONS [0001] This application claims priority to and is a continuation of U.S. patent application Ser. No. 17/163,423, (Attorney Docket No. CYTL-0001-U01), filed Jan. 30, 2021, and entitled “TRIAL DESIGN PLATFORM”, published as U.S. 2021-0241859 A1. [0002] U.S. patent application Ser. No. 17/163,423 claims the benefit of priority to: [0003] U.S. Provisional Patent Application Ser. No. 62/968,874 (Attorney Docket No. CTYL-0001-P01), filed Jan. 31, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”; [0004] U.S. Provisional Patent Application Ser. No. 63/002,197 (Attorney Docket No. CTYL-0001-P02), filed Mar. 30, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”; [0005] U.S. Provisional Patent Application Ser. No. 63/002,253 (Attorney Docket No. CTYL-0001-P03), filed Mar. 30, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”; [0006] U.S. Provisional Patent Application Ser. No. 63/037,977 (Attorney Docket No. CTYL-0001-P04), filed Jun. 11, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”; [0007] U.S. Provisional Patent Application Ser. No. 63/085,700 (Attorney Docket No. CYTL-0001-P05), filed Sep. 30, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”; and [0008] U.S. Provisional Patent Application Ser. No. 63/086,474 (Attorney Docket No. CYTL-0001-P06), filed Oct. 1, 2020, and entitled “CLINICAL TRIAL DESIGN PLATFORM”. [0009] Each of the foregoing applications is incorporated herein by reference in its entirety for all purposes.

SUMMARY
[0010] The success and the performance of a clinical trial depends on the design of the trial. Different choices for the design of a trial may result in very different costs, completion times, and/or other performance parameters for the trial. A trial design platform, systems, and methods are described herein for evaluation and/or comparison of designs for a clinical trial. Evaluation and/or comparison may include a large number of design options. Embodiments of the current disclosure may be used to evaluate hundreds, thousands, or even millions of design options for a clinical trial

and may be used to find the optimal or near-optimal design for a trial.
[0011] The success of the clinical trial often depends on the ability to recruit a satisfactory number of patients, suitable to participate in the clinical trial. The number of suitable patients available to be recruited for a clinical trial is, in turn, typically a function of the sites selected for the clinical trial. The selection of sites for a clinical trial may include considerations and tradeoffs between hundreds or even thousands of site selections. Embodiments of the current disclosure may provide for a site selection platform, systems, and methods for evaluation and/or comparison of site selection options for a clinical trial.
[0012] The success of the clinical trial often depends on the availability of resources needed to conduct the clinical trial. The selection of sites for a clinical trial, with respect to optimizing available resources, may include considerations and tradeoffs between hundreds or even thousands of site selections. Embodiments of the current disclosure may provide for a resource optimization platform, systems, and methods for evaluation and/or comparison of site selection options with respect to optimizing resource availability for a clinical trial. In embodiments, the platform, systems, and methods described herein may be used to evaluate hundreds, thousands, or even millions of site selection options for a clinical trial and may be used to find the optimal or near-optimal resource availability for a trial.

Description

BRIEF DESCRIPTION OF THE FIGURES
[0013] FIG. **1** is a block diagram of a platform for providing global optimization of clinical trial designs, in accordance with an embodiment of the current disclosure;
[0014] FIG. **2** is a diagram of a process for globally optimizing clinical trial designs, in accordance with an embodiment of the current disclosure;
[0015] FIG. **3** is a schematic diagram of an apparatus for determining globally optimum designs, in accordance with an embodiment of the current disclosure;
[0016] FIG. **4** is a schematic diagram of an apparatus for determining globally optimum designs, in accordance with an embodiment of the current disclosure;
[0017] FIG. **5** is a flow chart depicting a method for determining globally optimum designs, in accordance with an embodiment of the current disclosure;
[0018] FIG. **6** is a flow chart depicting a method for determining globally optimum designs, in accordance with an embodiment of the current disclosure;
[0019] FIG. **7** is a flow chart depicting a method for determining globally optimum designs, in accordance with an embodiment of the current disclosure;
[0020] FIG. **8** is a schematic diagram of an apparatus for evaluating designs, in accordance with an embodiment of the current disclosure;
[0021] FIG. **9** is a flow chart depicting a method of evaluating designs, in accordance with an embodiment of the current disclosure;
[0022] FIG. **10** is a flow chart depicting a method of evaluating design, in accordance with an embodiment of the current disclosure;
[0023] FIG. **11** is a schematic diagram of an apparatus for evaluating designs, in accordance with an embodiment of the current disclosure;
[0024] FIG. **12** is a block diagram of an interface for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure;
[0025] FIG. **13** is a schematic diagram of another embodiment of an interface for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure;
[0026] FIG. **14** is a block diagram of two distinct views of the interface of FIG. **12**, in accordance

with an embodiment of the current disclosure;
[0027] FIG. **15** is a diagram of user types corresponding to the views of FIG. **14**, in accordance with an embodiment of the current disclosure;
[0028] FIG. **16** is a flow chart depicting a method for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure;
[0029] FIG. **17** is a flow chart depicting another method for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure;
[0030] FIG. **18** is a schematic diagram of an apparatus for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure;
[0031] FIG. **19** is a schematic diagram of an interactive interface for an advisor for guiding a user through configuration of trial design simulations and/or systems for optimizing clinical trial design, in accordance with an embodiment of the current disclosure;
[0032] FIG. **20** is a schematic diagram of another embodiment of the interactive interface of FIG. **19**, in accordance with an embodiment of the current disclosure;
[0033] FIG. **21** is a schematic diagram of a prompt of the interactive interface of FIG. **19**, in accordance with an embodiment of the current disclosure;
[0034] FIG. **22** is a block diagram depicting stages of configuring a clinical trial design optimization process, in accordance with an embodiment of the current disclosure;
[0035] FIG. **23** is flow chart depicting a method for guiding a user through configuration of trial design simulations and/or systems for optimizing clinical trial design, in accordance with an embodiment of the current disclosure;
[0036] FIG. **24** is a flow chart depicting another embodiment of the method of FIG. **23**, in accordance with an embodiment of the current disclosure;
[0037] FIG. **25** is a block diagram of an apparatus for guiding a user through configuration of trial design simulations and/or systems for optimizing clinical trial design, in accordance with an embodiment of the current disclosure;
[0038] FIG. **26** is a flow chart depicting a method for augmenting simulated data, in accordance with an embodiment of the current disclosure;
[0039] FIG. **27** is a schematic diagram of an apparatus for augmenting simulated data, in accordance with an embodiment of the current disclosure;
[0040] FIG. **28** is a is a flow chart for evaluating designs, in accordance with an embodiment of the current disclosure;
[0041] FIG. **29** is a flow chart depicting a method for evaluating designs, in accordance with an embodiment of the current disclosure;
[0042] FIG. **30** is a flow chart showing aspects of utilizing virtual populations, in accordance with an embodiment of the current disclosure;
[0043] FIG. **31** is a flow chart for utilizing virtual populations and counterfactual data, in accordance with an embodiment of the current disclosure;
[0044] FIG. **32** is a flow chart depicting a method for evaluating designs with counterfactual data, in accordance with an embodiment of the current disclosure;
[0045] FIG. **33** is a flow chart depicting a method for evaluating designs with counterfactual data, in accordance with an embodiment of the current disclosure;
[0046] FIG. **34** is a schematic depicting a circuit for evaluating designs with counterfactual data, in accordance with an embodiment of the current disclosure;
[0047] FIG. **35** is a is a schematic diagram of an apparatus for determining designs from user interactions, in accordance with an embodiment of the current disclosure;
[0048] FIG. **36** is a is a schematic diagram of an apparatus for determining designs from user interactions, in accordance with an embodiment of the current disclosure;

[0049] FIG. **37** is a flow chart depicting a method for determining designs from user interactions, in accordance with an embodiment of the current disclosure;
[0050] FIG. **38** is a flow chart depicting a method for determining designs from user interactions, in accordance with an embodiment of the current disclosure;
[0051] FIG. **39** shows aspects of a card interface, in accordance with an embodiment of the current disclosure;
[0052] FIG. **40** is a flow chart depicting a method for design analysis using a card interface, in accordance with an embodiment of the current disclosure;
[0053] FIG. **41** is a schematic diagram of an apparatus for design analysis using a card interface, in accordance with an embodiment of the current disclosure;
[0054] FIG. **42** is a schematic diagram of an apparatus for design analysis using a card interface, in accordance with an embodiment of the current disclosure;
[0055] FIG. **43** shows aspects of a tornado interface, in accordance with an embodiment of the current disclosure;
[0056] FIG. **44** shows aspects of a heatmap interface, in accordance with an embodiment of the current disclosure;
[0057] FIG. **45** is a schematic diagram of an embodiment of the platform **104** having a primary algorithm, in accordance with the current disclosure;
[0058] FIG. **46** is a flow chart depicting a workflow of the primary algorithm of FIG. **45**, in accordance with an embodiment of the current disclosure;
[0059] FIG. **47** is a schematic diagram of an apparatus that implements the primary algorithm of FIG. **45**, in accordance with an embodiment of the current disclosure;
[0060] FIG. **48** is a graph showing aspects of Pareto analysis in accordance with an embodiment of the current disclosure;
[0061] FIG. **49** is a table showing aspects of Pareto analysis in accordance with an embodiment of the current disclosure;
[0062] FIG. **50** is a schematic diagram of an apparatus for determining optimum designs using Pareto analysis, in accordance with an embodiment of the current disclosure;
[0063] FIG. **51** is a is a schematic diagram of an apparatus for determining optimum designs using Pareto analysis, in accordance with an embodiment of the current disclosure;
[0064] FIG. **52** is a flow chart depicting a method for determining globally optimum designs with Pareto analysis, in accordance with an embodiment of the current disclosure;
[0065] FIG. **53** is a flow chart depicting a method for determining globally optimum designs with Pareto analysis, in accordance with an embodiment of the current disclosure;
[0066] FIG. **54** depicts aspects of convex hull (CH) analysis in accordance with an embodiment of the current disclosure;
[0067] FIG. **55** depicts aspects of convex hull analysis in accordance with an embodiment of the current disclosure;
[0068] FIG. **56** is a is a schematic diagram of an apparatus for determining optimum designs using convex hull analysis, in accordance with an embodiment of the current disclosure;
[0069] FIG. **57** is a is a schematic diagram of an apparatus for determining optimum designs using convex hull analysis, in accordance with an embodiment of the current disclosure;
[0070] FIG. **58** is a flow chart depicting a method for determining globally optimum designs with convex hull analysis, in accordance with an embodiment of the current disclosure;
[0071] FIG. **59** is a flow chart depicting a method for determining globally optimum designs with convex hull analysis, in accordance with an embodiment of the current disclosure;
[0072] FIG. **60** shows aspects of robustness analysis in accordance with an embodiment of the current disclosure;
[0073] FIG. **61** shows aspects of robustness analysis in accordance with an embodiment of the current disclosure;

[0074] FIG. **62** is a schematic diagram of an apparatus for determining robustness of designs, in accordance with an embodiment of the current disclosure;
[0075] FIG. **63** is a flow chart depicting a method for determining robustness of designs, in accordance with an embodiment of the current disclosure;
[0076] FIG. **64** is a flow chart depicting a method for determining robustness of designs, in accordance with an embodiment of the current disclosure;
[0077] FIG. **65** is a is a schematic diagram of an apparatus for evaluating design with simulated annealing, in accordance with an embodiment of the current disclosure;
[0078] FIG. **66** is a is a flow chart evaluating design with simulated annealing, in accordance with an embodiment of the current disclosure;
[0079] FIG. **67** is a flow chart depicting a method for evaluating a design with simulated annealing, in accordance with an embodiment of the current disclosure;
[0080] FIG. **68** is a flow chart depicting a method for evaluating a design with simulated annealing, in accordance with an embodiment of the current disclosure;
[0081] FIG. **69** is a flow chart depicting a method of simulating clinical trial designs based in part on a Delaunay interpolation, in accordance with an embodiment of the current disclosure;
[0082] FIG. **70** is a schematic diagram of an apparatus for implementing the method of FIG. **69**, in accordance with an embodiment of the current disclosure;
[0083] FIG. **71** is a schematic diagram of a recommendation component for recommending clinical trial designs, in accordance with an embodiment of the current disclosure;
[0084] FIG. **72** is a schematic diagram of a recommendation engine, in accordance with an embodiment of the current disclosure;
[0085] FIG. **73** is a diagram depicting a relationship between sets of clinical trial designs, Pareto designs, convex hull designs, and recommended designs, in accordance with an embodiment of the current disclosure;
[0086] FIG. **74** is another diagram of the recommendation engine of FIG. **72**, in accordance with an embodiment of the current disclosure;
[0087] FIG. **75** is a diagram of a set of recommended clinical trial designs, in accordance with an embodiment of the current disclosure;
[0088] FIG. **76** is a diagram of a visualization of recommended clinical trial designs, in accordance with an embodiment of the current disclosure;
[0089] FIG. **77** is a diagram of another visualization of recommended clinical trial designs, in accordance with an embodiment of the current disclosure;
[0090] FIG. **78** is a flow chart depicting an embodiment of a method of recommending clinical trial designs, in accordance with the current disclosure;
[0091] FIG. **79** is a flow chart depicting another embodiment of the method of FIG. **78**, in accordance with the current disclosure;
[0092] FIG. **80** is a flow chart depicting another embodiment of the method of FIG. **78**, in accordance with the current disclosure;
[0093] FIG. **81** is a schematic diagram of an apparatus for implementing the method of FIG. **78**;
[0094] FIG. **82** is a diagram of a simulation queue, in accordance with an embodiment of the current disclosure;
[0095] FIG. **83** is a flow chart depicting a method for management and optimization of clinical trial designs, in accordance with an embodiment of the current disclosure;
[0096] FIG. **84** is a schematic diagram of an apparatus for management and optimization of clinical trial designs, in accordance with an embodiment of the current disclosure;
[0097] FIG. **85** is a block diagram of a simulation engine marketplace, in accordance with an embodiment of the current disclosure;
[0098] FIG. **86** is a block diagram of a simulation engine, in accordance with an embodiment of the current disclosure;

[0099] FIG. **87** is a diagram of an interface with fields populated based at least in part on a header section of a simulation engine in accordance with an embodiment of the current disclosure;

[0100] FIG. **88** is a flow chart depicting a method for using a simulation marketplace in accordance with an embodiment of the current disclosure;

[0101] FIG. **89** is a flow chart depicting another method for using a simulation marketplace in accordance with an embodiment of the current disclosure;

[0102] FIG. **90** is a schematic diagram of an apparatus for using a simulation marketplace in accordance with an embodiment of the current disclosure;

[0103] FIG. **91** is a diagram for a process for benchmarking and/or normalizing simulation engines, in accordance with an embodiment of the current disclosure;

[0104] FIG. **92** is a flow chart depicting a method for benchmarking and/or normalizing simulation engines, in accordance with an embodiment of the current disclosure;

[0105] FIG. **93** is a schematic diagram of an apparatus for benchmarking and/or normalizing simulation engines, in accordance with an embodiment of the current disclosure;

[0106] FIG. **94** is a block diagram of a plurality of clinical trials and corresponding clinical trial designs for optimization, in accordance with an embodiment of the current disclosure;

[0107] FIG. **95** is a block diagram of a permutation set of the clinical trial designs of FIG. **94** and corresponding combined performance criteria, in accordance with an embodiment of the current disclosure;

[0108] FIG. **96** is a flow chart depicting a method for optimization of clinical trial designs across a plurality of clinical trials, in accordance with an embodiment of the current disclosure;

[0109] FIG. **97** is a flow chart depicting another embodiment of the method of FIG. **96**, in accordance with the current disclosure;

[0110] FIG. **98** is a schematic diagram of an apparatus for optimization of clinical trial designs across a plurality of clinical trials, in accordance with an embodiment of the current disclosure.

[0111] FIG. **99** is a flow chart depicting a method for determining robustness of a clinical trial design, in accordance with an embodiment of the current disclosure;

[0112] FIG. **100** is a flow chart depicting another method for determining robustness of a clinical trial design, in accordance with an embodiment of the current disclosure;

[0113] FIG. **101** is a schematic diagram of an apparatus for determining a robustness of a clinical trial design, in accordance with an embodiment of the current disclosure;

[0114] FIG. **102** is a flow chart depicting a method for updating a clinical trial, in accordance with an embodiment of the current disclosure;

[0115] FIG. **103** is a flow chart depicting another method for updating a clinical trial, in accordance with an embodiment of the current disclosure;

[0116] FIG. **104** is a block diagram of a platform for providing global optimization of site selection for clinical trial designs, in accordance with an embodiment of the current disclosure;

[0117] FIG. **105** is a diagram of a process for globally optimizing site selection for clinical trial designs, in accordance with an embodiment of the current disclosure;

[0118] FIG. **106** is a schematic diagram of an apparatus for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0119] FIG. **107** is a schematic diagram of another apparatus for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0120] FIG. **108** is a flow chart depicting a method for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0121] FIG. **109** is a flow chart depicting another method for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0122] FIG. **110** is a flow chart depicting another method for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0123] FIG. **111** is a flow chart depicting another method for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0124] FIG. **112** is a flow chart depicting an apparatus for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0125] FIG. **113** is a diagram of a platform with an interface for collaborative configuration of a site selection for optimization of patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0126] FIG. **114** is a flow chart depicting a method for collaborative configuration of a site selection for optimization of patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0127] FIG. **115** is a schematic diagram of an apparatus for collaborative configuration of a site selection for optimization of patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0128] FIG. **116** is a flow chart depicting another method for collaborative configuration of a site selection for optimization of patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0129] FIG. **117** is a diagram of a platform for configuring a system for globally optimizing patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0130] FIG. **118** is a flow chart depicting a method for predicting an initial site selection with respect to patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0131] FIG. **119** is a schematic diagram of an apparatus for predicting an initial site selection with respect to patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0132] FIG. **120** is a diagram of a platform/system for generating an interactive interface for exploration/evaluation of spaces related to patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0133] FIG. **121** is a flow chart depicting a method for generating an interactive interface for exploration/evaluation of spaces related to patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0134] FIG. **122** is a schematic diagram of an apparatus for generating an interactive interface for exploration/evaluation of spaces related to patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure;

[0135] FIG. **123** is a flow chart depicting a method for updating patient recruitment, in accordance with an embodiment of the current disclosure;

[0136] FIG. **124** is a flow chart depicting another method for updating patient recruitment, in accordance with an embodiment of the current disclosure;

[0137] FIG. **125** is a block diagram of a platform for providing global optimization of resource availability for clinical trial designs, in accordance with an embodiment of the current disclosure;

[0138] FIG. **126** is a diagram of a process for globally optimizing resource availability for clinical trial designs, in accordance with an embodiment of the current disclosure;

[0139] FIG. **127** is a schematic diagram of an apparatus for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0140] FIG. **128** is a schematic diagram of another apparatus for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0141] FIG. **129** is a flow chart depicting a method for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0142] FIG. **130** is a flow chart depicting another method for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0143] FIG. **131** is a flow chart depicting another method for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0144] FIG. **132** is a flow chart depicting another method for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0145] FIG. **133** is a flow chart depicting an apparatus for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0146] FIG. **134** is a diagram of a platform with an interface for collaborative configuration of a site selection for optimization of availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0147] FIG. **135** is a flow chart depicting a method for collaborative configuration of a site selection for optimization of availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0148] FIG. **136** is a schematic diagram of an apparatus for collaborative configuration of a site selection for optimization of availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0149] FIG. **137** is a flow chart depicting another method for collaborative configuration of a site selection for optimization of availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0150] FIG. **138** is a diagram of a platform for configuring a system for globally optimizing availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0151] FIG. **139** is a flow chart depicting a method for predicting an initial site selection with respect to optimizing available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0152] FIG. **140** is a schematic diagram of an apparatus for predicting an initial site selection with respect to available resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0153] FIG. **141** is a diagram of a platform/system for generating an interactive interface for exploration/evaluation of spaces related to availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0154] FIG. **142** is a flow chart depicting a method for generating an interactive interface for exploration/evaluation of spaces related to availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0155] FIG. **143** is a schematic diagram of an apparatus for generating an interactive interface for exploration/evaluation of spaces related to availability of resources for a clinical trial, in accordance with an embodiment of the current disclosure;

[0156] FIG. **144** is a flow chart depicting a method for updating site selection according to available resources, in accordance with an embodiment of the current disclosure;

[0157] FIG. **145** is a flow chart depicting another method for updating site selection according to available resources, in accordance with an embodiment of the current disclosure;
[0158] FIG. **146** depicts aspects of a view of an organization of a platform, in accordance with an embodiment of the current disclosure;
[0159] FIG. **147** is a schematic diagram of a system for efficient resource allocation in accordance with an embodiment of the current disclosure;
[0160] FIG. **148** is a flow chart depicting a method for efficient resource allocation in accordance with an embodiment of the current disclosure;
[0161] FIG. **149** is a schematic diagram of a system for determining a score in accordance with an embodiment of the current disclosure;
[0162] FIG. **150** is a flow chart depicting a method for determining a score, in accordance with an embodiment of the current disclosure;
[0163] FIG. **151** is a flow chart depicting a method for score transformation, in accordance with an embodiment of the current disclosure;
[0164] FIG. **152** is a flow chart depicting a method for determining a collaborative session sequence, in accordance with an embodiment of the current disclosure;
[0165] FIG. **153** is a flow chart depicting a method for generating a collaborative interface, in accordance with an embodiment of the current disclosure;
[0166] FIG. **154** is a schematic diagram of a system for generating a collaborative interface in accordance with an embodiment of the current disclosure;
[0167] FIG. **155** is a diagram of a hierarchy of convex hulls in accordance with an embodiment of the current disclosure;
[0168] FIG. **156** is a flow chart depicting a method determining a design hierarchy based on convex hull peeling, in accordance with an embodiment of the current disclosure;
[0169] FIG. **157**(*a-e*) is a diagram depicting a method for determining a convex hull for a scenario, in accordance with an embodiment of the current disclosure;
[0170] FIG. **158** is a flow chart depicting a method for determining a scenario convex hull, in accordance with an embodiment of the current disclosure;
[0171] FIG. **159** is a diagram depicting an apparatus for convex hull peeling, in accordance with an embodiment of the current disclosure;
[0172] FIG. **160** is a schematic diagram of a system for providing adaptive replication in clinical trial design simulation, in accordance with an embodiment of the current disclosure;
[0173] FIG. **161** is a schematic diagram for an apparatus for providing adaptive replication in clinical trial design simulation, in accordance with an embodiment of the current disclosure;
[0174] FIG. **162** is a flow chart depicting a method for providing adaptive replication in clinical trial design simulation, in accordance with an embodiment of the current disclosure;
[0175] FIG. **163** is a schematic diagram of a system for providing enhanced simulated annealing, in accordance with an embodiment of the current disclosure;
[0176] FIG. **164** is a schematic diagram of an apparatus for providing enhanced simulated annealing, in accordance with an embodiment of the current disclosure;
[0177] FIG. **165** is a diagram of a design space having neighboring clinical trial designs, in accordance with an embodiment of the current disclosure;
[0178] FIG. **166** is a diagram of a convex hull tunnel, in accordance with an embodiment of the current disclosure;
[0179] FIG. **167** is a flow chart depicting a method for providing enhanced simulated annealing, in accordance with an embodiment of the current disclosure;
[0180] FIG. **168** is a flow chart depicting another method for providing enhanced simulated annealing, in accordance with an embodiment of the current disclosure;
[0181] FIG. **169** is a flow chart depicting yet another method for providing enhanced simulated annealing, in accordance with an embodiment of the current disclosure;

[0182] FIG. **170** is a schematic diagram of a system for design exploration and search, in accordance with an embodiment of the current disclosure;
[0183] FIGS. **171**(*a-b*) are diagrams of a quick search data structure, in accordance with an embodiment of the current disclosure;
[0184] FIG. **172** is a flow chart depicting a method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0185] FIG. **173** is a flow chart of another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0186] FIG. **174** is a flow chart depicting another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0187] FIG. **175** is a flow chart depicting another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0188] FIG. **176** is a diagram of an interface for design exploration and search, in accordance with an embodiment of the current disclosure;
[0189] FIG. **177** is flow chart depicting another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0190] FIG. **178** is flow chart depicting another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0191] FIG. **179** is flow chart depicting another method for design exploration and search, in accordance with an embodiment of the current disclosure;
[0192] FIG. **180** is a diagram of a design space, in accordance with an embodiment of the current disclosure; and
[0193] FIGS. **181**(*a-k*) are diagrams of an example project, in accordance with an embodiment of the current disclosure.

DETAILED DESCRIPTION

[0194] Clinical trials (herein, also referred to as a “trial” or “study”) may be used to assess, examine and evaluate drugs, devices, procedures, treatments, therapies, and the like. Clinical trials may be used to evaluate the efficiency, performance, and/or effectiveness of treatments for subjects. Embodiments of the current disclosure may also optimize for clinical trial resources, which may include drugs/drug supply subject to the trial, devices subject to the trial, administrative personnel, and/or equipment needed to administer a procedure/drug/device subject to the trial.
[0195] The success and the performance of a clinical trial depends on the design of the trial. In some cases, a wrong choice in the design of a trial may reduce the usefulness of the trial even if the trial is executed without error. In some cases, different choices for the design of a trial may result in very different costs, completion times, and/or other performance parameters for the trial.
[0196] The design of clinical trials may include considerations and tradeoffs between hundreds or even thousands of design options. Traditionally, the design of trials has been based on heuristics and experienced professionals to determine which set of parameters will result in a design that is likely to produce a successful trial. However, traditional approaches are not capable of evaluating more than a handful of design options and tradeoffs and may often miss design options that may result in better performance. The cost of a clinical trial may often exceed tens of millions or even hundreds of millions of dollars and may take years to complete, thus, small differences in the performance of a trial design may result in large impacts on the overall cost and time associated with corresponding trials.
[0197] The complexity of a trial design often requires aspects of statistical expertise, clinical design expertise, and software expertise, which may not be available in many organizations. As such, many organizations fallback on the use of generic study designs due to their inability to find optimal or near-optimal study designs.
[0198] A trial design platform, systems, and methods are described herein for evaluation and/or comparison of designs for a clinical trial. In embodiments, evaluation and/or comparison may

include a large number of design options. In some embodiments, the platform, systems, and methods described herein may be used to evaluate hundreds, thousands, or even millions of design options for a clinical trial and may be used to find the optimal or near-optimal design for a trial.

[0199] The trial design platform may be used for trial design. In embodiments, a trial design platform may support a team in collaborating and surfacing all the inputs that are key to consider for preparing and selecting an optimal design. The trial design platform may use cloud and distributed computing so the team can simulate hundreds of millions of study design variants across all those inputs. The trial design platform may present the team with prioritized options and visualizations to enable the interrogation of the drivers of value. As used herein, a "team" may include a single individual or a group of individuals. Embodiments of the platforms disclosed herein may provide for collaboration within a single organization and/or across multiple organizations. In embodiments, an organization may be a business entity and/or a regulation authority, e.g., a governmental agency, and/or other entity charged with oversight and/or certification of clinical trials.

[0200] A trial design platform may enable a team to quickly identify optimal designs and the factors that most strongly drive performance factors, strategic goals, and the like. A trial design platform, as described herein, may leverage emerging technologies to provide options for advanced simulations, distributed computing, visualizations, and the like. The trial design platform may leverage methodological knowledge, analysis of the business value of different design choices, and/or analysis of regulatory risk and operational complexity to determine optimum or near optimum study designs. The trial optimization platform may determine optimum or near optimum study designs by leveraging a novel workflow, speed and/or computing innovations, and/or powerful visualizations for study analysis and optimization.

[0201] A trial design platform may improve how data and processes are used to make better decisions on clinical trial design. Improvements may result from recognizing which innovative designs might significantly increase goals. Improvements may be obtained by communicating the benefits of specific trial designs in a way that that intuitively allows a variety of team members to understand the design of a trial and/or possible options for the design of the trial. A trial design platform may support a team in collaborating and surfacing all the inputs that are key to consider for preparing and selecting an optimal design. The trial design platform may present the team with prioritized options and insightful visualizations to enable interrogation of the drivers of value.

[0202] FIG. **1** shows an embodiment of a platform for evaluation and comparison of trial designs for treatments for subjects. As used herein, treatments may include procedures, diagnostic tests, devices, diets, placebos, drugs, vaccines, and the like. Treatments may include combinations of drugs, devices, procedures and/or therapies. References to subjects throughout this disclosure should also be understood to be references to people, animals, plants, organisms and other living elements.

[0203] The platform **104** may provide for a system for providing users with facilities and methods for designing, evaluating, and/or comparing designs. The facilities described herein may be deployed in part or in whole through a machine that executes computer software, modules, program codes, and/or instructions on one or more processors, as described herein, which may be part of or external to the platform **104**. Users may utilize the platform **104** to identify trial designs for criteria, evaluate the designs, compare designs, determine optimal designs, and the like.

[0204] A user may interact with the platform **104** through one or more user devices **102** (e.g., computer, laptop computer, mobile computing device, and the like). The platform **104** may be implemented and/or leverage one or more computing resources **150** such as a cloud computing service **152**, servers **154**, software as a service (SaaS), infrastructure as a service (IaaS), platform as a service (PaaS), desktop as a Service (DaaS), managed software as a service (MSaaS), mobile backend as a service (MBaaS), information technology management as a service (ITMaaS), and the like. The platform **104** may be provided or licensed on a subscription basis and centrally hosted (e.g., accessed by users using a client (for example, a thin client) via a web browser or other application, accessed through or by mobile devices, and the like). In embodiments, elements of the platform **104** may be implemented to operate on various platforms and operating systems. In embodiments, interfaces for the user device **102** through which the users may interact with the platform may be served to the user device **102** through a webpage provided by a server of the platform **104**, an application, and the like.

[0205] The platform **104** may include one or more facilities such as a configuration facility **106**, simulation facility **110**, analysis facility **108**, interfaces facility **112**, data facility **138**, and computation resources **150**.

[0206] The configuration facility **106** may include advisors **114**, which may include one or more wizards, tools, algorithms, recommenders, configuration elements, questioners, and the like. Advisors may be used to receive data and/or define or develop space definitions **116**. Space definitions **116** may include aspects of criteria space. As used herein, criteria space may include the set of parameters and values of the parameters that define goals for a design. Criteria space may define initial parameters for narrowing the design space before optimization. Parameters may include goals of designs, endpoints, primary objectives, secondary objectives, and the like. Criteria space may define values, ranges of values, types, ranges of types, and the like that may define general characteristics of a trial design.

[0207] Space definitions **116** may include aspects of design space. As used herein, design space may include the set of parameters and values of the parameters that define different options and variations of designs. Parameters may include design type, dose of drug, frequency of drug, maximum duration, patient inclusion/exclusion criteria, randomization type, and the like. The design space may include all possible permutations of the parameters. For example, one design type may be configured with different doses of a drug and different frequency of the administration of the drug. The design space may include all possible permutations of the different doses of the drug for all the different frequencies of the administration of the drug. The design space may include all the permutations of all the parameters associated with design. The design space may include millions of possible design variations. A trial design platform may evaluate all permutations of parameters of the design space. A trial design platform may evaluate a partial set of permutations of parameters of the design space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically defined, such as according to the criteria parameters.

[0208] Space definitions **116** may include aspects of scenario space. As used herein, scenario space may include the set of parameters and values of the parameters that define different options and variations of scenarios associated with designs. Scenario space may define the parameters of the environment associated with a design. Parameters may include population enrollment rate, dropout rate, population statistics, and the like. The scenario space may include all possible permutations of the parameters. For example, one scenario may be configured with a range of values for population enrollment rate and a range of values for patient dropout rate. The scenario space includes all possible permutations of the population enrollment rate and the patient dropout rate. The scenario space may include all the permutations of all the parameters associated with scenarios. The scenario space may include millions of possible scenario variations. A trial design platform may evaluate all permutations of parameters of the scenario space. A trial design platform may evaluate a partial set of permutations of parameters of the scenario space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically or semi-automatically defined, such as according to the criteria parameters.

[0209] Space definitions **116** may include aspects of performance space, e.g., **316** (FIG. **3**). As used herein, performance space may include the set of parameters and values of the parameters that define the evaluation criteria for a design. Parameters may include: net present value (NPV), expected NPV, incremental NPV, study cost, incremental study cost, study budget, incremental study budget, time to complete, incremental time to complete, time to market, incremental time to market, clinical utility, incremental clinical utility, probability of regulatory acceptance, incremental probability of regulatory acceptance, probability of success, incremental probability of success, statistical power, incremental statistical power, number of patients, incremental number of patients, number of sites, incremental number of sites, study complexity, incremental study complexity, operational complexity, incremental operational complexity, dose selected, incremental dose selected, statistical design, incremental statistical design, peak revenue, revenue at year five (5), other revenue numbers, incremental revenue, market introduction, whether market introduction beats competition entry, number of treatment arms, hypothesis superiority/equivalence/non-inferiority, other choices around statistical design, treatment effect, hazard ratio, and other choices around estimating the characteristics of the patient population, response, and safety profile, screening criteria, dropout rate, and other choices around modeling/estimating the characteristics and behaviors of the patient population and other factors that impact how the study evolves and its likelihood of achieving its goals (how slowly/quickly patients enroll, etc.), site payments and other choices around operational aspects of the study that can impact how the study evolves and its likelihood of achieving its goals, cost per patient, cost per site, or other cost factors, selections made in other projects (across users within customer companies or organizations and across all users of the platform), priorities set by the customer company or organization, and/or other user-defined filters based on available inputs and outputs of the platform or in the systems and methods described herein. In embodiments, any of the parameters and variables described herein may be incremental parameters and variables. Designs may be evaluated and compared against all of the parameters of the performance space or a subset of the parameters of the performance space. A set of designs may be evaluated for one or more of the performance parameters. The performance parameters and the values of the performance parameters of designs define the performance space of the set of designs.

[0210] The configuration facility **106** may include a combinations component **118**. The combinations component **118** may automatically or semi-automatically define the design space and/or scenario space that may be evaluated by the platform.

[0211] The simulation facility **110** of the platform **104** may, based on the space definitions from the configuration facility **106**, evaluate the trial designs. The simulation facility **110** may include models **126**. As used herein, a model includes the combination of parameters and the values that describe a design and the scenario under which the design is evaluated.

[0212] Models **126** may include hundreds or even thousands of models. Models **126** may include deviation specifications for one or more of the parameters of the models. Deviation specification may define a range of values, a distribution of values, and/or a function of values for one or more parameters of a model. The deviation specifications may be based on expected or previously measured distributions or variations in design parameters.

[0213] The simulation facility **110** may include engines **128**. As used herein, engines may relate to the codification of a design that can receive model parameters and run a simulation to generate an output. The output of the engines **128** may be a predicted behavior for a design for one or more scenarios and/or conditions. Engines **128** may evaluate a design with analytical methods, mathematical methods, numerical methods, simulation, and/or the like. As used herein, simulation refers to the execution of a model using an engine. A simulation may be a single execution of model (one simulation instance) or a simulation run that includes more than one simulation instance. Evaluating a design may include a simulation run to determine performance of the design. Evaluating a design may include using a Monte Carlo approach to simulate a design for different values according to the deviation specifications and using statistical methods to determine the performance of the design from a simulation run.

[0214] The simulation facility **110** may include search/exploration component **130**. The search/exploration component may facilitate modification of model parameters for simulation. The search/exploration component **130** may adaptively modify or generate models for simulations based on simulation results of other models/designs and/or based on triggers and data from other facilities of the platform **104**.

[0215] The analysis facility **108** may be configured to analyze simulation results of designs. The analysis facility **108** may include a filtering component **120**. The filtering component **120** may be configured to use one or more numerical and/or analytical methods to evaluate and compare the performance of evaluated designs. The filtering component may identify optimal or near-optimal designs for one or more performance parameters. The filtering component may search the performance space and identify a set of optimal and/or near optimal designs for one or more performance parameters.

[0216] The analysis facility **108** may include a recommendation component **122**. The recommendation component **122** may provide design recommendations. The design recommendations may be based on optimal or near-optimal designs determined by the filtering component **120**. Recommendations may be adaptive based on settings, feedback, selections, triggers, and the like from the user, and/or other facilities in the platform **104**.

[0217] The analysis facility **108** may include an augmenting component, **124**. The augmenting component may supplement simulation results with real-world data.

[0218] The interfaces facility **112** may be configured to provide visualizations and interfaces for comparing, searching, and evaluating simulated designs. Visualization component **132** may provide for one or more interfaces to visualize the performance of designs and facilitate comparison of designs by a user. The feedback analysis component **134** may track user actions associated with the interfaces and visualization to determine patterns and/or preferences for designs. The tradeoff advisor component **136** may analyze and provide data and guidance for evaluating tradeoffs between two more designs.

[0219] The platform **104** may include and/or provide access to one or more data facilities **138**. Data in the data facilities may include design histories **140**, simulation data **142**, site data **144**, resource data **146**, population data **148**, and the like.

[0220] FIG. **2** shows aspects of an embodiment of a process for trial design. The process may include four or more stages. Facilities of the platform **104** may be configured to implement the stages of the process. The stages of the process may include a configure stage **202**. The configure stage **202** may define one or more the spaces associated with the trial design. The configure stage **202** may define one or more of criteria space **210**, design space **212**, scenario space **214**, and/or performance space **216**. The configure stage **202** may utilize one or more advisors, wizards, algorithms, and the like for defining the spaces. In some embodiments, the different spaces associated with the configuration stage **202** may be defined by different members of a team based on the expertise of the members. In some cases, members of a team may have different specializations. For example, some members may specialize in scenarios, while others may specialize in design definitions. Separating the inputs may allow different team members to independently optimize and improve specific models without affecting other inputs. In some embodiments, the inputs may be separated into two or more types based on convenience, expertise, flexibility, and the like.

[0221] The stages of the process may include an evaluate stage **204**. The evaluate stage **204** may configure models **218** for evaluation using simulation **220** and analytical methods **224**. The stage may include various methods of enhancing computation and simulation using parallelization and resource management **222**.

[0222] The stages of the process may include an augment stage **206**. The augment stage **206** may add real-world data to the simulation data. Financial data **226**, regulatory data **228**, revenue data **230**, and the like may be added to the and used to augment data from simulations.

[0223] The stages of the process may include an explore and analyze stage **208**. The explore and analyze stage **208** may include filtering methods and algorithms **232** for identifying optimal designs. The stage may include generating and interacting with visualizations **234** and tradeoff analysis tools **236** to compare and select designs.

[0224] In embodiments, the platform may be configured for identification and confirmation of globally optimal trial designs. Optimality of trial designs may be in relation to optimality criteria. Optimality criteria may be determined in relation to the performance space of designs. Optimality may be in relation to one or more performance parameters and the values of the performance parameters. An optimal design may be a design that achieves a most desirable value for one or more specific performance parameters. A most desirable value may depend on the performance parameter and may be different for each performance parameter. In some cases the most desirable value may be the highest value of a performance parameter. In some cases, the most desirable value may be the lowest value of a performance parameter. In some cases, the most desirable value may be a range of values, a specific value, a function of values, and the like. For example, in some cases an optimal design with respect to a cost performance parameter may be a design that has the lowest cost and achieves the goals of the clinical trial. As another example, an optimal design with respect to a time performance parameter may be a design that has the highest NPV and achieves the goals of the clinical trial. Optimality may be determined for different design types and/or different phases of a trial. In embodiments different optimality criteria may be used for different designs and/or different phase of a trial.

[0225] In embodiments, an optimum design is a design that achieves most desirable values for two or more specific performance parameters. In the case of optimality for multiple performance parameters, optimality may require a tradeoff between the parameter values. For example, a design that has the lower cost may have a low NPV and therefore may not be desirable. The optimality of a design may be based on a function of performance parameters. In some cases, a function may be a weighted sum of the performance parameters. A function, or a set of functions, may be used to generate an overall score (or a set of scores) and the score may be used to determine the optimality of the design. A highest score, a specific score, lowest score, and the like may be considered optimal depending on the function used to compute the score.

[0226] In embodiments, optimality may be evaluated according to Pareto optimality. Pareto optimal designs may be designs where no individual performance parameter can be better off without making at least one other individual performance parameter worse off. In some cases, optimality may be determined using convex hull analysis.

[0227] In some cases, one design may be globally optimum. In some cases, more than one design may be globally optimum. In some cases, no designs may be globally optimum. In some embodiments, optimality of designs may be relative to a benchmark. A known design, a set of historical designs, and/or the like may be used as a benchmark. Designs may be considered optimal if they meet, exceed, and/or are within a threshold distance of the benchmark design performance parameters.

[0228] Performance parameters that may be used to determine design optimality may be user defined, system defined, algorithmically defined, and/or the like. In some cases, users may specify a subset of performance parameters that should be used to identify optimal designs. A user may define optimality criteria by defining ranges, values, characteristics, and the like of the parameter values that may be considered desirable and/or optimal. Interactive graphical interfaces may be provided to a user to evaluate different designs based on one or more optimality criteria. Interactive interfaces may allow a user to explore different designs by changing scoring methods, weights associated with the criteria, and the like.

[0229] In embodiments, the characteristics of performance parameters for evaluated designs may be analyzed by the platform to determine if any of the parameters may be less important for optimality. For example, analysis may include evaluation of ranges, variability, and other statistical analysis. If one or more performance parameters for all evaluated designs is within a desirable range, or the performance parameter is almost equal for all of the evaluated designs, the

performance parameter may be removed and identified as less significant for optimality and, in some cases, may not be factored in when determining optimality. Prior to determining optimality on based on performance parameters, the performance parameters and the values of the performance parameters may be grouped, filtered, normalized, and the like.
[0230] Optimality of designs may be redefined automatically, semi-automatically, in response to user input, and/or the like. The criteria for optimality of designs may change as designs are evaluated by the platform. For example, initial optimality criteria may produce no optimal designs. In response to no optimal designs being determined, the criteria may be changed (relaxed, increased, decreased, etc.) until at least one design is considered optimal. In another example, optimality criteria may change in response to user feedback. Users may evaluate initial designs found to be optimal and provide feedback (direct feedback and/or indirect feedback that can be derived from user actions and inactions). The feedback from the user may be used to change how optimality is determined, which performance parameters are used to determine optimality, the values of the performance parameters that are considered optimal, and/or the like.
[0231] In some embodiments, performance parameters may be grouped, ordered, and/or organized into one or more hierarchies, groups, and/or sets. Two or more different optimality criteria may be used in parallel to determine multiple sets of optimal designs under different criteria. Two or more different optimality criteria may be used sequentially to determine optimal designs. One criteria may first be used to identify a first set of optimal designs under first criteria. A second set of criteria may then be used on the first set to reduce the set of optimal designs.
[0232] In embodiments, a design may be globally optimum if the design is optimal with respect to all possible design options. In embodiments, a design may be globally optimum if the design is optimal with respect to possible design options for one or more criteria. In embodiments, a design may be globally optimum if the design is optimal with respect to a large percentage (such as 80% or more) of possible design options for one or more criteria. In embodiments, a design may be globally optimum if the optimality of the design is within a high confidence level (90% confidence) with respect to possible design options for one or more criteria.
[0233] Traditional methods for evaluating designs cannot determine global optimum designs since they evaluate one, several, or a small subset of design options. Traditional methods do not consider all or almost all of the design options and cannot find a global optimum.
[0234] Trial designs may involve numerous variables, parameters, considerations, tradeoffs, and the like resulting in a very large number of possible variations. A large number of possible variations makes study design and optimization using traditional methods difficult. In many cases, traditional methods may fail to explore or consider the complete space of possible trial design options and may miss or never consider globally optimal designs. Using traditional methods, the number of design variations that may be explored in a reasonable time is limited. In some cases, only one (1) statistical design and only three (3) clinical scenarios may be evaluated. The best design study of the limited number of variations may not result in a globally optimal design. A locally optimum design chosen from a limited number of considered designs may represent one (1) local maximum but may be far from the globally optimum design. When 10,000 or more clinical scenarios are considered, a globally optimum design may be distinguished from the many locally optimum designs. However, consideration of 10,000 clinical scenarios cannot be practically performed using traditional methods as it would require an estimated 50,000 hours or more to complete.
[0235] In embodiments, the platform and methods described herein may evaluate thousands or even millions of design options enabling a determination of a global optimum design. In many cases, the globally optimum design may have significant advantages over locally optimum designs. In one example, a globally optimum design may require less time to complete than other designs.
[0236] Referring again to FIG. **1**, the platform **104** may receive and/or determine performance space using the configuration facility **106**. Performance space may be defined in the space

definitions component **116**. The performance space may be configured based input from users and/or based on data **138** such as history data **140** and/or simulation data **142**. In one instance, performance space may define optimality criteria. Optimality criteria may define performance parameters, performance values, functions, methods, and algorithms for evaluating optimality and/or global optimality of designs. In one instance optimality criteria may be configured by the user or determined from benchmark designs from history **140** and/or simulation **142** data. In another instance, optimality criteria may be defined from simulation data from the simulation facility **110**. Optimality of designs may be determined in the analysis facility **108**. The filtering component **120** may be used to determine one or more sets of globally optimum designs from the designs evaluated by the simulation facility **110**.

[0237] FIG. **3** shows aspects of an apparatus for determining global optimality of designs. In embodiments, the optimality analysis component **302** may be part of the analysis facility **108** of the platform **104**. The optimality analysis component **302** may receive data from simulated designs **312** and determine one or more sets of optimal designs **322**, **324**. The optimality analysis component **302** may include one or more circuits for determining optimality of designs. In embodiments, the optimality analysis component **302** may include circuits for determining optimality based on optimality functions **328**. Optimality functions **328** may determine optimality of designs based on different weighting of performance factors of the simulated designs. In embodiments, the optimality analysis circuit **302** may include circuits for determining optimality based on benchmark analysis **304**. Benchmark analysis circuit **304** may determine optimality of designs based on a comparison of performance parameter values to one or more benchmark designs such as from historical data **314** and/or simulation data **312**. In embodiments, the optimality analysis circuit **302** may include circuits for determining optimality using sequential analysis **308** and/or parallel analysis **310**. Sequential analysis circuit **308** and parallel analysis circuit **310** may use one or more different optimality functions **328** in parallel or sequentially to determine optimal designs. In embodiments, the optimality analysis circuit **302** may include circuits for dynamically modifying optimality criteria **306**. User inputs **320**, simulation data **312**, and/or the determined sets of optimal designs may be monitored and analyzed to determine modifications to optimality criteria. In embodiments, the optimality analysis circuit **302** identifies a confidence level **326** associated with the optimality of sets of optimal designs. In the case where simulation data **312** may not include simulations of all design options for the criteria space **318**, the optimality circuit **302** may determine, based on the simulated designs, a confidence level that the determined optimal designs are indeed optimal for a given optimality criteria.

[0238] FIG. **4** shows aspects of an apparatus for determining global optimality of designs. In embodiments, the apparatus may include an optimality analysis circuit **414** which may be part of the analysis facility **108** of the platform **104**. In embodiments, the apparatus may include a data processing circuit **406** structured to interpret/obtain design data **402** of a clinical trial design. In some embodiments the design data **402** may be outputs of simulation data of trial designs. The data processing circuit **406** may transform the design data **402** into a format suitable for use by the various circuits in the apparatus. For example, the design data **402** may be received by the data processing circuit **406** and determine and identify performance parameters in the data. In some embodiments, some performance parameters may be grouped, filtered, converted, normalized, and the like.

[0239] The apparatus of FIG. **4** may further include an optimality determining circuit **408** structured to receive processed design data from the data processing circuit **406**. The optimality determining circuit **408** may identify globally optimum designs **412** based on one or more optimality criteria. In some embodiments, the globally optimum designs **412** may be provided as an output of the apparatus. In some embodiments, globally optimum designs **412** may be further processed by the design analysis circuit **410**. The design analysis circuit **410** may analyze the globally optimum designs **412**, determine characteristics of the designs, and receive feedback data

404 about the designs. The design analysis circuit may, based on the determined characteristics, determine modifications for optimality criteria used in the optimality determining circuit **408**. Using modified optimality criteria, the optimality determining circuit **408** may determine a new set of globally optimum designs **412**.

[0240] As shown in FIG. **5**, a method for determining globally optimum designs may include simulating all design options for a design criteria **502**. The method may further include determining an optimality criteria for evaluating simulated designs **504**. Optimality criteria may be a function of one or more performance values for each design such as a weighted sum of the values, a comparison of the values, and the like. The method may include searching for globally optimum designs in the simulated designs using the determined optimality criteria **506**. The globally optimum designs may be recommended to one or more users **508**.

[0241] As shown in FIG. **6**, a method for determining globally optimum designs may include simulating design options for a design criteria **602**. The method may further include determining a first optimality criteria for evaluating simulated designs **604**. The method may further include determining a first optimality criteria for evaluating simulated designs **606**. In the next step, the method may include determining a first set of optimum designs using the first optimality criteria, the first set may be determined from the simulated designs **608**. The method may further include determining a second set of optimum designs using the second optimality criteria, the second set may be determined from the first set of designs **610**. The globally optimum designs may be recommended to one or more users **612**.

[0242] As shown in FIG. **7**, a method for determining globally optimum designs may include simulating design options for a design criteria **702**. The method may further include determining a first optimality criteria for evaluating simulated designs **704**. In the next step, the method may include determining a first set of optimum designs using the first optimality criteria, the first set may be determined from the simulated designs **706**. The method may further include identifying characteristics of designs in the first set of globally optimum designs **708**. The method may further include determining a second optimality criteria for evaluating simulated designs based on the identified characteristics **710**. The next step of the method may include determining a second set of globally optimum designs using the second optimality criteria from the simulated designs **712**.

[0243] In embodiments, the platform may be configured for identification and confirmation of globally optimal trial designs across one or more of design space, scenario space, criteria space, or performance space. In embodiments, the determination of an optimum design requires a careful balance to ensure that relevant parameter permutations are considered but that time, cost, and the like are not wasted on needless simulations and evaluation of designs that are not relevant. In embodiments, the platform enables the surfacing and consideration of all relevant parameters for evaluating a design while not needlessly wasting resources.

[0244] In embodiments, the platform may support global optimization of clinical trial design by connecting criteria space, design space, scenario space and performance space. The platform may provide users with visualizations for interactive exploration of the spaces. The platform may support global optimization by enabling design optimization and exploration across different styles of explorations. Users of different experience, knowledge, and/or expertise may explore or optimize for elements that are within their expertise/knowledge and share and explore data with users of the same or different expertise/knowledge.

[0245] In embodiments, globally optimum trial design may include defining criteria space. In some embodiments, defining and configuring criteria space may be a prerequisite to defining and configuring other spaces. Configuration space may be at least partially defined and configured by a user. In some embodiments, expert users may define all or a large portion of the criteria space. In some embodiments, a user may directly define a portion of the criteria space and/or provide general aspects or goals for the study and the platform may use one or more advisors (such as the design advisor described herein), historical data, and AI/ML models of historical study data to define and configure the criteria space. In embodiments, the criteria space definitions may be used by the platform to determine parameters for design space, scenario space, and/or performance space. In embodiments, the scenario space parameters may be automatically reviewed for consistency and errors and any contradictions in parameters may be flagged for review by a user.

[0246] In embodiments, scenario space parameters may be analyzed to determine the breadth of the constraints of the parameters. In some cases, the platform may determine or estimate aspects such as size of the design space (for example, number of design options that will need to be simulated), complexity of the design space (for example, number of parameters) size of the scenario space (for example, number of scenarios that will need to be simulated), complexity of the scenario space (for example, number of parameters), size of the performance space (for example, number of performance parameters that need to be tracked in simulation), and the like based on the configuration of the criteria space. The estimates on sizes, complexity, and the like may provide a guide as to the breadth of the criteria space definitions. The estimates may be determined from historical data, may be algorithmically determined, and/or estimated via one or more tables that provide a correspondence between the criteria space parameters and other spaces.

[0247] In some cases, criteria space may be identified (automatically by the platform or by the user) as being too constricting (such as not resulting in a meaningful number of design options for simulation) or to broad (such as resulting in an extremely large number of design options to be simulated) and the platform may identify ways to broaden and/or narrow the criteria space. In one embodiment, parameters of the criteria space may include relations and dependencies. The platform may surface and identify criteria space parameters to add (typically to narrow the breadth) or to remove certain constraints from the criteria space (typically to increase the breadth) based on the relations and dependencies in the parameters.

[0248] In embodiments, the criteria space definitions may be used to define the design space. Design space definitions may include ranges of values for one or more design space parameters. The design space may be developed by defining design options by taking a cross product of all the permutations of the values of the design space parameters. Each of the resulting design options may be verified to determine if the permutation of parameters for the design resulted in a valid design option and/or consistent with the criteria space constraints. Invalid permutations may be removed or flagged to avoid needless simulation.

[0249] In embodiments, the criteria space definitions may be used to define the scenario space. Scenario space definitions may include ranges of values for one or more scenario space parameters. The scenario space may be developed by defining scenario options by taking a cross product of all the permutations of the values of the scenario space parameters. Each of the resulting scenario options may be verified to determine if the permutation of parameters for the scenario resulted in a valid scenario option and/or consistent with the criteria space constraints. Invalid permutations may be removed or flagged to avoid unnecessary simulation.

[0250] In embodiments, a cross product of all the valid scenario options from the scenario space and all the valid design options from the design space may be used to generate models for simulation. Each of the resulting scenario-design permutations may be verified to determine if the permutation resulted in a valid permutation and/or is consistent with the criteria space constraints. Invalid permutations may be removed or flagged to avoid unnecessary simulation.

[0251] In some embodiments, the set of scenario-design permutations may be pruned to remove permutations that are determined to have poor performance parameters or are predicted to not meet the criteria. In some cases, a database of previous simulations may be compared to the set of permutations to identify preliminary predictions.

[0252] Models for the valid scenario-design permutations may be simulated using one or more engines to determine performance of the designs. The simulations may track and evaluate performance space of each design according to the criteria space definitions. The simulated data may be analyzed to determine optimum designs. Various visualizations and analysis interfaces (such as card interfaces, heat maps, and tornado diagrams as described herein) may be provided by the platform for visualizing and identifying performance of designs. The systematic development of criteria, design, scenario, and performance spaces and their respective permutations ensures that all relevant design options are considered and evaluated for determining globally optimum design options.

[0253] Referring to FIG. **1**, the configuration facility **106** of the platform **104** may include components for defining the criteria space, design space, scenario space, and performance space. In embodiments, advisor components **114** may be used to define criteria space and further define space definitions using the space definitions component **116**. The combinations component **118** may determine permutations and combinations and may identify invalid or unnecessary combinations of parameters for a criteria. The combinations may be used to define models in the models component **126** for simulation. The models may be simulated by the simulation facility **110** and analyzed by the analysis facility **108**.

[0254] FIG. **8** shows aspects of an apparatus for defining criteria, design, scenario, and performance spaces for trial design. In embodiments, the space definition component **802** may be part of the configuration facility **106** of the platform **104**. The space definition component **802** may receive specifications for user input **820** or from one or more input/design advisors **830**. The inputs may identify definitions and constraints on one or more spaces. From the input, the criteria definitions component **804** may identify criteria parameters that may identify constraints on the study. In embodiments size/complexity estimator **808** may provide data and estimates with respect to how criteria definitions relate to the number of design options and scenario options that will be simulated for the criteria. Estimates may be determined from previous simulation data **818**. The size/complexity estimator **808** may initiate criteria revisions. In some embodiments, parameter relations component **806** may surface settings and parameter relations to identify constrains and/or parameters that may be added, removed, or redefined in the criteria. A validity checker component **810** may verify that criteria space parameters are consistent and may flag any issues that should be addressed. Based on the criteria space definitions **822**, the design parameters component **812** may determine ranges and values for one or more design parameters that meet the criteria. The design parameters component **812** may identify valid permutations of the design parameters and define the design space **824**. Based on the criteria space definitions **822**, the scenario parameters component **814** may determine ranges and values for one or more scenario parameters that meet the criteria. The scenario parameters component **814** may identify valid permutations of the scenario parameters and define the scenario space **826**. The performance parameters component **816** may identify performance parameters that should be tracked based on the criteria and define the performance space **828**.

[0255] As shown in FIG. **9**, a method for evaluating a design may include obtaining a criteria for a trial design study **902**. The criteria may be obtained from the user or from other parts of the platform based on a user input and/or historical data. The method may further include determining permutations for designs based on the criteria **904** and determining permutations for scenarios based on the criteria **906**. For example, depending on the criteria, it may be possible to affirmatively determine design permutations or scenario permutations that are feasible in view of the criteria, and/or it may be possible to determine specific design permutations or scenario permutations that are not feasible in view of the criteria (e.g., cannot possibly provide a result that satisfies the criteria). For example, if a user inputs as a design criterion a specific maximum drug dose, then only design permutations having a dose of drug equal to or less than the specified maximum drug dose will be included (all other design permutations are infeasible in view of specified criterion, because it is not possible for them to achieve a drug dose that does not exceed the specified maximum). Alternatively or in addition, if a user inputs as a scenario criterion a specific range of patient dropout rates (for example), then only scenario permutations having a patient dropout rate within the specified range will be included. Furthermore, the method may include generating combinations using the permutations of designs and scenarios **908**. In some embodiments, the combinations may be exhaustive, i.e., the combinations to be simulated include each possible design permutation combined with each possible scenario permutation (or, if infeasible permutations are first excluded, the combinations to be simulated include each feasible design permutation combined with each feasible scenario). Alternatively, in some embodiments, some combinations may be removed based on predicted performance. As discussed further below, a variety of heuristics, algorithms, filters, or the like may be used to predict that certain combinations are improbable or unlikely to achieve a desirable outcome. In some embodiments, analysis of data from past trials, or information input by one or more users, may indicate improbable combinations for which simulation would be of minimal value. For example, historical trial data and/or guidelines based on user experience may indicate a direct relationship between trial duration and patient dropout rates, such that a patient dropout rate below a certain level is unlikely to be achieved for a trial having a duration that exceeds a certain time period. Therefore, although combinations having certain patient dropout rates and certain trial durations may satisfy all selected criteria, it can be predicted that such combinations either cannot be achieved as a practical matter or cannot result in a satisfactory trial outcome. Therefore, such combinations can be removed prior to the simulation. As another example, analysis of past trial data may indicate that drug doses below a certain level are rarely effective in treatment of certain conditions, and combinations involving low drug doses may be predicted to perform poorly and therefore be removed prior to simulation. Also, as discussed further below, a scoring system may be implemented to predict performance and determine combinations that should be removed prior to simulation. The combinations that are determined to be appropriate for simulation (which may be all possible combinations in some embodiments or a subset of combinations in other embodiments) may be simulated **910** and the performance of the simulated designs may be determined and analyzed **912**. The evaluated performance parameters may be based on the criteria and/or based on goals or performance objectives other than the obtained criteria.

[0256] As shown in FIG. **10**, a method of evaluating designs may include obtaining a criteria for trial design study **1002**. The method may further include predicting design simulation requirements based on the criteria **1004**. The predictions may include how many simulations will need to be performed, the cost of the simulations, the time for the simulations, and the like. For example, based on the obtained criteria, a number of potential design permutations may be determined, and a number of potential scenario permutations may be determined. A cross product of the number of design permutations and the number of scenario permutations can indicate the number of combinations to be simulated, and based on system parameters that number can be used to also determine, for example, the time required to simulate that number of combinations, the cost of the simulations, and the like. The method may include modifying the criteria based on the predictions **1006**. The criteria may be modified to constrain the criteria to reduce the number of needed simulations or broaden the criteria to include more design options for simulation. As one example, if the predicted number of required simulations is very large for when an obtained criteria relates to a maximum trial duration, the criteria may be modified to include both a maximum and a minimum trial duration (in situations where a very short trial duration is deemed unlikely to provide a successful result). In some embodiments, controls (for example, slider bars) may be provided to a user to adjust values for selected criteria so that the user can quickly see the impact that changes to the criteria have on the predicted number of required simulations, the duration of the simulation, the cost of the simulation, etc. The method may include generating design and scenario combinations based on the modified criteria **1008** and determining performance parameters that should be determined based on the criteria **1010**. The combinations may be simulated to obtain the performance parameters determined for each design. The method may further include simulating combinations and determining performance designs **1012**.

[0257] FIG. **11** shows aspects of an apparatus for determining designs. In embodiments, the apparatus may include a space definition circuit **1102** which may be part of the simulation facility **110** of the platform **104**. In embodiments, the apparatus may include a criteria analysis circuit **1104** structured to interpret/obtain criteria data **1112**. The criteria data may be analyzed by the simulation prediction circuit **1120** to determine aspects of simulation time, design options, and the like that are consistent with the criteria. The predictions **1122** from the simulation prediction circuit **1120** may be provided to a user and feedback **1114** may be received for modification of the criteria. The design space circuit **1106** and the criteria space circuit **1108** may generate the design and performance parameters from the criteria. The combinations circuit **1110** may generate design-scenario combinations **1118** for simulation. In some embodiments, a validity circuit **1124** may determine the validity of any combinations **1118** or any design space or scenario space parameters and the invalid options may be removed. The combinations **1118** and the performance space **1116** determined from the criteria by the space definition circuit **1102** may be used to simulate and analyze designs.

[0258] Referring to FIG. **12**, an embodiment of an interface **1210** for configuring and managing an execution flow **1212** for a clinical trial design evaluation is shown. In embodiments, the interface **1210** may form part of the configuration facility **106** (FIG. **1**). The interface **1210** may also be provided by a system separate from the platform **104** (FIG. **1**) and communicate with the platform **104** via one or more application programming interfaces (APIs) or otherwise. The interface **1210** may be provided as a graphical user interface on one or more user devices **102** (FIG. **1**).

[0259] As can be seen in FIG. **12**, the execution flow **1212** defines, in part, one or more processes and the order in which they occur for conducting one or more clinical trial design evaluations. The interface **1210** may include a canvas area **1214** for visualizing/editing/creating the execution flow **1212** using nodes **1216** and arcs **1218**. For example, nodes **1216** and/or arcs **1218** may be dragged on and/or off the canvas area **1214**, wherein the nodes **1216** and arcs **1218** on the canvas area **1214** define, in part, the execution flow **1212**.

[0260] Each node **1216** may represent one or more modules and/or processes included in the execution flow **1212**, wherein the arcs **1218**, e.g., arrows, connect the nodes **1216** so as to define the flow of data from one node **1216** to another. Non-limiting examples of the types of processes the nodes **1216** may represent include: an execution engine from component **128** (FIG. **1**); reception and/or obtaining one or more of design criteria, performance criteria/parameters, scenario criteria; a search/exploration module from component **130** (FIG. **1**), e.g., simulated annealing; visualizations and/or interfaces to be presented from component **132** (FIG. **1**); and/or any type of parameter, model/engine, and/or visualization described herein. Users of the interface **1210** may change the configuration of the execution flow **1212** by changing nodes **1216**, adding nodes **1216**, removing nodes **1216**, moving arcs **1218** to change the flow of outputs from one node **1216** to the next, and/or the like.

[0261] Illustrated in FIG. **13** is another embodiment of an interface **1310** for configuring and managing an execution flow for a clinical trial design evaluation, in accordance with an embodiment of the current disclosure. A first node **1312** may represent a set of design parameters to be acquired/obtained and sent to a second node **1314**, as indicated by arc **1316**. Node **1314** may represent an engine that processes the set of design parameters to generate outputs as represented by arc **1318** and node **1320**. Arc **1322** depicts the outputs being communicated to an unconfigured node **1324**. As shown in FIG. **13**, a menu **1326** may be generated within and/or near the unconfigured node **1324** and provide options for configuring the node **1324**. For example, using the menu **1326** a user may configure the node **1324** to represent a sensitivity analysis, e.g., a tornado plot, a visualization, and/or an optimization method/engine, e.g., simulated annealing. The menu **1326** may also provide a general option to save the state of the interface **1310** and/or corresponding execution flow **1328**. Node **1330** represents a visualization that has not yet been incorporated into the execution flow **1328**, i.e., no arcs connect node **1330** into the execution flow **1328**. In embodiments, the interface **1310** may include a menu **1332** that provides a user with options to add parameter input nodes **1334**, engine nodes **1336**, arcs **1338**, visualizations **1340**, complex arcs **1342**, e.g., forks, a save option **1344**, and/or the like.

[0262] Referring now to FIGS. **14** and **15**, in embodiments, the interface may be configured for different user types/target audiences. Distinct instances/views of the interface may be generated wherein each instance/view is tailored for a particular user type/role and/or a configuration level. In embodiments, an instance/view may be for defining analysis aspects and may include a focus, as well as additional interfaces and/or options for viewing and/or editing greater details of the execution flow, e.g., specifying algorithms, performance criteria, and the like. In embodiments, an instance/view may be for defining design and/or scenario aspects and may include, for example, additional interfaces and options for importing design parameters from a previous analysis. Analysis templates, e.g., collections of nodes **1216** and arcs **1218**, may be used in the execution flow **1212** to provide a baseline configuration. Analysis templates may include templates for a low-cost analysis (i.e., use of low-cost engines), exhaustive analysis, and heatmap analysis (i.e., which visualizations are to be provided). In embodiments, different views may depict aspects of the same data to different users at the same time. For example, a user associated with a regulatory organization may see only results of the analysis, while another user may have access to additional features that provide for configuration of the analysis. Changes to the configuration of the analysis may propagate across multiple views in real-time.

[0263] User types may include simulation engine designers, visualization designers, optimization professionals and/or the like, and may be subdivided into skill levels, e.g., expert, intermediate, and/or novice. Configuration levels may provide for different levels of access over parts of an execution flow and may be categorized as high, medium, or low, wherein a high level provides for more access than a medium level which provides for more access than a low level. In embodiments, other classification schemes for user types and configuration levels are provided.

[0264] For example, a first instance/view of the interface **1410** may be configured for a first user type **1510** and a second instance/view of the user interface **1412** may be configured for a second user type **1512**. In embodiments, the user types, e.g., **1524**, may correspond to skill levels and/or different specialties with respect to clinical trial design. For example, the first user type **1510** may be a subcategory of a user type **1514** corresponding to a simulation engine designer. User type **1510** may correspond to an expert simulation engine designer and have sibling types corresponding to intermediate simulation engine designer **1516** and/or novice simulation engine designer **1518**. User type **1512** may be a subcategory of a user type **1520** corresponding to a visualization designer. User type **1512** may correspond to a novice visualization designer and have a sibling corresponding to an expert visualization designer **1522**.

[0265] Accordingly, view **1410** provides user type **1510** access to more functionality and/or control over configuration of the execution flow **1212** within an engine **1414** as compared to view **1412** for user type **1512**. For example, interface **1410** provides access to nodes **1416** and **1418** within the engine node **1414**, while interface **1412** provides only high-level access to the engine node **1414**. Thus, interface **1410** allows an expert simulation designer **1510** to configure the execution flow **1212** internal to an engine while interface **1412** prevents a non-expert simulation engine designer **1512** from doing the same.

[0266] In embodiments, different user types may define parts of the execution flow concurrently. In other words, embodiments may provide for users to collaborate (concurrently or asynchronously) to design, conduct simulations, and perform analysis on clinical trial designs during both pre-simulation and post-simulation stages. For example, user type **1510** may configure the internals of the engine node **1414** at the same time user type **1512** configures a visualization node **1420**. Thus, as will be appreciated, users in different geographic regions, e.g., cities, states/provinces, and/or countries, may work together on the same execution flow **1212**. In embodiments, authentication and access control may be used to identify and authenticate users and control access to one or more functions and/or resources accessible by the platform. In embodiments, users may have different permissions allowing different access and actions. For example, some users may be provided with the ability for configuring a flow but require another user or another authorization level to execute the flow.

[0267] Turning now to FIG. **16**, a method **1600** for configuring an execution flow for a clinical trial design evaluation is provided. The method **1600** includes configuring an execution flow for a clinical trial design evaluation using a configurable interface **1610**, as described herein. The configurable interface **1210** (FIG. **12**) may include at least one node element **1216** and at least one arc element **1218**. The execution flow **1212** may be defined, in part, via the at least one node element **1216** and the at least one arc element **1218** (FIG. **12**), as disclosed herein. The method **1600** includes executing the clinical trial design evaluation using the execution flow **1612**. The method **1600** includes reconfiguring at least one of the at least one node element or the at least one arc element in the execution flow **1614**. Reconfiguring may include one or more of adding, removing, moving, and/or otherwise adjusting the at least one node element and/or the at least one arc element. The method **1600** further includes executing the clinical trial design evaluation using the reconfigured execution flow **1616**.

[0268] FIG. **17** depicts another method **1700** for configuring an execution flow for a clinical trial design evaluation. The method **1700** includes configuring an execution flow for a clinical trial design evaluation using a configurable interface **1710**, as disclosed herein. The execution flow **1212** may be defined using at least one node element **1216** and at least one arc element **1218**, as described herein. The method **1700** further includes determining a first user type interacting with the execution flow **1712**, e.g., attempting to and/or preparing to configure the execution flow **1212**. The method **1700** further includes configuring a first view of the execution flow for the first user type **1714**. The method **1700** further includes determining a second user type interacting with the execution flow **1716** e.g., attempting to and/or preparing to configure the execution flow **1212**. The method **1700** further includes configuring a second view of the execution flow for the second user type **1718**.

[0269] Illustrated in FIG. **18** is an apparatus **1800** for configuring an execution flow for a clinical trial design evaluation. The apparatus **1800** includes an interface configuration circuit **1810** structured to generate interface data **1812** corresponding to a configurable interface having a node element **1216** (FIG. **12**) and an arc element **1218** (FIG. **12**). The node element **1216** and the arc element **1218** define execution flow data **1814** for a clinical trial design evaluation, i.e., the flow data **1814** corresponds to the execution flow **1212** (FIG. **12**). The apparatus **1800** further includes a user input circuit **1816** structured to interpret user input data **1818** based at least in part on the node element **1216** and the arc element **1218**. The apparatus **1800** further includes an interface reconfiguration circuit **1820** structured to reconfigure the execution flow data **1814** to generate, based at least in part on the user input data **1818**, reconfigured execution flow data **1822**. The apparatus **1800** may include an evaluation circuit **1824** structured to generate evaluation data **1826** via executing the clinical trial design evaluation based at least in part on the reconfigured execution flow data **1822**. The apparatus **1800** may further include an evaluation processing circuit **1828** structured to transmit the evaluation data **1826**.

[0270] In embodiments, apparatus for configuring execution flow may enable configuration and manipulation of scenario, design, performance, and criteria spaces. Each space may be separately configured by different users. Each space may be associated with one or more different nodes in the execution flow. The nodes corresponding to each space may be modified and/or replaced with a different version of the node to change aspects of any one of the spaces.

[0271] Referring to FIG. **19**, an advisor **1900**, e.g., an interactive wizard or algorithm, for guiding a user through configuration of trial design simulations, and/or systems for optimizing clinical trial design selection, is shown. In embodiments, the advisor **1900** may be used for pre-simulation configuration of the platform **104**, updating of the platform **104** during simulation runs, and/or for configuring the platform **104** for post-simulation analysis, e.g., configuring searches such as those provided by the search/exploration component **130** (FIG. **1**). For example, a user may first log on to the platform **104** and specify via a user interface, e.g., **112** (FIG. **1**) that they wish to being a new design evaluation. The platform **104** may then launch an embodiment of the interactive wizard or algorithm which may then present the user with a series of initial questions/prompts designed to determine general design and/or performance criteria for one or more designs. The interactive wizard or algorithm may then ask additional questions/prompts to determine more specific ranges and/or values for the design and/or performance criteria. Based on the user's inputs/answers to the questions/prompts, the platform may affirmatively determine design permutations or scenario permutations that are feasible in view of the criteria, and/or it may be possible to determine specific design permutations or scenario permutations that are not feasible in view of the criteria (e.g., cannot possibly provide a result that satisfies the criteria). For example, if a user inputs as a design criterion a specific maximum drug dose, then only design permutations having a dose of drug equal to or less than the specified maximum drug dose will be included (all other design permutations are infeasible in view of specified criterion, because it is not possible for them to achieve a drug dose that does not exceed the specified maximum). Alternatively, or in addition, if a user inputs as a scenario criterion a specific range of patient dropout rates (for example), then only scenario permutations having a patient dropout rate within the specified range will be included.

[0272] In embodiments, the interactive wizard or algorithm may include a method of generating combinations that uses the permutations of designs and scenarios. In some embodiments, the combinations may be exhaustive, i.e., the combinations to be simulated include each possible design permutation combined with each possible scenario permutation (or, if infeasible permutations are first excluded, the combinations to be simulated include each feasible design permutation combined with each feasible scenario). Alternatively, in some embodiments, some combinations may be removed based on predicted performance. As discussed further below, a variety of heuristics, algorithms, filters, or the like may be used to predict that certain combinations are improbable or unlikely to achieve a desirable outcome. In some embodiments, analysis of data from past trials, or information input by one or more users, may indicate improbable combinations for which simulation would be of minimal value. For example, historical trial data and/or guidelines based on user experience may indicate a direct relationship between trial duration and patient dropout rates, such that a patient dropout rate below a certain level is unlikely to be achieved for a trial having a duration that exceeds a certain time period. Therefore, although combinations having certain patient dropout rates and certain trial durations may satisfy all selected criteria, it can be predicted that such combinations either cannot be achieved as a practical matter or cannot result in a satisfactory trial outcome. Therefore, such combinations can be removed prior to the simulation. As another example, analysis of past trial data may indicate that drug doses below a certain level are rarely effective in treatment of certain conditions, and combinations involving low drug doses may be predicted to perform poorly and therefore be removed prior to simulation. Also, as discussed further below, a scoring system may be implemented to predict performance and determine combinations that should be removed prior to simulation. The combinations that are determined to be appropriate for simulation (which may be all possible combinations in some embodiments or a subset of combinations in other embodiments) may be simulated and the performance of the simulated designs may be determined and analyzed. The evaluated performance parameters may be based on the criteria and/or based on goals or performance objectives other than the obtained criteria.

[0273] In embodiments, the advisor **1900** may be integrated into the platform **104**, or the advisor **1900** may be a standalone system apart from the platform **104**. In embodiments, the advisor **1900** may assist in obtaining input from a user to determine trial design criteria and/or trial design parameters, e.g., values for one or more of criteria space, design space, and/or scenario space, as described herein. User input may be obtained via one or more interactive interfaces, e.g., **1910**, structured to generate one or more questions/user prompts, e.g., **1912**. User inputs may be compared to historical data, such as data stored in data facility **138** (FIG. **1**), e.g., previous designs, inputs, and/or outcomes, having similar criteria as that defined by the user input. As will be appreciated, assisting a user through the clinical trial design optimization process may reduce the amount of time and/or resources (including computing resources and/or associated costs) spent on research and/or simulating sub-optimal clinical trial designs for a given clinical trial. Further, the advisor **1900** may be able to make recommendations for trial design criteria and/or trial design parameters that may provide for improved efficiencies over similar trial design optimizations performed by a human.

[0274] Accordingly, in embodiments, the interactive interface **1910** may be a graphical user interface wherein the prompts **1912** may be textboxes, popup dialogue boxes, verbal questions played through a sound and/or video file, e.g., .mp4, .wav, etc. The interface **1910** may be provided though a web interface, e.g., provided through cloud services **152** (FIG. **1**). The interface **1910** may be generated locally on a user device **102** (FIG. **1**) and communicate with the platform **104** through one or more application programing interfaces (APIs). Further, while FIG. **19** depicts the interface **1910** as a graphical user interface, a non-limiting example of a command line version of the interface **2010** with textual prompts **2012** is shown in FIG. **20**.

[0275] As shown in FIG. **19**, in embodiments, the prompts **1912** may include one or more of: a prompt **1914** to determine a duration of a clinical trial; a prompt **1916** to determine a number of recommended designs to provide; a prompt **1918** to determine a type of a model to use for simulation and/or searching/exploration, e.g., whether Pareto and/or convex hull analysis should be performed; a prompt **1920** to determine whether simulated annealing should be performed; a prompt **1922** to determine total costs of a clinical trial; and/or other prompts **1924** for determining any other criteria relevant to determining a globally optimized design for a clinical trial.

[0276] Turning now to FIG. **21**, a non-limiting example of a prompt **2100** is shown. In embodiments, the prompt **2100** may include a presentation window **2110** having a message box **2112** which may display a textual question to the user, e.g., "What types of optimization engines would you like to use?" The prompt **2100** may also include one or more input fields **2114** for receiving the user input. The input fields **2114** may include text boxes, radio buttons, sliders, dropdown menus, checkboxes, and/or other suitable widgets for receiving user input.

[0277] In embodiments, the prompt **2100** may include recommendation fields **2116** which may present one or more recommended values to a user for one or more trial design criteria and/or design parameters. For example, a user may inform the interface **1910** that they intend to optimize a clinical trial of a titration design. The advisor **1900** may then query one or more databases in the data facility **138** (FIG. **1**) and present the user with one or more recommendations **2116** for one or more trial design criteria and/or trial design parameters. For example, the advisor **1900** may recommend, for a particular trial design, that that a Pareto analysis be performed in conjunction with a convex hull analysis. The advisor **1900** may also provide a recommendation **2116** for an estimated cost of the clinical trial. In embodiments, the recommendations **2116** may be single values and/or ranges for values. In embodiments, a recommendation field **2116** may correspond to an input field **2114**. For example, an input field **2114** may be structured to receive a user input defining a number of simulations to run, and a corresponding recommendation field **2116** may recommend a specific value or a range for the user to enter into the input field **2114**. In embodiments, a recommendation **2116** may be in response to a user selection, e.g., users who select option "A" usually select option "B" and/or usually do not select option "C". For example, a user may select a first option "A" and then select a second option "C", wherein upon selecting option "C" a recommendation is generated informing the user that most users who pick option "A" select either options "B" or "D" instead of option "C".

[0278] In embodiments, the user inputs may be compared to historical clinical trial designs selected by traditional (human) experts. For example, the data facility **138** (FIG. **1**) may include a history of past clinical trial design selections from a plurality of experts, e.g., humans who have extensive experience optimizing clinical trial designs. The advisor **1900** may receive one or more user inputs and query the data facility **138** for past trial designs having trial design criteria and/or trial design parameters that are the same, and/or nearly the same, as those defined by the user input. The advisor **1900** may then generate and present recommendations **2116** for other trial design criteria and/or trial design parameters, outside of the ones corresponding to the user input. In other words, in embodiments, the advisor **1900** may generate recommendations **2116** for design criteria and/or trial design parameters for which a user may not have yet specified and/or know. For example, past clinical trial designs may be categorized (based on type of trial, success of the trial, date of the trial, cost of the trial, and the like). Past clinical trials may be compared, clustered, analyzed, and the like to determine variations, similarities, and the like for trials in the same category. In some cases, based on one or more of the clustering, similarities, and/or variations the platform may generate statistics about the one or more features of past clinical trials in each category. The statistics may be used to determine features of trial designs that are common in a category and features that are uncommon. In some cases, common and uncommon features may correspond to desirable and undesirable features respectively. Features that are identified as common may be suggested to a user while features that are uncommon may be flagged for reconsideration. In another example, the platform may generate a dynamically changing score for the trial design configuration. The score may be a prediction of the likelihood that the study will results in a useful design for the study. As a user enters data about design details they wish to evaluate, the problem they study is meant to address, and the like, the platform may compare the inputs with a historical record of similar studies and the outcome of the studies (such as if the study resulted in a selected design, was the design implemented, how successful was the design when implemented, and the like). The system may compare the entered data to the database and develop a score according to the similarity of the entered parameters to historically successful studies. In some cases, similarity may be based on a function of all the parameters. The score may be updated in real time as users enter or change parameters, ranges of values, and the like. The score may provide a rough guide as to how close the study is to a successful study and what aspects of the parameters may be changed to make the study closer to a successful study.

[0279] In embodiments, artificial intelligence/machine learning approaches may be used to generate the prompts **1912** (FIG. **19**) and/or other suggestions for a user. The artificial intelligence/machine learning may be trained via supervised learning. For example, in embodiments, the artificial neural network may be trained to estimate an expected cost, net present value (NPV), expected NPV, incremental NPV, study cost, incremental study cost, study budget, incremental study budget, time to complete, incremental time to complete, time to market, incremental time to market, clinical utility, incremental clinical utility, probability of regulatory acceptance, incremental probability of regulatory acceptance, probability of success, incremental probability of success, statistical power, incremental statistical power, number of patients, incremental number of patients, number of sites, incremental number of sites, study complexity, incremental study complexity, operational complexity, incremental operational complexity, dose selected, incremental dose selected, statistical design, incremental statistical design, peak revenue, revenue at year five (5), other revenue numbers, incremental revenue, market introduction, whether market introduction beats competition entry, number of treatment arms, hypothesis superiority/equivalence/non-inferiority, other choices around statistical design, treatment effect, hazard ratio, and other choices around estimating the characteristics of the patient population, response, and safety profile, screening criteria, dropout rate, and other choices around modeling/estimating the characteristics and behaviors of the patient population and other factors that impact how the study evolves and its likelihood of achieving its goals (how slowly/quickly patients enroll, etc.), site payments and other choices around operational aspects of the study that can impact how the study evolves and its likelihood of achieving its goals, cost per patient, cost per site, or other cost factors, selections made in other projects of a clinical trial design based on past examples. In embodiments, the artificial intelligence/machine learning may be trained on a training set that includes clinical trial designs created by experts and/or designs made by other non-expert users. Some embodiments of the training set may not account for the outcomes of past clinical trial designs. Some embodiments of the clinical trial training set may account for the outcomes of past clinical trial designs. In such embodiments, the artificial intelligence/machine learning may structure the prompts **1912** to guide a user towards a likely outcome, e.g., a likely global optimum design. In embodiments, the artificial intelligence may be trained via unsupervised learning, e.g., policy-based learning. For example, the artificial intelligence may be directed to make recommendations **2116** based on reducing the expected cost of a clinical trial.

[0280] Moving to FIG. **22**, in embodiments, the advisor **1910** may generate and present the prompts **1912** based on one or more stages **2200**. For example, a first plurality of prompts **2212** may correspond to a first stage **2214** of a clinical trial design configuration process, a second plurality of prompts **2216** may correspond to a second stage **2218** of the clinical trial design configuration process, a third plurality of prompts **2220** may correspond to a third stage **2222** of the clinical trial design process, and so on. One or more of the stages **2214**, **2216**, **2218**, and/or **2220** may correspond to stages, of a clinical trial, e.g., “phase 0”, “phase 1”, “phase 2”, “phase 3”, etc., to include substages of a “phase”. In embodiments, a user's inputs to a first plurality of prompts **2212** may determine the aspects of a subsequent plurality of prompts **2216**. For example, a user may input a type of trial design in response to the first plurality of prompts **2212**, and the second plurality of prompts **2216** may seek to elicit input from the user specific to the type of trial.

[0281] Illustrated in FIG. **23** is a method **2300** for guiding a user through configuration of the platform **104** (FIG. **1**). Th method **2300** may include generating an interactive interface **2310**, presenting, via the interactive interface, one or more prompts to a user **2312**. The prompts may be structured to determine one or more trial design criteria. The method **2300** may further include evaluating historical design selections **2314** to identify one or more trial design parameters based at least in part on or more trial design criteria.

[0282] In embodiments, the advisor may be configured to query and derive configurations for the designs, scenario, performance, and criteria space separately. The advisor and interfaces associated therewith may be configured to separate questions, wizards, and other interfaces such that configurations for the spaces are derived separately. The advisor may be configured to allow a first user configure the design space and another user configure the scenario space. In embodiments, user inputs such as type of therapeutic to be tested, budget, and the like may be used to configure the design space and or criteria space. In embodiments, user inputs such as number of patients may be used to configure the scenario space. In embodiments, user inputs such as desired cost or time to completion may be used to configure the performance space.

[0283] Turning to FIG. **24**, in embodiments, the method **2300** may further include simulating one or more clinical trial designs **2410**. The simulations may be based at least in part on the one or more trial design parameters. The method **2300** may further include presenting, via at least one of the prompts, a recommended value for the one or more trial design criteria and/or the trial design parameters **2412**. The method **2300** may further include generating the recommended values via artificial intelligence based at least in part on the historical trial design selections **2414**. In embodiments, evaluating the historical trial design selections **2314** may include evaluating the historical trial design selections via artificial intelligence **2416**.

[0284] Illustrated in FIG. **25** is an apparatus **2500** for implementing the method **2300**. The apparatus **2500** may be integrated into one or more servers **154**, user devices **102**, and/or other suitable computing devices. As shown in FIG. **25**, the apparatus **2500** may include an interface generation circuit **2510** structured to generate interactive interface data **2512** that includes one or more user prompts **1912**, in accordance with those described herein. The apparatus **2500** may include an interface processing circuit **2514** structured to transmit the interactive interface data **2512**, and a user input circuit **2516** structured to receive user input data **2518** defining one or more trial design criteria and/or trial design parameters. The apparatus **2500** may include a historical evaluation circuit **2520** structured to identify one or more trial design parameters **2522** based at least on part on the trial design criteria via evaluating historical data **2524** corresponding to previously simulated clinical trial designs. The apparatus **2500** may further include a simulation circuit **2526** structured to simulate one or more clinical trial designs based at least in part on the trial design parameters. The apparatus **2500** may further include a recommendation circuit **2528** structured to generate a recommended value **2530** for the trial design criteria and/or the trial design parameters. In embodiments, the recommendation circuit **2528** may be further structured to generate the recommended value **2530** based at least in part on historical trial design selections **2532**.

[0285] Referring now to FIG. **26**, embodiments of the current disclosure may provide for augmentation of simulated data with additional/supplemental data, e.g., real-world data. Real-world data may include actual data from clinical trial sites, patients, clinical trials, and/or other entities and aspects related to one or more parameters used to evaluate clinical trial designs as disclosed herein. For example, simulated data, also referred to herein as simulated outputs, may be generated via simulating one or more clinical trial designs. The simulated data may include relative and/or general values.

[0286] Relative values may include values related to an objective or subjective scale. Relative values may include a scale (i.e., 0-1, 1-10, 1-100) and/or designators (i.e., high, medium, low). For example, evaluation data may include a relative scale of a complexity of a trial which may be based on the number of personnel involved, the steps in a protocol of the trial, and the like. Real-world data such as regulatory approval times may be used to estimate how long it will take to receive regulatory approval for the study. Real world data, e.g., **3104** (FIG. **31**), may include a history of the time required to receive approval for studies with similar relative complexity rating. The relative values may be supplemented with the real-world data by substitution and evaluation with respect to historical data and real-world data.

[0287] General values may include values or placeholders that may be mapped or representative of other data. The mapping and placeholder may comprise metadata. For example, a simulation output of a design may specify general values such as number of sites and patients needed for a study. Real-world cost data may be used to determine the real-world cost (in a local currency such as dollars, for example) for the trial based on the number of sites and number of patients. Real-world data may include an average cost for a patient and an average cost per site. The general values may be supplemented with the real-world data by computing or substituting the real-world cost associated with the number of patients and sites.

[0288] The simulations of the clinical trial designs may be based on one or more design space parameters, criteria space parameters, scenario space parameters, and/or additional types of input parameters suitable for simulating clinical trial designs. In certain aspects, one or more of the input parameters to the simulations of the clinical trial designs may have an estimated and/or predicted value. For example, the manufacturing cost of a subject drug for an intended clinical trial may be unknown at the time the simulations of the possible clinical trial designs (for testing the subject drug) are first executed/run. In such a case, the initial simulations of the clinical trial designs may use an estimated (or predicted) price of the subject drug. The estimated price of the subject drug, and/or other input parameters, may be based at least in part on historical data. Real data may then be used in computations to relate the simulation data to real-world or current values. Thus, in the foregoing example, the actual price of the subject drug, when it becomes available, could be used to augment the initial simulations.

[0289] Real-world data may also be used to associate relative values with real-world absolute values. For example, simulation data may identify general or relative parameters that may influence cost. Additional data (such as current cost data) may be used to determine how these general parameters translate to real dollar values. Relative data may be substituted with additional data to provide current values for cost, time, and other performance data. Relative and absolute values may be tagged with metadata for marking for substitution.

[0290] As shown in FIG. **26**, a method for augmentation of simulated data **2600** may include obtaining a set of simulation outputs for a set of clinical trial designs **2610**. The method **2600** may further include obtaining a set of supplemental data **2612**. The method **2600** may further include determining a relationship between at least one simulation output of the set to at least one supplemental data of the set **2614**. The method **2600** may further include generating modified supplemental data based at least in part on the relationship **2616**. The method **2600** may further include generating a substitute of the at least one simulation output based at least in part on the modified supplemental data **2618**. The method **2600** may further include transmitting the substitute **2620**.

[0291] Illustrated in FIG. **27** is an apparatus **2700** for performing aspects of the method **2600** (FIG. **26**). In embodiments, apparatus **2700** may be one or more processors, as described herein, that form part of the augmenting component **124** of the analysis facility **108** of the platform **104**. In embodiments, the apparatus **2700** may be one or more processors of a mobile electronic device, e.g., a tablet or smart phone. The augmenting component **124** may receive data evaluation data such as from the simulation facility **110**. The augmenting component **124** may analyze the data from the simulation facility **110** and identify elements in the data based on tags, values, locations, and the like. The augmenting component **124** may compile or group data that are related (such as data that is related to and/or may affect the cost of a trial). The augmenting component **124** may group data and determine relative scales or values for the data (such as 1-10 scale for complexity). The grouped and scaled data may be identified with tags or other identifiers for matching with real-world data during the substitution and/or supplementing process.

[0292] Accordingly, referring now to FIGS. **26** and **27**, in embodiments, the apparatus **2700** may include a simulated output processing circuit **2710** structured to interpret/obtain **2610** a simulated output dataset **2712** of a clinical trial design. In certain aspects, the simulated output processing circuit **2710** may be in communication with (or integrated with) a network interface card, wherein the simulated output dataset **2712** is received over a corresponding network connection. The simulated output processing circuit **2710** may transform the simulated output dataset **2712** from a network transportation format into a different format suitable for use by the various circuits in the apparatus **2700**. For example, the simulated output dataset **2712** may be received by the simulated output processing circuit **2710** as a series of packets, wherein the simulated output processing circuit **2710** may reassemble the packets into a complete data structure. In embodiments, the simulated output dataset **2712** may be distributed across multiple databases. In certain aspects, the simulated output dataset may include relative data and/or general data.

[0293] The apparatus **2700** may further include a supplemental processing circuit **2714** structured to interpret/obtain **2612** supplemental data **2716**. Non-limiting examples of supplemental data include: costs of a clinical trial; time to completion of a clinical trial; NPV of a clinical trial; actual personnel costs of a clinical trial; or actual facility costs of a clinical trial. In embodiments, the supplemental data **2716** may be derived, e.g., collected, from one or more clinical trial sites **144**. The apparatus **2700** may further include a relation determining circuit **2718** structured to determine **2614** a relationship **2720** between the simulated output dataset **2712** and the supplemental data **2716**. Non-limiting examples of relationships include related units, related data tags, timestamps, user defined relationships, semantic analysis, and/or the like. In certain aspects, the relationship **2720** may be based at least in part on metadata, labels and/or unit values. The apparatus **2700** may further include a supplemental data modification circuit **2722** structured to generate **2616** modified supplemental data **2724** based at least in part on the relationship **2720**. Non-limiting examples of modified supplemental data include financial data, regulatory data, revenue data, and the like. The apparatus **2700** may further include a substitute circuit **2726** structured to generate **2618**, based at least in part on the modified supplemental data **2724**, substitute data **2728** of/for the simulated output dataset **2712**. Non-limiting examples of substitute data **2728** may include costs, time, number of personnel, available sites, number of enrolled patients, and/or the like. The apparatus **2700** may further include a substitute data provisioning circuit **2730** structured to transmit **2620** the substitute data **2728**. The substitute data provisioning circuit **2730** may be in communication with, or integrated into, a network interface card that communicates with one or more remote devices via a network. The substitute data provisioning circuit **2730** may format the substitute data **2728** into a network specific format.

[0294] In certain aspects, the apparatus **2700** may further include a graphical user interface circuit **2732** structured to generate graphical user interface data **2734** for generating a graphical user interface that facilitates user control over augmentation of the simulated data. As such, the apparatus **2700** may further include a user input data processing circuit **2736** structured to interpret user data **2738** entered into the graphical user interface. For example, the graphical user interface may provide for the user to enter the supplemental data **2716** and/or provide instructions to the apparatus **2700** as to where and how the supplemental data **2716** may be acquired, e.g., downloaded from remote databases.

[0295] In embodiments, the substitute data **2728** may be used to replace corresponding parameters that were used to generate the simulated output dataset **2712** so that new simulations can be executed/run with more accurate data. In certain aspects, the substitute data **2728** may be included in one or more reports and/or displays, e.g., via the graphical user interface provided by the graphical user interface circuit **2732**. For example, the graphical user interface may depict differences between the simulated output dataset **2712** and the substitute data **2728**. In embodiments, the graphical user interface may depict differences between the simulated output dataset **2712** and an updated simulated output dataset derived from re-running the clinical trial design simulations, used to generate the simulated output dataset **2712**, with the substitute data **2728**.

[0296] As will be appreciated, use of supplemental data **2716**, as described herein, may provide for improved accuracy with respect to simulating clinical trial designs. Further, by providing for the ability to augment simulated outputs, embodiments in accordance with method **2600** and/or apparatus **2700** may provide for earlier planning of a clinical trial, as possible clinical trial designs can be first simulated with estimated data, thus enabling other planning processes to begin and/or proceed, with the simulated data being adjusted based on real data at a later point in time.

[0297] In some embodiments the simulation models may include various parameters and data that are used by simulation engines to evaluate designs. Model parameters may be separated into different categories. Model parameters may be separated based on delineated expertise of teams. In some cases, members of a team may have different specializations. For example, some members may specialize in building human behavior models, while others may specialize in trial design models. Separating or grouping the parameters may allow different team members to independently optimize and improve specific aspects of models. In some embodiments, the model parameters may be separated into two or more types based on convenience, expertise, flexibility, and the like. Separation of parameters may provide for new and faster methods for simulation, analysis, optimization, and the like when the separation of parameters is at least partially maintained and propagated through the simulation and analysis components of the platform.

[0298] In embodiments, model parameters may be separated into at least two types or categories. Model parameters may be grouped to include parameters that define the trial design space and clinical scenario space. The trial design space may include one or more parameters that are related to protocol design, dosing algorithms, subject selection, demography, blinding of subjects, measurements to be performed, study length, and the like. The trial design space may include one or more trial design types with a combination of design variables. The trial design may specify how data will be analyzed. The design space may further include deviation models for one or more of the parameters of the design models. Deviation models may be based on expected or previously measured distributions or variations in the design.

[0299] Trial design space may further include experimental design data, adaptation rules data, and analysis model data. The experimental design data may include data, parameters, variables, and the like related to sample size, number of sites, accrual durations, allocation ratio, and the like. The adaptation rules data may include data, parameters, variables, and the like that specify the number of interim analyses, the timing of the interim analyses, boundaries, and the like. The analysis model data may include data, parameters, variables, and the like that specify test statistics, type one (1) error, and the like. In embodiments, each data, parameter, variable, and the like may have a set and/or a range of acceptable, realistic, or practical values. In embodiments, a set of trial designs may be generated wherein each trial design may have a different combination of data, parameters, variables, and the like. In some cases, the combination of different possible data values, parameters, and/or variables may result in thousands or millions of different trial design options.

[0300] Scenario space may include environmental and external factors that may affect trial design. In some embodiments, scenario data may include one or more mathematical or numerical models and methods that are related and/or describe one or more of human behavior, disease progress, drug behavior, and the like. Scenarios may include a combination of environmental variables that provide a specification or guidelines for generating virtual patient populations for a design study. Human behavior inputs may include trial execution characteristics, including how subjects adhere to regimen, dropout rates, and the like. Drug behavior may include models of drug behavior in a body and may include pharmacokinetic and pharmacodynamic models. The inputs may further include deviation models for one or more of the parameters of the models. Deviation models may be based on expected or previously measured distributions or variations in aspects such as human behavior, demographics, and the like. In embodiments, a plurality of different scenarios may be generated as potential inputs to the platform wherein each scenario may include different aspects of human behavior, disease progress, and drug behavior, and the like.

[0301] In embodiments, simulation models may be generated by combining two or more categories of inputs, such as by combining design space and scenario space. In embodiments, design space and scenario space may be defined separately and combined to generate models that include the two spaces. Generating the models from the two spaces may involve generating permutations of the two spaces. In one embodiment, a cross product between each scenario in the scenarios space and each design in the design space may be used to generate models. In this configuration, a large number of models may be generated from a much smaller set of designs and scenarios. In embodiments, millions of models may be created from design and scenario spaces that correspond to only thousands of designs and scenarios.

[0302] In some embodiments, the trial and clinical spaces models may be selectively combined, such that some instances of trial designs and clinical scenario models are not combined to create simulation models. The selective combination may reduce the number of simulation models that are simulated by the system, thereby reducing computation time. In some embodiments, a variety of heuristics, algorithms, filters, and the like may be used to select a subset of all possible combinations of trial and scenario spaces to reduce the number of simulation models, eliminate improbable combinations, and the like. In some embodiments, models may be scored before they are simulated. The scoring may be based, at least in part, on the feasibility, probability, practicality, or the like of the scenario-design combination for each model.

[0303] In embodiments scoring may be based on rating and/or priority associated with the design space parameters and/or scenario space parameters in each model. Ratings and/or priority may be provided by a user and/or other parts of the system. In some embodiments, rating and/or priority may be determined from historical data from previous simulations and design studies. The ratings and/or priority may be determined based on the number of occurrences of the parameter in the historical data in similar designs studies. In some embodiments the ratings and/or priority may be determined on the number of occurrences of the parameters in designs that were identified as optimal or desirable in previous designs studies. Ratings and/or priority score may be used to determine a relevancy score. The relevancy score may be computed as function of the ratings and priority score such that the higher the ratings and/or priority score the higher the relevancy score. Models that score below a threshold may be flagged or removed such that they are not simulated.

[0304] After the simulation models are created, the platform may execute and evaluate the simulation models. In embodiments, each simulation model (i.e., a specific combination of a trial design and scenario) may be evaluated over the course of numerous simulation runs, and the number of simulations may vary depending on the project stage. Each simulation run may be based on a different deviation of the trial design and/or scenario according to the respective deviation models. Results from multiple simulation runs for a particular simulation model may be analyzed to determine performance parameters.

[0305] In embodiments, results of simulations may be organized and grouped according to their relation to design and scenario space. Performance parameters of each model after simulation may be grouped to show relations of each parameter to one or more aspects of a design and/or scenario models. The relations may be used to refine aspects of the design space and/or scenario space for additional evaluation.

[0306] Referring to FIG. **28**, a flow chart for the evaluating designs may include defining design space **2802** and scenario space **2804**. The design space and scenario space may be used to determine combinations **2806** that are used to define models **2808** for simulation **2810**. The combinations may be analyzed **2812** by one or more filtering components **2814** that may rate and rank the combinations. The simulation data may be analyzed to determine desirable and/or optimum designs. Based on the analysis, the design and/or scenario spaces may be modified to generate more combinations for simulation.

[0307] As shown in FIG. **29**, a method for evaluating designs may include obtaining a design space **2902** and a scenario space **2904**. The set of simulation models may be generated by combing different permutations of the design space and scenario space **2906**. The simulation models may be scored and filtered **2908**. The method may further include simulating the filtered set of simulation models **2910** and analyzing the simulation results **2912**.

[0308] In embodiments, simulations may require population models, e.g., **3106** (FIG. **31**), to evaluate a design for virtual subjects. Population models may define characteristics of subjects in a clinical trial. A trial design may define aspects of subjects that should be included in a trial. A trial design may define inclusion and exclusion criteria for subjects based on characterizations of demography, disease status, and the like.

[0309] In embodiments, for a simulation, virtual subjects may be selected from population models. A population model may include subject models that include various subject characteristics such as demography data, survival models (control and treatment), dropout rate (control and treatment), expected responses, and the like. Characteristics of subjects in a population model may be associated with different distributions. The distributions of parameters of the population model may correspond to real-world population models. In embodiments, when a subject is included in a simulation, a population model may be evaluated to determine characteristics for a subject for one simulation instance. For each simulation instance, the population model may be evaluated (with a random value for selection) to identify a new subject and the subject may be selected based on inclusion/exclusion criteria of the trial.

[0310] In embodiments, a virtual population, e.g., **3102** (FIG. **31**), may be pre-generated. The virtual population may be generated according to a population model and/or real-world population data. The virtual population may be a list or other data structure that includes thousands or even millions of different virtual subjects. Each subject in the virtual population may be associated with characteristics such as demography data, survival models, dropout rate, expected responses, and the like for each subject. For a simulation, a subject may be selected from the virtual population (randomly or based on another function) for simulation of a trial design.

[0311] FIG. **30** shows aspects of utilizing virtual populations for simulation. A virtual population **3002** may be generated from population models **3006** and/or from real world population data **3004**. The virtual population **3002** may include data representing individual subjects (virtual patients) and characteristics of the subjects. The virtual population may be generated to have a specific distribution of characteristics for the subjects. The distribution of characteristics may be consistent with real-world data for a specific population or sub-population. The virtual population may include data for hundreds, thousands, or even millions of subjects. In some embodiments, multiple different virtual populations may be generated with different distributions of characteristics for the subjects.

[0312] In embodiments, a virtual population **3002** may be pre-generated before simulation start or may be generated in real time during simulation. In some embodiments, subjects may be generated as they are needed and/or requested for simulation using population models and the subjects may be added to a virtual population each time it is generated. The virtual population may grow as simulations and analysis of designs progresses. The virtual population may be a data structure (such as a database, list, table, and the like) that may be configured to retrieve data for a subject or a group of subjects randomly, according to specific subject characteristics, according to an unique identifier of the subject, and the like. Subjects in the virtual population may be used for simulation of trials. Simulation instance **3014** may include characteristics of a subject. The subject for the simulation may be selected from the virtual population **3002**. A simulation instance may evaluate a design for the subject for a specific design and scenario combination **3014**. Simulations may include a plurality of simulation instances **3014**, **3016**, **3018** using different subjects from the virtual population and variations of design and scenario combinations **3008**, **3010**, **3012**.

[0313] In embodiments a subject for a simulation instance **3008** may be selected from the virtual population **3002** randomly, based on a function of the characteristics of the subjects, by a unique identifier associated with each subject, and the like. In embodiments, each simulation instance may be associated with a unique identifier of a subject used for simulation. The virtual population may be used for all simulations of a study. Simulations instances may be reproduced with the same subject from the virtual population by saving a unique identifier associated with the subject with the simulation instance in a simulation history record.

[0314] In embodiments pre-generated virtual populations may have several benefits over subject selection from a population model. Subject selection from a virtual population may decrease computation time since a population model does not need to be evaluated for simulation instance and requires a simpler selection from a population (such as a selection from a list or table). Virtual populations provide for enhanced reproducibility given a constant population and improved accuracy of results across multiple simulations given constant population. In embodiments, due in part to the reproducibility aspects, pre-generated virtual populations may enable easier and faster computations of counterfactual data.

[0315] In embodiments, simulations may include determination of counterfactual data for a trial. Counterfactual data may relate to data that would have been observed under different (often conflicting) configurations of a trial. For example, if a trial provides data about an outcome of a patient that receives a therapy, counterfactual data may be data that relates to an outcome of the same patient if they did not receive a therapy. Normally, counterfactual data cannot be observed in a real-world trial. Continuing with the example, a patient, in a real-world trial can receive a therapy or not receive a therapy, but not both since the two configurations are conflicting. In a real-world trial, a patient can only be in one of two groups and therefore only one possible configuration of trial can be observed. The data related to a configuration that is not observed by a trial may be counterfactual data.

[0316] In another example, a trial may have missing data when patients drop out of the trial. The missing data is the data that would have been observed had the patient not dropped out of the trial. Missing data cannot be observed in a real-world trial but may be determined using simulation.

Missing data (which may be a type of counterfactual data) may be determined by simulating a trial design configuration for when a patient drops out of the trial and a configuration where the same patient does not drop out of the trial.

[0317] A trial design simulation may determine what is expected to happen in a trial and what could have happened in a trial given a different configuration (such as counterfactual data). Counterfactuals may be used to determine estimands for a true effect of a treatment. In embodiments, counterfactual data may be used to determine how good a trial is at estimating the estimands of interest using the observables of a trial. In embodiments, estimands determined from counterfactual data may be used to configure a trial design parameter (such as population size) to enable a trial design to come close to estimating the estimands.

[0318] FIG. **31** shows aspects of a platform that utilizes counterfactual data in a simulation and design scenarios **3108**, **3110**, **3112**, **3126**, **3128**, and **3130**. In embodiments, simulations may include simulations **3114**, **3116**, **3118** to determine what is expected to happen in a trial **3134** and another set of counterfactual simulations **3120**, **3122**, **3124** to determine what could have happened in a trial given a different configuration. For example, one simulation **3114** may simulate an outcome if patient A received a treatment and another counterfactual simulation **3120** may simulate an outcome if patient A did not receive a treatment. In embodiments, the trial data **3134** may be used to determine the estimator **3136** of a design. In embodiments, the trial data **3134** may be compared to the counterfactual data **3132** to determine estimand for the trial **3138**. A performance of a trial may be evaluated as to how close the estimator of trial is to the estimands. A trial for which the estimator is close to the estimands may be considered desirable.

[0319] As shown in FIG. **32**, a method for evaluating designs with counterfactual data may include simulating a configuration of a trial design to determine trial data **3202**. The method may further include simulating a second configuration of a trial design to determine counterfactual data **3204**. The trial data and the counterfactual data may be compared to determine an estimand for an outcome of the trial **3206**. The method may further include determining, for the outcome of the trial, the estimator of the trial design **3208**, and scoring the design based on a distance of the estimator to the estimand **3210**.

[0320] As shown in FIG. **33**, a method for evaluating designs with counterfactual data may include determining observable data for a trial **3302**. The method may further include determining counterfactual data for a trial design **3304**. An estimand may then be determined from the observable data and the counterfactual data **3306**. The method may also include determining, from the observable data, the estimator for the design **3308**. The design may be modified or other variations of the design may be explored (such as a design with a different population) such that the difference between the estimator and estimand are within a threshold **3310**.

[0321] FIG. **34** shows aspects of an apparatus for evaluating design with counterfactual data. In embodiments, the design evaluation circuit **3402** may receive simulation data from a simulation circuit **3412** and counterfactual simulation data from a counterfactual simulation circuit **3410** the data may be for a design. An estimand determining circuit **3404** may be configured to determine an estimand for an outcome using the input data. An estimator circuit **3406** may be used to determine the estimator for the design. An evaluation circuit **3408** may be configured to determine how well the estimator estimates the estimand. A distance measure, such as a difference or other statistical measure may be determined. Based on the measure the design may be scored and the design evaluation circuit **3402** may output a design score parameter **3414** based on the difference.

[0322] Interactive methods can be used in the process of evaluating designs, conducting simulations, configuring a design study (such as pre-simulation)s, and the like. Interactive methods may be methods in which a person or an alternate algorithm acts as a decision-maker and interacts with the methods, systems, and platform to indicate a preference for aspects of the outcomes and/or input. The preferences may be used to determine other inputs and/or outputs that relate to the preferences.

[0323] In embodiments, interactive methods may be used to identify preferences for trial designs. The preferences in trial designs may be used to identify optimum designs based on the preferences. The preferences in trial designs may be used to identify other designs that are similar to the preferences, surface design options that are complementary to the preferences, determine ranking of desired aspects of designs, determine unwanted features, and the like.
[0324] In embodiments, interactive methods may include providing a comparison and tracking selections in response to the comparison. In embodiments, configuration parameters may be presented to a user. Aspects of criteria space, design space, scenario space, and performance space may be presented before simulation. Parameters may be presented as a comparison between different parameters and/or values of the parameters. User input may an interaction between the values or parameters shown. Interactions may be used to identify preferences for parameters and/or values for parameters.
[0325] In embodiments, results of simulations may be presented to a user. Performance of simulated designs may be presented to a user via an interactive interface. In one embodiment, the interactive interface may present results of simulations as a comparison between two or more simulated designs. User input may include a selection of a preference between the designs, saving of one or more of the presented designs, indicating an interest in one or more parameters of the design and the like.
[0326] Interactive interfaces may be used to present two or more performance parameters of a simulated design to a user. In one embodiment the user may specify a preference for a design. Based on the tracking of the selection, one or more user preferences may be determined. User preferences may be identified from the user selecting a design, saving a design, dismissing a design, moving a design, and the like. In embodiments, preferences may be determined by identifying differences between the presented designs the designs associated with a user action.
[0327] In some embodiments, designs presented for consideration in an interactive interface may be selected based on results of optimality determination based on Pareto analysis and/or CH analysis. In some embodiments, designs presented for consideration in an interactive interface may be selected randomly from the set of designs.
[0328] Designs presented for consideration in an interactive interface may be selected such that an interaction with of one or more design in the interface provides useful information about preferences of a user. Designs may be selected for presentation may be selected such that they are substantially similar is most parameters and different with respect to a small number of parameters (such less than 10). Having substantially similar designs for comparison may provide a clear indication which parameters and/or values are preferrable to a user when an interaction with the designs is observed. In embodiments, designs may be selected such they represent very different designs. The designs may represent different ends of the spectrum with respect to the overall design (designs may differ in more than 10 parameters). Having designs that represent vastly different designs for comparison may provide a clear indication of the overall properties and types of designs that are preferred.
[0329] In embodiments, information inferred from interactions may be directly related to the parameters and values for which interactions were received. In some embodiments, information inferred from interactions may be derived for parameters and values for which interactions were received. Interactions related to one parameter or a design may provide additional information about other parameters. For example, interactions related to cost of a study may be used to determine preferences for the cost and/or other related parameters such a duration (longer studies may typically be more expensive), number of patients (more patients may require more sited and more cost), and the like.
[0330] In embodiments, interactive interfaces for identifying preferences for designs may be iterative and may require multiple interactions from a user to determine preferences. In the case of an interactive interface based on a comparison, the interface may iterate over multiple cycles of

presenting designs and receiving user selections. In each iteration, the interactive interface may present a different set of designs for consideration and monitor user interactions with the designs. In each iteration, the set of designs may be strategically selected to determine different aspects of preferences from user interactions. For example, in first iteration the designs shown on the interface may be selected to identify preference for design type, in the second iteration, the designs may be selected to identify preference for a first parameter.
[0331] Once preferences are identified designs, such as optimal designs, may be determined for the preferences.
[0332] In embodiments, interactive methods may be used to identify regions of interest and/or identify additional designs for simulation. Initial simulations may be coarse grained simulations. Coarse grained simulations may not be exhaustive but may be used to provide a course grid of designs that provides an overview of the designs and performance for identified criteria by simulating subset of the possible combinations. Some of the simulated designs from the coarse set of simulations may be presented to a user. User interactions with the presented designs may be used to identify types of designs and parameters of the designs that may be further explored with simulation.
[0333] In embodiments, an interactive method for identifying regions of interest may include an interface such as a map that shows relative and/or absolute performance of designs and their parameters. The interactive interface may be used to visualize the locations of designs in the performance space. Users may select regions of interest and the platform may be directed to identify designs that may be in the regions of interest for further simulation and evaluation.
[0334] In embodiments, an interactive method for identifying regions of interest may include an interface that identifies one or more designs from the coarse grid of designs. The designs and the properties and performance of the designs may be presented to a user and the user interactions with aspects related to the design may be tracked. Based on the interactions, user preference for the design may be determined. Additional designs may be presented to the user to determine preference for additional designs. Based on the interactions and preferences for designs, a region or an area in the design space may be identified as being an area of interest. An area of interest may include an area around a design (such as all designs within an P-distance of a design). An area of interest may be an area between two designs. An area of interest may be an area bounded by three or more designs (such as a triangular area bounded by three designs). The area of interest may be used as a guide for additional simulations. Additional simulations may be conducted on the designs that are in the area of interest.
[0335] In embodiments, interactive interfaces may be in connection with sensitivity analysis of designs. Interactions with the interface may be monitored to determine preferences for designs with respect to sensitivity and/or robustness of the designs. User interactions with interfaces for interacting with graphical elements for specifying filters, designs, regions, and the like may be tracked to determine which aspects of a design the user analyzes the most with respect to sensitivity of the design. The interactions may be tracked to determine minimum and/or maximum acceptable values for one or more parameter variations.
[0336] In embodiments, user interactions with interactive interfaces may be recorded and saved. In some embodiments, interactions with interactive interfaces may be processed to derive relevant data from the interaction and only the derived relevant data may be stored. In some embodiments, the derived data and the raw interaction data may be stored. Aspects of presented data in the interactive interfaces, interactions from users, sequence of interactions to achieve an outcome, and other aspects related to interactive interfaces may be saved. Interactions data, along with design data, design data, scenario data, and the like may be used to train one or more AI and/or ML models for identifying user preferences from interactions. The models may be trained on the previous interactions, presented data, and other aspects of the design study relevant to the interaction such as the criteria space, design space, scenario space, and performance space

definitions. The trained models may be used to predict which designs should be presented to the user to maximize information obtained from the interactions from the user with the presented designs. The models may be trained to determine user preferences based on the interactions and the final selections. The use of trained models may reduce the number of iterations and amount of interactions that need to be observed to identify preferences and/or identify other designs or regions of interest.

[0337] As shown in FIG. **35**, the interfaces component **3502** may include component for generating visualizations **3504**. The visualizations may include data related to simulated trial designs **3510**. The visualizations may present data related to trials and receive user input data **3512** that is indicative of user interactions with the interface and the presented data on the interface. The apparatus may include a feedback analysis component **3506** for tracking and analyzing the user input and interactions **3512**. The feedback analysis component **3506** may analyze interactions to determine design preferences, regions of interest, and the like. In some embodiments, the feedback analysis component **3506** may receive data related to user interactions which may include AI/ML model trained on the previous interaction data **3508**. The feedback analysis component **3506** may determine preferences **3514** for designs, parameters of designs, regions of interest **3516** for designs and the like based on the interactions.

[0338] FIG. **36** shows aspects of an apparatus for determining preferences from user interactions. In embodiments, the interfaces circuit **3602** may include a user input circuit **3604** and a simulation results processing circuit **3606**. The user input circuit **3604** may process interaction data **3612** from a user. The interaction data **3612** may relate to user interactions with data and components of an interactive interface. The interface may, during the interaction, display design data that is received from a recommendation circuit **3610**. The simulation processing circuit **3606** may further include a criteria determination circuit **3608** that may be configured to analyze processed user interaction data from the user input circuit **3604** and data provided in the interface from the simulation results processing circuit **3606** and determine user preferences. The preferences may include design preferences **3614** and/or regions of interest **3616**.

[0339] As shown in FIG. **37**, a method for determining design using user interactions may include obtaining trial design simulation results from a set of trial designs **3702** and recommending a first subset of trial designs to a user **3704**. The recommendations may be via one or more interactive graphical interfaces. The method may include receiving feedback from the user via the interface **3706**. The feedback may include interaction data that relates to one or more of the recommended designs. The method may further include identifying characteristics of trial designs preferred by the user from the feedback **3708**. Using the determined characteristics, the method may determine new trials with the identified characteristics that have not been presented to the user **3710**. The new trials may be simulated **3712**. The method may be repeated at least some of the recommended designs being the new simulated designs.

[0340] Shown in FIG. **38** is a method for determining a design using user interactions. The method may include obtaining trial design simulations results for a set of trial designs **3802**. The method may further include providing a first subset of trial designs to a user **3804** and feedback from the user may be received from an interface **3806**. Based on the feedback, one or more regions of interest from the design space may be identified **3808**. The method may further include identifying a second set of trial designs that are within the region of interest **3810**.

[0341] In embodiments, the interactive graphical interfaces may include a card interface. A In embodiments, a card interface may be used to evaluate or determine aspects the criteria space, design space, scenarios space, and/or performance space.

[0342] In embodiments, a card interface may be used to evaluate simulated designs. The card interface may be configured to identify, based on user interactions with the interface, user preferences for designs, preferences for design parameters, optimality of designs, and the like. The card interface may be configured to identify, based on user interactions with the interface, regions or areas of interest in the design space that appear to have desirable designs. These areas may be further explored with further simulations and analysis.

[0343] In embodiments, the card interface may include depictions of elements referred herein as “cards” that represent one or more of the simulated trial options. Depictions of cards may include rectangular shapes that may group data or parameters associated with a simulated design. The cards may be depicted as rectangles, squares, circles, polygons, or other shapes. The graphical interface depicting cards may include one or more cards that are associated with different trial designs.

[0344] In embodiments, an initial set of cards may be populated on the graphical interface, such as when simulations are completed. In some embodiments, an initial set of cards may be populated on the graphical interface during the simulation before all of the simulations are finished based on available or intermediate data. A card may provide an intuitive grouping of data for a trial design allowing a user to easily determine the parameters and qualities of the trial design the card is associated with.

[0345] In many situations, the number of simulated trial designs may be large such as a thousand or even millions of simulated trial designs. In embodiments, the number of cards shown on the graphical interface may be less than the number of simulated trial designs. In some embodiments, the number of cards initially shown on the interface may be less than fifty (50) or may be less than ten (10). The number of cards initially shown may be determined based on the total number of simulated trial designs, a user preference, historical preference, or the like.

[0346] A number of cards may be initially shown on the interface. Each card may be associated with and show data related to a particular trial design of the set of simulated trial designs. The selection of the initial trial designs that are represented by the cards may be selected using an initial card selection criteria.

[0347] In some embodiments, the initial card selection criteria may be a random criteria wherein random trial designs from the set of simulated trial designs are selected. In some embodiments, the initial card selection criteria may be based on a selection of trial designs that have the best value for one or more parameters. In some cases, each card shown on the interface may represent a trial design that has a maximum value for a different parameter. In embodiments, initial cards shown may represent the trial design that is associated with the trial design that has the best value for each strategic goal. Depending on the parameter, the best value may be the maximum value, a minimum value, a median value, and the like and may depend on the parameter and the goals of the parameter.

[0348] In some embodiments, the initial card selection criteria may be based at least in part on historical data (such as associated with a particular user or organization). Trial designs may be selected that have similar parameters to trial designs that were ultimately selected or were finalists in other clinical trials.

[0349] In embodiments, the selection of trial designs for cards may be based on a function of one or more parameters and variables. In some embodiments, the selection of trial design candidates for cards may be based on a weighted value sum of one or more parameters and variables. The weighting may be based on a specific goal of the study or other design parameters or requirements. In some cases, two or more different functions may be used. In some cases, each card or some cards may be associated with a different selection function. In embodiments, selection of trial designs for cards may be based on Pareto and/or CH analysis. Pareto designs and/or CH-designs may be used to populate data in the cards.

[0350] FIG. **39** shows one embodiment of a graphical interface with cards associated with trial designs. The figure shows four cards elements **3902**, **3904**, **3906**, **3908** with each card showing seven parameter values of different trial designs. In this case, the four initial cards represent a trial design that has the best value for four (4) different strategic goals. The first card **3902** is representative of a trial design that maximizes the expected net present value (eNPV) of all the simulated design studies. The first card **3902** shows parameters of the trial design that maximizes the eNPV for the simulated trial designs. Other cards are representative of trial designs that maximize or minimize other design goals, such as the probability of success (POS), discounted cost, and study duration.

[0351] In embodiments, colors, shading, saturation, background color, and the like may be used to represent information regarding values of the parameters of a trial design shown on each card. In embodiments colors, shading, saturation, background color, and the like may be used to represent the relative value of a parameter with respect to all of the simulated trial designs. For example, a low relative value may be shown with a blue color, while a large relative value may be shown with a red color. In embodiments, colors, shading, saturation, background color, and the like may be used to represent the relative value of a parameter with respect to the values shown on the cards.

[0352] In embodiments, the graphical card interface may include designs for specifying filters **3910** for one or more parameters of the trial designs. Filters **3910** may affect which trial designs are displayed by the cards. In embodiments, the filters may affect the number of cards shown. Filters may be used to set global limits on specific parameters for all the displayed cards or may be applied differently to each card.

[0353] In embodiments, filters may be applied to cards that are configured to display cards that maximize or minimize a strategic goal. An applied filter may cause the card to display a trial design that provides the maximum or minimum for a strategic goal but also satisfies the bounds of the filter.

[0354] In embodiments, filters may be applied via one or more graphical controls. The controls may be different based on the type of parameter or variable the filter is being applied to. Parameters or variables that have real numbers, for example, may have different controls than parameters or variables that have Boolean values. In some embodiments, the filter controls may include sliders, dials, input boxes, and the like. The behavior of a control may depend on the values for the respective parameters or variables in the set of simulated trial designs. The behavior of the control may depend on the distribution of the values of the respective parameter or variable. For example, in the case of a slider control, the behavior of the slider control may be nonlinear with respect to the value the slider represents with respect to the position of the slider. The behavior of the slider may be different when the slider is in a position where there are many values for a variable or a parameter versus where there are no values for a variable or a parameter.

[0355] In embodiments, filter settings may be analyzed with respect to the one or more distributions, values, desired values, expected values, goals, trial goals, trial parameters, trial values, distribution of values, distributions or parameters, and the like. Filter settings may be analyzed to determine how adjusting one or more filters may impact what trial designs are displayed on one or more cards. For example, filter settings may be set to filter out all trial designs below a specific value of a parameter of the trial designs. However, the setting of the filter may filter out many trial designs that meet one or more strategic goals. In embodiments, the sensitivity of filter settings may be identified, and their sensitivity may be communicated to a user. In embodiments, a user may be provided with information to indicate that the user may consider adjusting one or more filter settings. The user may be provided with information as to how the settings may be changed. In some embodiments, the platform may adjust filters when the filters are determined to be too aggressive or determined to cause filtering of trial designs that would otherwise be good candidates for a trial or that a user should otherwise review. In some embodiments, the filters may be set to approximate values, and the platform may be configured to automatically set the filters to an actual value based on analysis of the trial designs and/or design objectives.

[0356] In some embodiments, filter settings may be analyzed with respect to a distribution of the values related to the filter. Users may be provided with information regarding the setting of the filter with respect to the distribution of the values. For example, in some cases, a variable may have a binomial distribution. The user may be provided with information regarding the setting of the filter and how the setting may be adjusted to consider a cluster or a specific distribution of values. In some cases, filters may be associated with one or more graphs or graphics that identify the distribution of the values associated with the filter. In some cases, a user may be provided with a graph or other indicators that provide information about the relation between a value associated with a filter and one or more strategic goals.

[0357] In embodiments graphics on a displayed card, around a displayed card, the like may provide additional information regarding the trial design displayed compared to other simulated trial designs not displayed. Graphics may be used to provide information regarding how many other trial designs are within a specified distance to the displayed trial design. Graphics such as variable shadows, lines, colors, and the like may provide a quick visual indication as to the number of similar trial designs are available to the trial design displayed on the card. In embodiments, graphics may indicate a depth of a deck of cards, the number of trial designs related to a card, the number of trial designs in the same category as a card, and the like.

[0358] In embodiments, cards in the card interface may be manipulated by a user. User interactions with the card interface may be tracked. Interactions may include manipulation of cards. Manipulation of cards may include actions that are performed by a user in the process of examining and selecting one or more trial designs. Manipulations may include selecting, ranking, moving, putting into a “shopping cart” or “favorites” category, comparing, and the like. The manipulations of the cards may be tracked by the platform to determine the preferences and/or goals of the user.

[0359] In embodiments, the platform may use the history of the interactions, such as the manipulations, to provide suggestions for filter settings and/or provide new cards that show additional trial designs for consideration. For example, the platform may identify a trend that cards with data related to trial designs with a cost exceeding a specific value are removed from consideration by a user. The platform may use the identified trend to determine additional trial designs below the cost and provide the designs for consideration to the user.

[0360] In embodiments, data related to objectives of an organization, historical data, customer data, and the like may be used to identify trial designs automatically. In embodiments, the automatically identified trial designs may be displayed to a user with a card for consideration. In embodiments, manipulation of cards may be used to identify preferences such as absolute values or variables or parameters, relative values, and correlations. In embodiments, the platform may find trial designs that are similar to those selected as “favorites” and present them as cards for consideration.

[0361] In embodiments, cards that were tagged as a favorite, saved in a shopping cart, or highly ranked by a user may be selected for display in a comparison table. Data related to the trial designs of the cards may be displayed in a table format, and the data may be compared by the user or exported for comparison or other purposes. In embodiments, the interface may include visual effects such as highlighting or emphasized (such as a darker border, a different color of border, a flickering of colors, and the like) to confirm user interactions and/or provide feedback that an interaction was analyzed to determine preferences.

[0362] In embodiments, the platform may determine preferences for characteristics of trial designs by presenting various trial designs in the form of cards for considerations. The trial designs may be strategically selected to explore preferences between tradeoffs between one or more parameters. In some embodiments, cards with selected values may be presented to a user allowing the user to select the card or provide other indications of interest in the card.

[0363] Based on the responses, the platform may determine which variables or parameters are important, as well as acceptable ranges for those variables and parameters. In another embodiment, the platform may simultaneously present two or more cards with contrasting values for parameters allowing the user to choose a favorite card or rate the relative interest in the cards. Based on the rating and selection, the platform may determine which parameters, variables, values, and the like the user is most interested in or that are more important to the trial. Cards presented to the user may reflect values of specific trial designs or may not be selected to explore preferences and may not be directly related to any specific trial design.

[0364] In embodiments, the platform may determine preferences for characteristics of trial designs by presenting various combinations of parameters. The platform may show parameter values that represent corner cases of one or more parameters. The platform may show values that represent a spectrum of values of one or more parameters or a combination of parameters to determine a user preference. For example, the platform may display cards to a user that represent different ranges of parameters such as a high cost or low cost. Based on user interactions with the cards, the platform may determine a user's preference for cost. In another example, the platform may determine user preferences for a tradeoff between parameters by presenting cards with two or more parameter values. For example, the user may be presented with one card that represents high cost and low time values. The user may be further presented with another card that represents low cost and high time values. Based on user selection of the cards, the platform may determine the user preferences for tradeoffs between cost and time for a study.

[0365] In embodiments, the platform may determine a trial design through one or more processes that may use various graphical interfaces for determining user preferences, user selections, refining results, receiving feedback, and/or the like. In some embodiments, a series of scripts, programs, algorithms, and wizards may analyze data, patterns in the data, user preferences from the data, and/or the like without direct or other use of a graphical user interface. In some embodiments, any combination of data analysis and graphical user interfaces may be used to narrow down a set of trial designs to one or more selected trial designs.

[0366] In embodiments, one or more, artificial intelligence algorithms, neural network, statistical analysis, and the like may be used to track user selections, analyze the history of trial design selections to suggest one or more filters and trial designs in view strategic goals, preferences, constraints, and the like.

[0367] As shown in FIG. **40**, a method for evaluating designs with user interactions in a card interface may include presenting a set of cards wherein each card is representative of a different trial design **4002**. Each card may include graphics that display one or more parameters associated with the card. The designs represented by the cards may be derived by Pareto analysis, CH analysis, and/or simulated annealing. The designs presented by the cards may be selected at least in part based on filters. In embodiments, filters may be configured by user input to select bounds and/or values on one or more parameters. The method may further include monitoring user interactions with the cards **4004**. Interactions may include selecting cards, moving cards, deleting cards, saving cards, changing filters, adjusting filter, and the like. Based on the interactions, the method may determine preferences for one or more values and/or parameters of designs **4006**. The method may further include presenting at least one new design based on the determined preferences **4008**. The new design may be presented on a new card that is added to the set of cards. The new design may be shown as a replacement for a previously shown design. The method may further include monitoring user interactions with the cards that include the new design **4010**. The interactions may be used to refine the determined user preferences **4012**. The new interactions, such as for example, a user selecting the new design, may indicate that the parameters of the new design are desirable.

[0368] FIG. **41** shows aspects of an apparatus for evaluating design with user interaction using a card interface. The apparatus may include a card interface component **4102**. The card interface component **4102** may be part of the interfaces facility **112** of the platform **104**. The card interface component **4102** may display and monitor an interactive card interface that enables interactive evaluation of designs. The card interface may include a card presentation component **4104** that may generate a card display for one or more simulated designs **4114**. The card presentation component **4104** may identify which values or parameters should be displayed for a design on a card. The card interface component **4102** may include a graphic enhancement component **4108** which may be configured to change the display of one or more aspects of a card to highlight a property, value, rating, ranking, and the like of the design displayed by the card. For example, the highlighting may be relative to other designs shown on the cards. Designs that have a parameter higher than the other designs displayed may have the parameter highlighted on the card of the design. The card interface component **4102** may include an interaction analysis component **4106** configured to monitor user input **4116** with the interface. Interaction analysis component **4106** may be configured to infer one or more preferences **4118** for one or more parameters of the designs based on the interactions. The interaction analysis component **4106** be configured to receive historical interaction data **4112** to identify patterns or trends in previous interactions and preferences to identify how interactions with the present interface relate to preferences. The preferences may be used by the card suggestion component **4110** to identify new designs to be displayed in a card. The new design may be consistent with the determined preferences **4118**. In some embodiments the new design may be selected to provide new information about preferences and may not be consistent with the preferences **4118**.

[0369] FIG. **42** shows aspects of an apparatus for evaluating design with user interaction using a card interface. In embodiments, the interfaces circuit **4202** may include an interaction analysis circuit **4204** and a simulation results processing circuit **4206**. The interaction analysis circuit **4204** may process interaction data **4214** from a user. The interaction data **4214** may relate to user interactions with data and components of an interactive interface. The interface may, during the interaction, display design data in a card interface. The design data may be received from a recommendation circuit **4212**. The interface circuit **4202** may further include a suggestion circuit **4208** that may be configured to analyze processed user interaction data from the interaction analysis circuit **4204** and data provided in the interface from the simulation results processing circuit **4206** and determine user preferences **4216** for designs. The interface circuit **4202** may include a graphic enhancement circuit **4210** for highlighting or emphasizing one or more parameters or values displayed on the card. The emphasizing may be due to the value being substantially (such as 10% or more) higher or lower than the other designs. The card suggestion circuit **4208** may identify which designs to present using the card interface. The card suggestion circuit **4208** may determine designs based on the determined preferences **4216**. The card suggestion circuit **4208** may determine designs to display on the card interface in order to determine new preferences.

[0370] In embodiments, the interactive graphical interfaces may include a tornado diagram interface that may be used to evaluate simulated designs. In embodiments, designs may be evaluated for their sensitivity to changes in scenarios and/or other parameters. A tornado chart is a type of sensitivity analysis that provides a graphical representation of the degree to which the result is sensitive to the specified independent variables. Tornado visualization may be configured for viewing trade-offs and obtain answers to what-if questions in real-time. In embodiments, an interactive tornado diagram for sensitivity analysis of promising designs may use categorization of design parameters, including: decision variable vector, scenario vector, performance criteria, and the like. The tornado diagrams may be configured to help in visually analyzing the effect of change in design and scenario vectors on the performance, and to identify the desirable design space combination to have optimum performance criteria values.

[0371] FIG. **43** shows example aspects of a tornado dashboard for evaluating sensitivity of design. In embodiments, the dashboard may include one or more tornado diagrams (three tornado diagrams are shown **4302**, **4304**, **4306**). In embodiments, tornado plots may be used to analyze the sensitivity of designs and decision variables with respect to performance criteria. A set of tornado plots that may be used to assess and compare the sensitivity of various designs and decision variables. In embodiments, an interface may be presented to a user allowing comparison of sensitivity designs and variables with respect to two or more performance criteria. In some embodiments, input elements **4308**, such as slides, text boxes, checkboxes, and the like, may be provided to change values of variables and options that are shown in the plots.

[0372] In embodiments, the interactive graphical interfaces may include a heatmap interface that may be used to evaluate simulated designs. A heatmap interface may show a magnitude of a performance parameters for different designs using colors and shading. The heatmap may be arranged in a grid or a matrix. The heatmap may be arranged such that one dimension may list designs while the other dimension may list parameters. In embodiments, the heatmaps may be clustered heatmaps where the parameters may be clustered according to different criteria.

[0373] A heatmap provides an interface to quickly visually compare, evaluate, and select designs. In embodiments a heatmap may provide for tens, hundreds, or even thousands of different designs with respect to tens, hundreds, or even thousands of different parameters or scenarios. In embodiments, a heatmap may be configured or configurable to show different relations and allow a user to compare and evaluate different designs against different parameters and/or scenarios. In embodiments, a heatmap may be configured or configurable to show different parameters for the designs. The heatmap elements may be filtered according to one or more filters. In embodiments, the elements may be reordered based on one or more criteria. Users may zoom or select a subsection of a heatmap.

[0374] In embodiments, users may evaluate designs by changing views of a heatmap or showing more than one heatmaps with different configurations. In embodiments, users may mark one or more designs in one heatmap or one configuration of a heatmap. The marking of a design in one heatmap or one configuration of a heatmap may be propagated to other heatmaps or configurations of heatmaps with the same design. The selected design may be highlighted or emphasized (such as a darker border, a different color of border, a flickering of colors, and the like) as a heatmap is reconfigured to show the selected design. In embodiments, a two or more designs may be selected and tracked between different heatmaps or heatmap configurations.

[0375] In embodiments, heatmaps may provide an option to display or emphasize optimal designs, Pareto designs, CH-designs, and/or other recommended designs. The designs may be highlighted and/or emphasized to show their location in the heatmap and may show animations or other indicators to show changes in locations of the designs in the heatmap when a heatmap is reconfigured. Designs and/or cells that are highlighted or emphasized may be deselected, dismissed, flagged, marked, and the like by the user. Designs that are dismissed may be deemphasized and no longer tracked in the heatmap. User interactions with the heatmap may be tracked to identify user preferences for designs. In some embodiments, a user may identify regions of the heatmap (such as by drawing or indicating an area such as a circle, square, or other shape) to indicate an area of interest or to indicate an area that does not include relevant designs. The areas that are indicated to not have designs may be filtered from the heatmap. Areas that are indicated as areas of interest may trigger additional simulations. For example, marking an area as an area of interest may trigger simulated annealing analysis to identify other designs that may be similar to those in the area of interest. In embodiments, selections of elements in the heatmap may trigger automatic updates to definitions of the criteria space, design space, scenario space, and/or performance space and may trigger additional simulations and/or additional analysis (such as recomputing P-designs, CH-designs, and the like).

[0376] In embodiments, heatmaps may provide features to emphasize some designs. In heatmaps with a large number of designs, the color and/or shading that represents a value of a design with respect to a parameter may have a small area on the interface. The small area of the color may make it difficult to distinguish the value represented by the color from nearby or neighboring colors. In some embodiments, the heatmap interface may identify cells that may be of interest to a user (such as representative of a high or desirable value) but may not be clearly visible due to small size or the colors of neighboring cells. In embodiments the cells may be emphasized with changing colors, flickering, distinguished borders, or other effects to distinguish the cell from surrounding cells.

[0377] FIG. **44** shows aspects of a heatmap. A heatmap **4402** may be displayed as a grid of cells.

The rows of the grid may correspond to different designs and the columns may be representative of different scenarios. Each cell may be colored or shaded to be representative of a value (such as a score) of the design for a scenario. The configuration of heatmap may be changed by changing aspects of the score, aspects of what designs and scenarios are represented, the ordering of the designs and scenarios, and the like. The score shown for each cell may be configured in a score definition part of the interface **4404**. The score definition part **4404** may provide for a configuration of the weights used for computing the score and/or the parameters used to calculate the score. The interface may include components to filter scenarios **4406** and components to filter designs **4408**. The interface may include options **4410** to configure the heatmap for displaying different aspects such as what score is shown, which design and scenarios are shown. The component **4410** may include preset options for filtering and configuring the heatmap. In embodiments, users may mark one or more cells in the heatmap. The marked heatmaps may be visually emphasized and may be tracked as the heatmap is reconfigured.

[0378] In embodiments, the interactive graphical interfaces may include a tradeoff advisor. A tradeoff advisor may include a graphical interface may provide one or more displays for selecting data for comparison and graphing. The tradeoff advisor may provide a display of heatmaps, scatter plots, tornado plots, and other graphs for visualizing relationships between aspects of the designs. In embodiments, relationships between strategic goals, variables, parameters, values, and the like may be automatically determined for a set of simulated trial options. In some cases, users may choose to select a parameter and/or strategic goal, and the platform may determine two (2) or three (3) or more variables and/or parameters that have the biggest impact on the selected parameter and/or strategic goals. The platform may generate one or more graphs showing the relationship between the parameters. For example, a user may select one output of interest (duration, cost, eNPV, probability of success, etc.). The platform may use sensitivity analysis to automatically put the two (2) or three (3) biggest drivers for that output on the two (2) or three (3) axes for a display chart. In embodiments, a user may select to show parameters or variables that have the biggest impact, lower impact, average impact, variable impact, and the like. The relationships may be used to set filters, rank importance of variables or parameters, and the like.

[0379] In embodiments, interactive interfaces (such as the card interface, heatmap interface, tornado interface and the like described herein) may be used to evaluate and configure parameters and/or criteria before simulation. Parameters and values of the parameters for design space, scenario space, criteria space, and/or performance space may be displayed using one or more interactive interfaces. Interactions may be received to configure one or more of the spaces. For example, heatmaps may be used to visualize scenario parameter values that have been determined for simulation. Regions in the heatmap may be identified using the interface to exclude some scenarios. In some cases regions in interest in the heatmaps may be identified to add additional parameters or ranges of values to the spaces.

[0380] In embodiments, interactive interfaces may include reporting and alert features. In embodiments, outputs of interfaces may be provided in report format for users. In embodiments, reports may be automatically generated and stored for documentation of design and analysis methodologies. In embodiments reporting may be based on the types and/or number of interactions observed. In some cases reporting may provide a summary of how interactions were interpreted and used to determine preferences and/or recommended designs.

[0381] Referring now to FIG. **45**, an embodiment of the architecture/analysis platform **104** (also shown in FIG. **1**) is depicted. The platform **104** may include a primary algorithm **4510** that controls and/or monitors the workflow of the platform **104**, e.g., queuing (ordering), cueing (invoking), starting and/or stopping execution of one or more algorithms and/or engines; procurement of inputs; delivery of outputs, performance, progress updates; and/or the like. While FIG. **45** depicts the primary algorithm **4510** as being within the analysis facility **108**, it is to be understood that, in embodiments, the primary algorithm **4510** may form part of, extend, and/or have access to one or more other components of the platform **104**, e.g., the configuration facility **106**, simulation facility **110**, interface facility **112**, data facility **138**, computing resources **150**, and/or the like. In certain aspects, the primary algorithm **4510** may interface with other algorithms/engines/modules and techniques such as simulated annealing **4516** modules, Pareto modules **4512**, convex hull modules **4514**, Monte Carlo modules **4516**, visualization tools/engines, recommendation algorithms/engines, and/or the like **4518**. As described in greater detail herein, embodiments of the primary algorithm **4510** may structure and/or control the flow of data through the platform **104**. Data flow through the platform **104** may be facilitated by data records that are stored and retrieved from one or more databases in data facility **138**. In other words, embodiments of the primary algorithm **4510** may provide for a configuration of the platform **104**, also referred to herein as a platform configuration. A data record may include one or more variable types, e.g., string, integer, long, scalar, etc., in rows and columns. Data records may conform to a relational schema so that several data records collectively represent a higher-level data object. As used herein with respect to the platform **104**, the terms "configuration" and "platform configuration" include the arrangement, sequencing, and/or manipulation of one or more components of the platform **104**, e.g., sequencing of models and/or engines, sequencing and/or configuration of algorithms, control of data flow and/or the like. In certain aspects, the platform configuration may be based on data analysis, user inputs, and/or the like.

[0382] For example, FIG. **46** depicts a method/workflow execution control structure of an embodiment of the primary algorithm **4510**. The primary algorithm **4510** may include obtaining a trial design specification for a clinical trial design **4610** and obtaining one or more component specifications for one or more components of the platform **4612**. A component specification may include one or more levels of specification. For example, in one level, the component specification may include specific configurations of components such as which algorithms will be used, order of execution, the types and versions of simulation engines, and/or the like. In another level, the component specification may include high-level, and/or generalized, descriptions/objectives that may specify how long a design study should take and/or a cost of performing the design study. In the case of a high-level description, the component specification may be used to automatically, or semi-automatically, identify details of a configuration to achieve the high-level description. For example, based on a high-level specification of a cost, a configuration may limit the number of designs simulated, the number of simulation runs for each design, the fidelity of the simulations, number of analysis algorithms executed, and the like. The one or more components may include an engine, one or more algorithms, models, databases, computing resources, storage resources, and/or any other component of the platform **104** described herein. The algorithms may include Pareto analysis algorithms, convex hull algorithms, simulated annealing algorithms, Monte Carlo algorithms, recommendation algorithms, and/or the like. The trial design specification may include a simulation time, a runtime, a type of analysis, a performance criteria, and/or the like. In embodiments, the trial design specification may include a preference for a number of recommended designs, a type of visual output, a type of interactive interface, and/or the like. The one or more component specifications may include a cost, a runtime, a required resource, a version, and/or the like.

[0383] The primary algorithm **4510** may further include determining, based at least in part on the trial design specification and the one or more component specifications, a configuration for the analysis platform **4614**. The configuration may be a data file and/or other type of data structure that defines various aspects of the platform **104**, e.g., sequencing and/or type of algorithms, location of inputs, and/or any other type of configurable property of the platform **104** described herein. For example, in embodiments, the configuration may call for filtering simulated trial designs by first applying a Pareto algorithm followed by applying a convex hull algorithm. The configuration may then call for the results of the convex hull algorithm to be assessed via simulated annealing to detect if the current results are a local maxima or minima with respect to the desired performance criteria. In embodiments, the primary algorithm **4510** may include executing an analysis of the clinical trial design **4616** via the analysis platform **104**, as described herein, using the configuration. As further shown in FIG. **45**, in certain aspects, the primary algorithm **4510** may include transmitting the configuration **4618**. Determination of the configuration **4614** may include determining an order of execution for one or more analysis algorithms **4620**. In certain aspects, the configuration may be based on historical data and/or derived/predicted via machine learning. For example, artificial intelligence may be used to recognize and/or recommend particular configurations as being suitable for a particular type of clinical trial.

[0384] In one example, the primary algorithm may determine a configuration of the analysis platform based in part on the number of designs that are expected to be simulated for a study. The primary algorithm, may, before simulations are executed, analyze the configuration for simulation to determine or estimate the number of designs for which performance parameters will be determined. The number of designs may be estimated based on the number of design/scenario parameters (the number of parameters may correlate to the number of designs that will be simulated), based on the types of simulations scheduled (exhaustive simulations, partial simulations, or based on simulated annealing). The primary algorithm may determine which analysis algorithms should be executed to provide the user with sufficient (not too many) recommended designs. In one instance, if exhaustive simulations are scheduled, the primary algorithm may configure the analysis platform for the convex hull algorithms to reduce the number of design suggestion. In another instance, if partial simulations are scheduled, the primary algorithm may configure the analysis platform for Pareto algorithms in order to provide for a sufficient number of recommended designs.

[0385] Turning to FIG. **47**, an apparatus **4700** for implementing the primary algorithm **4510** is shown. The apparatus **4700** may be one or more processors, as described herein, that form part one or more servers, e.g., computing resources **150** (FIG. **1**). The apparatus **4700** may include a specification receiving circuit **4710** structured to interpret trial design specification data **4712** and one or more component specification data **4714**. The apparatus **4700** may further include a configuration determination circuit **4716** structured to generate platform configuration data **4718** based at least in part on the trial design specification data **4712** and the one or more component specification data **4714**. The apparatus **4700** may further include an evaluation circuit **4720** structured to analyze the clinical trial design via the analysis platform **104**, as described herein. In embodiments, the evaluation circuit **4720** may generate evaluation data **4722** which may be transmitted by the apparatus **4700** via an evaluation data provisioning circuit **4724**. The apparatus **4700** may further include a graphical user interface circuit **4726** structured to generate graphical user interface data **4728** configured to provide a graphical user interface. The apparatus **4700** may further include a user input processing circuit **4730** structured to interpret user input data **4732**.

[0386] In certain aspects, the apparatus **4700** may provide for results and/or intermediate data of the analysis of one or more clinical trials to be transmitted and/or accessed by a user interface (which may be provided by the graphical user interface circuit **4726**) for review, analysis, visualization, and manipulation. The user interface may receive user input data **4732** for design selections, parameters, and/or the like. The apparatus **4700** may provide an interface (which may be provided by the graphical user interface circuit **4726**) for interacting with external tools and/or engines for simulation and/or analysis. In some embodiments, the apparatus **4700** may record and/or track the processes and/or inputs for a session and/or design study. The apparatus **4700** may track the sequence of steps and/or algorithms/engines used for the analysis of data and may further record and/or track user selections and/or actions. The apparatus **4700** may analyze recorded sequences of processes, user actions, and/or selections to learn from past actions and results to determine the most appropriate (i.e., the fastest, the most accurate, etc.) sequence of algorithms for providing user recommendations. In embodiments, the apparatus may learn via artificial intelligence, e.g., a neural network, as disclosed herein. In embodiments, the primary algorithm

4510 may facilitate communication between any two or more of the algorithms described herein. For example, the platform may track and record which platform configurations resulted in a faster design consensus. The platform may track which platform configuration and which combination of analysis configuration resulted in less time between when designs were presented/recommended to a user and when a final design was selected. Faster time for selection may be indicative that the platform provided the user with recommended designs that were acceptable since the user spent less time considering other options or performing additional simulations and/or analysis. The system configuration that was related to faster consensus may be tagged as more favorable. Based on the tags, the platform may analyze a configuration of simulation configurations and analysis configurations.

[0387] In embodiments, analysis of design options may include a Pareto analysis. A Pareto optimal analysis may be used for algorithmic generation of design recommendations. Pareto analysis may be used to determine one or more Pareto optimal designs (also referred herein as “Pareto designs” or “P-designs”). Initial selections of a set of candidates for best or optimal designs may be selected using a Pareto frontier that is generated by the Pareto designs.

[0388] Pareto analysis may identify designs that are Pareto optimal for the one or more performance parameters. Pareto optimal designs may be designs where no individual performance parameter can be better off without making at least one other individual performance parameter worse off. The set of Pareto optimal designs may form a Pareto frontier. Pareto optimality may be used as an optimality criteria.

[0389] Referring again to FIG. **1**, the filtering component **120** (FIG. **1**) may include Pareto analysis. The filtering component **120** may include circuits, components, and algorithms for enabling Pareto analysis. The filtering component **120** may receive simulation data from the simulation facility **110** and analyze the simulated data to identify one or more designs using Pareto analysis techniques. The identified designs may be recommended to a user.

[0390] FIG. **48** shows a graphical representation of aspects of Pareto analysis. FIG. **48** further shows a graph with points wherein each point corresponds to a trial design. The graph shows the performance of each trial design with respect to two trial design parameters (e.g., maximum probability of technical success and maximum time to patent expiry) that may have been determined by simulation. As depicted in **48**, it may be the case that the higher the number of the parameter, the more desirable the parameter is. Points in the top right quadrant (represented by box **4802**) of the graphs may relate to designs having more desirable performance parameter values. In the illustrated example, Pareto analysis is used to determine Pareto optimum designs in the top right quadrant **4802**. As further shown, the Pareto designs are connected by a line that is the Pareto frontier **4804**. As will be appreciated, the Pareto designs represent designs where no individual performance parameter can be better off without making at least one other individual performance parameter worse off.

[0391] The Pareto frontier may be computed for a subset of all the trial designs. In some cases, the Pareto frontier may be computed for trial designs that have at least a threshold value for one or more performance parameters. In the example of FIG. **48**, the Pareto frontier is determined only for the trial designs that are in the top right section/quadrant **4802** of the graph and relate to a threshold of at least 90% in both the two performance parameters considered. The thresholds may be based on the goals considered, may be set by a user, algorithmically determined, and/or the like. FIG. **48** also shows trial designs that do not meet the 90% threshold for the two performance parameters are omitted from consideration, and a Pareto frontier is determined only for the designs that meet the thresholds.

[0392] In embodiments, the Pareto designs (and, hence, the Pareto frontier) may be determined using various methods such as, but not limited to, a scalarization algorithm, a skyline query, weighted sums, and/or the like.

[0393] In embodiments, Pareto designs may be identified as globally optimum designs and the

Pareto designs may be recommended to a user. In some embodiments, Pareto designs may be identified as initial globally optimum designs and they may be used to refine the optimality criteria to identify other globally optimum designs for the new criteria. In some embodiments, interactive methods can be used in which a person, or an alternate algorithm, acts as a decision-maker and interacts with the method to indicate a preference for designs (such as preference among initial Pareto designs). In such embodiments, the method may use the preference information to determine other trial designs (and modify optimality criteria) based on the preference of designs. In embodiments, the Pareto designs can be used to elicit the user's preferences by interactively querying the user to make comparisons between designs.

[0394] Trial designs that are on or near the Pareto frontier may be selected as initial choices for evaluation by a user. One or more of the designs may be presented to a user to evaluate and provide feedback. Feedback may include data related to acceptance of a trial design, rejection of a trial design, identification of one or more parameters or features of a trial design, and/or the like. In embodiments, the one or more trial designs from the Pareto frontier may be presented to a user using cards, tornado diagrams, heatmaps, and/or other similar interfaces as described herein.

[0395] In some cases, the platform may receive feedback, e.g., user feedback, regarding recommended Pareto designs. Based on the feedback, optimality criteria may be changed. Changes in optimality criteria may include eliminating designs from consideration. When designs are eliminated from considerations, a Pareto analysis may be performed on the remaining designs which may result in new Pareto designs. In some cases, a change in optimality criteria may include a new and/or modified criteria that provides for a “second best” Pareto frontier to be computed. A “second best” Pareto frontier may include designs that are Pareto optimal when the initial Pareto designs are eliminated. The second best Pareto designs may represent a second “level” of a Pareto frontier. In some cases, multiple “levels” of Pareto frontiers may be computed. In some cases, recommendations to users may include designs from the second best Pareto frontier and/or other levels, e.g., “third best”, “fourth best”, etc. Recommendations to designs in other levels may identify other design types that may be preferrable. Recommendations to designs in other levels may identify design that are more robust than designs in the first level and may be more desirable due to their robustness even if they have worse performance with respect to other performance parameters. In embodiments, interfaces such as tornado diagrams, card interfaces, heatmaps, and the like (including as described herein) may be used to evaluate initial recommendations determined using initial optimality criteria. Received feedback regarding the designs may be used to refine recommendations and optimality criteria used to determine globally optimum designs.

[0396] In embodiments, the optimality criteria may be modified according to the number of Pareto designs that are identified. Pareto designs may sometimes cluster. Some Pareto designs may be very close to other Pareto designs. Differences in the designs may be small and/or within the expected simulation error of the designs. In some cases, the Pareto designs which are close together may be filtered or grouped together. In some cases, a first Pareto design may be used to temporarily represent one or more other Pareto designs that are close to the first Pareto design to reduce the number of Pareto designs that are considered.

[0397] Pareto analysis may be configured to separate Pareto designs that are twins (designs that have equal or nearly equal performance parameters or observables such as cost, power, and/or time, twins may be designs that are within simulation error for example) and/or siblings (designs that are similar with respect to performance parameters or observables). In some cases, similarity for twin and/or sibling determination may be based on thresholds, such as designs that are within an ε-box of each other. In embodiments, one or more first designs may be considered within an ε-box of a second design when the one or more first designs are within a ball of radius P from the second design. Designs that are twins or siblings may be flagged or marked for further analysis if they are deemed to have desired performance as the twins or siblings may represent different design options that can be used to achieve similar performance criteria.

[0398] In embodiments, the Pareto analysis may further identify dominated designs. Dominated designs may be designs that are dominated by one or more other Pareto designs. Dominating Pareto designs may be better for one or more of the dominated designs for one or more design criteria. From the dominated designs, Pareto analysis may identify designs that are clustered by the dominating Pareto designs. The designs that are clustered may be identified using ε-criteria. The ε-criteria may be a threshold as to how far the dominated designs may be from the dominating Pareto designs to be included in the set of clustered designs. The ε-criteria may be a measure as to how similar designs should be to be clustered together. The threshold and similarity measures may be directed to the performance parameters of each design, such as the cost, duration, etc., of each design. For example, for performance parameter p, a design may be within ε-criteria if a design is within p±ε.
[0399] Pareto designs may be filtered or grouped, and one or more other Pareto designs that are within P of another Pareto design may be represented by one Pareto design. In other words, a dominating Pareto design may represent one or more dominated Pareto designs. In one example, the set of Pareto designs may be filtered to a smaller set of ε-filtered designs. The size of the set of P-filtered designs may be adjusted, e.g., made larger or smaller, by selecting the value of ε. In some cases, ε may be selected to be about 0.001, and/or about 0.055, and/or about 0.15. The ε-filtered designs may remove designs that are within ε-distance of another design. In some cases, the ε may be selected such that the number of ε-filtered designs is less than a predetermined and/or desired number such as one hundred (100), ten (10), or less than ten (<10). The ε-filtering may be performed with respect to performance parameters, design parameters, scenario parameters, and the like. In embodiments, ε-filtering may reduce the number of designs recommended to a user, and may increase the range or variety of designs that are recommended to a user by eliminating designs that are close to one another. In embodiments, ε-filtering may reduce clutter on a user interface and/or the number of computations performed.
[0400] In some embodiments, ε-filtered designs may be recommended and/or evaluated by a user to determine if the set includes designs with design criteria that are desirable. When a design from the ε-filtered designs is selected, the Pareto designs that were ε-filtered may be provided to the user for further evaluation. The ε-filtered designs may have similar design criteria to the selected design but may relate to different types of designs. The user may evaluate different design types and design options that are within ε of the desired/selected design criteria.
[0401] Pareto analysis often requires new configurations and considerations when applied to clinical trial design optimization. In one aspect, clinical trial simulation (CTS) data is usually different from data in other applications. For example, in many other applications, points in criterion space are continuous or form a lattice while, in the current application, points correspond to discrete designs. In many other applications, there may be a very large number of points on the Pareto frontier and the focus may be to produce a handful of well spread out points on the Pareto frontier for a decision-maker to study closely to determine and/or select the best solution. CTS data, on the other hand, is typically highly clustered in certain regions of criterion space with substantial parts of the space being empty due to practical limits and constraints, e.g., continuous adaptation after each subject) and/or due to there being a handful of design types for a particular trial (fixed SS, SSR, Group Sequential, tailored innovative designs and the like).
[0402] Pareto analysis for the clinical trial optimization applications may be designed to cluster dominated designs into Pareto clusters and provide an input consisting of only Pareto designs to convex hull algorithms in preparation for creating convex hull clusters with a simple geometrical structure in the criterion space. Additional unique aspects, of some embodiments, include a focus on interactive clinical trial simulations linked with visualizations of performance criteria space, design factors space, and/or scenarios. Links between Pareto designs and close but dominated designs may be generated as a byproduct of finding the Pareto set. Dominated designs may be preferred for qualitative reasons (e.g., complexity in trial execution, sensitivity to extreme

downside scenarios). Pareto points that are close to other points may be automatically suppressed in a corresponding visualization (e.g., because they are unimportant due to being in the area within the margin of model error). Dominated designs can be unmasked when needed (e.g., when the designs are qualitatively different). Hierarchical level two (2), level three (3), etc. Pareto sets may be generated by rerunning the analysis. In embodiments, the analysis may accommodate constraints on design parameters, and dynamically updating the Pareto set by removing designs, adding new designs and scenarios, and/or changing prior probabilities of scenarios. In embodiments, the analysis may be applied in stages to first find Pareto points in clusters of similar design sets (e.g., changes of one parameter change, qualitatively different). In embodiments, the analysis may be useful for gaining insight into design improvements. In embodiments, clustering points in design space distances are natural and may be efficient for users to gain insights. In embodiments, the analysis may be integrated with a simulated annealing engine that uses weights and/or target criteria points in unexplored regions.

[0403] Pareto analysis may provide for organization and/or analysis of data that is comprehensible and/or provides for a focus to designs that are optimal or near-optimal. The Pareto analysis may determine the hierarchies of design sets for consideration. In embodiments, one set in the hierarchy may be ε-filtered Pareto designs, another may be all Pareto designs, and/or another hierarchy may be designs that are within ε of the Pareto designs. The design space may be explored using the hierarchies to find designs that have the desired criteria and further to find designs that achieve the desired criteria with desired or acceptable design types.

[0404] In embodiments, Pareto analysis may be a two-pass analysis. In the first pass, the simulation records (e.g., summary records) may be sorted by maximum and/or minimum values of the performance parameters. Various sorting algorithms (including those described herein) may be used. In the second pass, after the records are sorted, each record may be compared with all the records that follow in the ordered set to identify which records are ε-dominated by the record. After the second pass, the algorithm may provide a set of Pareto designs which are not ε-dominated by any other design and/or Pareto clusters of dominated designs linked to one-or-more Pareto designs. If $\varepsilon=0$ for all performance criteria, then the full set of Pareto designs may be produced. If $\varepsilon>0$ for some performance criteria, then the set of ε-filtered Pareto designs may be produced, which is a subset of the full set of Pareto designs since some of the Pareto designs from the full set may be ε-dominated by other Pareto designs.

[0405] FIG. **49** shows aspects of the Pareto analysis using numerical examples. As shown in FIG. **49**, each row in the table represents a design with the performance parameter values listed in the columns. In the depicted example, all of the designs are Pareto designs identified by a unique "PSet" number. In the first pass of the algorithm/engine, the P-designs are sorted, and the designs with the highest power, the lowest cost, and the lowest duration are determined (PSet 1, 2, 3, respectively). In the second pass, the top three (3) P-designs (PSet 1, 2, 3) are compared to all remaining designs according to the selected ε for each performance parameters. Based on the values of ε, some of the remaining designs may be classified dominated by one of the first three (3) P-designs. As further shown in the example of FIG. **49**, PSet 7, 13, and 19 are determined to be dominated by PSet 1 for the ε values chosen (denoted by "−1" in the EPSet column). The algorithm may proceed to the next Pareto design after all the ε designs for the first Pareto design were determined. The next Pareto design considered may be a design that has not been identified as ε-dominated design. In this example, PSet 2 is next determined to dominate PSet 8, 11, 17, and 20 designs (denoted by "−2" in the EPSet column). The analysis may proceed to iteratively process all the Pareto designs that are not dominated by other designs to determine the set of ε-filtered Pareto designs. In this example, the ε-filtered Pareto designs (designs denoted by positive numbers by the EPSet column) are a subset of the Pareto designs and includes nine (9) designs. The algorithm may be iterated multiple times, and some designs may be dominated by more than one Pareto design.

[0406] In embodiments, the ε-filtered Pareto designs may be used for initial recommendations and/or consideration for users. The designs dominated by each ε-filtered design may be further recommended or provided for consideration when a design from the ε-filtered set if selected for further analysis by a user.

[0407] In embodiments, the Pareto analysis may be configured to quickly update the identified Pareto designs when new designs are introduced as inputs to the algorithm. The set of identified Pareto designs may be augmented incrementally by the algorithm as new designs are identified/simulated and added to the design space.

[0408] FIG. **50** shows aspects of an apparatus for determining globally optimum designs using Pareto analysis. In embodiments, the Pareto analysis component **5002** may be part of the analysis facility **108** of the platform **104**. The Pareto analysis component **5002** may receive data from simulated designs **5012** and determine one or more sets of optimal designs **5022** which may include Pareto designs **5024**, dominated designs **5026** (designs that are dominated by Pareto designs), ε designs **5028** (designs that are within a distance ε of Pareto designs). The Pareto analysis component **5002** may include one or more circuits for determining recommended designs. The circuits in the Pareto analysis **5002** may be selectively enabled according to user input **5020**, ε values **5014**, and other inputs. In embodiments, the Pareto analysis component **5002** may include circuits for determining Pareto optimality using Pareto algorithms **5030**. In embodiments, the Pareto analysis component **5002** may include circuits for determining optimality using ε filtering **5004**. Epsilon filtering circuit **5004** may determine designs that are within epsilon of Pareto designs. The Pareto analysis component **5002** may include Pareto level analysis circuit **5032**. Pareto level analysis circuit **5032** may determine one or different levels of Pareto designs and Pareto frontiers. In embodiments, the Pareto analysis circuit **5002** may include circuits for dominated designs analysis **5006**. Dominated designs analysis circuit **5006** may identify designs that are dominated by one or more Pareto designs and filter the designs and/or recommend the designs according to user input **5020** and/or epsilon values **5014**. In embodiments, the Pareto analysis circuit **5002** may include circuits for twins/siblings analysis **5008**. Twins/siblings analysis circuit **5008** may identify designs that are twins and/or siblings to one or more Pareto designs and filter the designs and/or recommend the designs according to user input **5020**. In embodiments, the Pareto analysis circuit **5002** may include circuits for clustered design analysis **5010**. Clustered design analysis circuit **5010** may identify designs that are clustered with one or more Pareto designs and filter the designs and/or recommend the designs according to user input **5020**.

[0409] FIG. **51** shows aspects of an apparatus for determining global optimality of designs. In embodiments, the apparatus may include an optimality analysis circuit **5116** which may be part of the analysis facility **108** of the platform **104**. In embodiments, the apparatus may include a data processing circuit **5108** structured to interpret/obtain design data **5102** of a clinical trial design. In some embodiments the design data **5102** may be outputs of simulation data of trial designs. The output processing circuit **5108** may transform the design data **5102** into a format suitable for use by the various circuits in the apparatus. For example, the design data **5102** may be received by the data processing circuit **5108** and determine and identify performance parameters in the data. In some embodiments, some performance parameters may be grouped, filtered, converted, normalized, and the like.

[0410] The apparatus of FIG. **51** may further include an optimality determining circuit **5110** structured to receive processed design data from the data processing circuit **5108**. The optimality determining circuit **5110** may identify globally optimum designs **5114** based on Pareto analysis. In some embodiments, the globally optimum designs **5114** may be provided as an output of the apparatus. In some embodiments, globally optimum designs **5114** may be further processed by the design analysis circuit **5112**. The design analysis circuit **5112** may analyze the globally optimum designs **5114** and determine characteristics of the designs, receive feedback data **5104** about the designs. The design analysis circuit may, based on the determined characteristics determine modifications for optimality criteria used in the optimality determining circuit **5110**. The optimality determining circuit **5110** may modify optimality criteria of Pareto analysis. The modifications may include epsilon filtering of Pareto designs, determining multiple levels of Pareto designs, clustering of Pareto designs, determining dominated Pareto designs, and/or the like. Using modified optimality criteria, the optimality determining circuit **5110** may determine a new set of globally optimum designs **5114**.

[0411] As shown in FIG. **52**, a method for determining optimum designs using Pareto analysis may include obtaining trial design simulations **5202**. The method may further include determining one or more score for each trial design based on the performance parameters **5204**. The method may include evaluating Pareto optimality for each design to determine Pareto frontier **5206**. Designs not on the Pareto frontier may be filtered **5208**. Designs on the Pareto frontier may be presented for further analysis **5210**.

[0412] As shown in FIG. **53**, a method for determining optimum designs using Pareto analysis may include obtaining trial design simulations **5302**. The method may further include evaluating optimality for each design using Pareto analysis **5304**. The method may include identifying optimal designs based on the Pareto analysis **5306**. The optimum designs may be evaluated **5308**. Evaluation may include feedback from user, statistical analysis, and the like. Based on the evaluation, the Pareto analysis may be modified **5310**. Modifications may include determining epsilon-distance designs, clustering, determining second level Pareto designs, filtering sibling and twin designs, and the like.

[0413] In embodiments Pareto analysis includes consideration of performance **5016** (FIG. **50**), design, scenario, and criteria **5018** (FIG. **50**) spaces. Pareto optimality is determined with respect to performance parameters of the performance space. The performance parameters may be evaluated using simulation for different designs defined by the design space. Each design in the design space is evaluated for different scenarios of the scenario space. The performance, design, and scenario spaces are defined according to the criteria space definitions.

[0414] In embodiments, analysis of design options may include convex hull (CH) analysis. A convex hull analysis may be used for algorithmic generation of design recommendations. Convex hull analysis may be used to determine one or more designs that are on a convex hull (also referred herein as convex hull designs or CH-designs). Initial selections of a set of candidates for best or optimal designs may be selected using a convex hull that is generated with convex hull analysis. Convex hull analysis may determine the smallest convex polygon shape that contains the designs.

[0415] Referring again to FIG. **1**, the filtering component **120** may include convex hull analysis. The filtering component **120** may include circuits, components, and algorithms for enabling convex hull analysis. The filtering component **120** may receive simulation data from the simulation facility **110** and analyze the simulated data to identify one or more designs using convex hull analysis techniques. The identified designs may be recommended to a user.

[0416] FIG. **54** shows a graphical representation of aspects of convex hull analysis. FIG. **54** shows a graph with points wherein each point corresponds to a trial design. The graph shows the performance of each trial design with respect to two trial design parameters (power and minimum study cost) that may have been determined by simulation. For these two performance parameters, the higher the number the more desirable. Points in the top right quadrant of the graphs relate to designs with the more desirable performance parameter values. In the example, convex hull analysis is used to determine CH-designs. The convex hull is a line **5404** and CH-design are vertices of the line **5404**. The convex hull contains or envelopes the other designs.

[0417] In embodiments, convex-hull designs are a subset of Pareto designs. They are often a fraction of the size of the set of Pareto designs. An important property of convex-hull designs is that they are that can be optimal with respect to a performance criteria that is a linear weighted criterion of the components of the multivariate performance parameters.

[0418] The convex hull of design may be computed for a subset of all the trial designs. In some cases, the convex hull may be computed for trial designs that have at least a threshold value for one

or more performance parameters.
[0419] In embodiments, various algorithms/engines may be used to compute convex hull points and may include brute force, gift wrapping, Graham scan, Jarvis, QuickHull, Qhull algorithms/engines, and/or the like. Computation of the convex hull of the designs may include additional data such as facet area and volume of the hull, facet normal vectors (weights for which the facet is optimal). Additional outputs may include triangular facets (such as Delaunay) or polygon (polyhedral) facets. In embodiments, outputs related to the facet area may be indicative of the number of designs from the CH-designs that are in the design space. Large facet areas may indicate that there are few design options in the design space area of the facet. Facet area information may be used as a basis for the exploration of the design space using simulated annealing algorithms/engines and/or the like.
[0420] In embodiments, CH-designs may be identified as desirable or optimum designs and the CH-designs may be recommended to a user. In some embodiments, CH-designs may be identified as initial globally optimum designs and they may be used to refine the optimality criteria to identify other globally optimum designs for the new criteria. In some embodiments, interactive methods can be used in which a person or an alternate algorithm acts as a decision-maker and interacts with the method to indicate a preference for designs (such as preference among initial CH-designs), and the method may use the preference information to determine other trial designs (and modify optimality criteria) based on the preference of designs. In embodiments, the CH-designs can be used to elicit the user's preferences by interactively querying the user to make comparisons between designs.
[0421] Trial designs that are on or near the convex hull may be selected as initial choices for evaluation by a user. One or more of the designs may be presented to a user to evaluate and provide feedback. Feedback may include data related to acceptance of the trial design, rejection of the trial design, identification of one or more parameters or features of the trial design, and the like. In an embodiment, the one or more trial designs from the convex hull may be presented to a user using the card, tornado, heatmaps, and similar interfaces described herein.
[0422] Convex hull analysis may output two or more sets of designs and may include the convex hull designs and clustered convex hull designs (such as designs that are non-reachable by weighting criteria). The sets of designs determined by convex hull analysis may represent a hierarchy of designs for recommendation and/or consideration by a user. The convex hull designs may be the first in the hierarchy and may be the first designs to be recommended or provided for consideration. The clustered convex hull designs may be below the convex hull designs on the hierarchy of designs for recommendation and/or consideration. The clustered convex hull designs may be provided for recommendation and/or consideration after the set of convex hull designs or if no designs in the set of convex hull designs are acceptable to a user. In some cases, the set of clustered convex hull designs may be larger than the set of convex hull designs.
[0423] Convex hull analysis may be configured to separate CH-designs that are have equal or nearly equal performance parameters or observables such as cost, power, and/or duration. In embodiments, designs that are within an ε-box of a design may be designs that are within a ball of radius P from a design. Designs that are twins or siblings may be flagged or marked for further analysis if they are deemed to have desired performance as the twins or siblings may represent different design options that can be used to achieve similar performance criteria.
[0424] CH-designs may be grouped, and one or more other designs that are within ε of a CH-design design may be represented by one CH-design. The size of the set of ε-filtered designs may be larger or smaller by selecting the value for ε. In some cases, ε may be selected to be 0.001, and/or 0.055, and/or 0.15.
[0425] Convex hull analysis for the clinical trial optimization applications may be designed to cluster dominated designs into convex hull clusters (CH-clusters). In embodiments, the analysis may accommodate constraints on design parameters, and dynamically updating the CH-design by removing designs, adding new designs and scenarios, and/or changing prior probabilities of

scenarios.

[0426] Convex hull analysis may provide for organization and/or analysis of data that is comprehensible and/or provides for a focus to designs that are optimal or near-optimal. The convex hull analysis may determine the hierarchies of design sets for consideration. In embodiments, one set in the hierarchy may be CH-design, another may be clustered CH-designs. In some embodiments, on CH-design hierarchy level may be the initial CH-designs.

[0427] The next hierarchy level may be CH-designs that are determined when the initial CH-designs are not deleted and so on. Platform may drill down into the hierarchies when initial levels do not provide acceptable designs.

[0428] In embodiments, inputs to convex hull analysis may include simulated trial designs. In some embodiments, inputs may be P-designs determined by the Pareto algorithm/engine. In some embodiments, the inputs may be a set of trial design simulation records from a simulation database. Inputs may further include levels of minimum meaningful difference for performance parameters (ε1, ε2, 3, . . .) specified by users or default values that are fixed or dynamic (data dependent). The values for (ε1, ε2, 3, . . .) may depend on the stage of design exploration (e.g., larger values in early stages and smaller values in later stages, when more accurate information has been obtained), user perspective/choice, and/or the like. In some cases, inputs may include upper and lower bounds for each performance parameter value.

[0429] FIG. **54** shows a graphical representation of aspects of convex hull analysis. In embodiments, outputs of convex hull analysis may include the set of convex hull designs (designs on vertices CH1, CH2, CH3, CH4, CH5). In the case where the inputs were Pareto designs, CH-design may be a subset of the Pareto designs. In the figure, Pareto designs correspond to vertices of line **5502** (FIG. **55**) (the Pareto frontier). Some vertices of the Pareto frontier correspond to the CH-designs (such as CH2 and CH3). In embodiments, outputs may further include clusters of P-designs for each convex hull facet (CHF), e.g., (CHF12, CHF23, CHF45) of the convex hull. Clusters may be determined by a right triangle formed by the ends of each facet forming convex hull facet clusters (CHF clusters). Convex hull facet clusters may be non-overlapping (i.e., each P-design belongs to exactly one CHF cluster). Each CH-design may be at the intersection of several facets so CHF clusters can be combined into a convex hull Pareto cluster (CHP cluster) for each CH-design. CHP clusters may be overlapping. As will be appreciated, this may provide a decomposition for the global problem of optimization into smaller local problems defined for a CHF or CHP clusters.

[0430] In embodiments, outputs of convex hull analysis may include facet area, volume of the hull, facet normal vectors (weights for which the facet is optimal). In embodiments, facet area, volumes of the hull, and normal vectors may be used by search algorithms such as simulated annealing to determine search trajectories and parameters. In embodiments convex hull analysis may be parallelized. Input designs may be partitioned into two or more sets and a CH-designs may be determined for each set in parallel. The CH-designs of each set may be combined and overall CH-designs may be determined. In some embodiments, convex hull analysis may support batch updating in collaborative environments.

[0431] FIG. **56** shows aspects of an apparatus for determining designs using convex hull analysis. In embodiments, the convex hull analysis component **5602** may be part of the analysis facility **108** of the platform **104**. The convex hull analysis component **5602** may receive simulated design data **5612** (which may include just P-designs from Pareto analysis) and determine one or more sets of optimal designs **5622** which may include CH—(designs that are within a distance epsilon of CH-designs). The convex hull analysis component **5602** may include one or more circuits for determining recommended designs. The circuits in the convex hull analysis component **5602** may be selectively enabled according to user input **5620**, epsilon values **5614**, and other inputs. In embodiments, the convex hull analysis component **5602** may include circuits for determining convex hull optimality using convex hull algorithms **5630**. In embodiments, the convex hull analysis component **5602** may include circuits for determining optimality using epsilon filtering

5604. Epsilon filtering circuit **5604** may determine designs, e.g., **5628**, that are within epsilon of CH-designs. In embodiments, the convex hull analysis circuit **5602** may include circuits for dominated designs analysis **5606**. Dominated designs analysis circuit **5606** may identify designs that are dominated by one or more CH-designs and filter the designs and/or recommend the designs according to user input **5620** and/or epsilon values **5614**. In embodiments, the convex hull analysis circuit **5602** may include circuits for twins/siblings analysis **5608**. Twins/siblings analysis circuit **5608** may identify designs that are twins and/or siblings to one or more CH-designs and filter the designs and/or recommend the designs according to user input **5620**. In embodiments, the convex hull analysis circuit **5602** may include circuits for clustered design analysis **5610**. Clustered design analysis circuit **5610** may identify designs that are clustered, e.g., **5626**, with one or more CH-designs and filter the designs and/or recommend the designs according to user input **5620**.

[0432] FIG. **57** shows aspects of an apparatus for determining global optimality of designs using convex hull analysis. In embodiments, the apparatus may include an optimality analysis circuit **5716** which may be part of the analysis facility **108** of the platform **104**. In embodiments, the apparatus may include a data processing circuit **5708** structured to interpret/obtain design data **5702** of a clinical trial design. In some embodiments the design data **5702** may be outputs of simulation data of trial designs. The output processing circuit **5708** may transform the design data **5702** into a format suitable for use by the various circuits in the apparatus. For example, the design data **5102** may be received by the data processing circuit **5708** and determine and identify performance parameters in the data. In some embodiments, some performance parameters may be grouped, filtered, converted, normalized, and the like. The apparatus of FIG. **57** may further include an optimality determining circuit **5710** structured to receive processed design data from the data processing circuit **5708**. The optimality determining circuit **5710** may identify designs **5714** based on convex hull analysis. In some embodiments, the designs **5714** may be provided as an output of the apparatus. In some embodiments, designs **5714** may be further processed by the design analysis circuit **5712**. The design analysis circuit **5712** may analyze the designs **5714** and determine characteristics of the designs, receive feedback data **5704** about the designs. The design analysis circuit may, based on the determined characteristics determine modifications for optimality criteria used in the optimality determining circuit **5710**. The optimality determining circuit **5710** may modify optimality criteria of convex hull analysis. The modifications may include epsilon, e.g., **5706**, filtering designs, determining multiple levels of CH-designs, clustering of designs, determining dominated CH-designs, and the like. Using modified optimality criteria, the optimality determining circuit **5710** may determine a new set of designs **5714** which may be recommended to a user.

[0433] As shown in FIG. **58**, a method for determining optimum designs using convex hull analysis may include obtaining trial design simulations **5802**. The method may further include determining one or more scores for each trial design based on the performance parameters **5804**. The method may include the convex hull for the designs **5806**. Designs not on the convex hull may be filtered **5808**. Designs on the convex hull may be presented for further analysis **5810**.

[0434] As shown in FIG. **59**, a method for determining optimum designs using convex hull analysis may include obtaining trial design simulations **5902**. The method may further include evaluating the designs to determine a convex hull **5904**. The method may include identifying optimal designs based on the convex hull **5906**. The optimum designs may be evaluated **5908**. Evaluation may include feedback from user, statistical analysis, and the like. Based on the evaluation, aspects of the convex hull analysis may be modified **5910**. Modifications may include determining epsilon-distance designs, clustering, determining second level CH-designs, and the like. New optimal designs may be identified using the modifications to the convex hull analysis.

[0435] In embodiments convex hull analysis includes consideration of performance **5616** (FIG. **56**), design, scenario, and criteria **5618** (FIG. **56**) spaces. Convex hull may be determined with respect to performance parameters of the performance space. The performance parameters may be evaluated using simulation for different designs defined by the design space. Each design in the design space is evaluated for different scenarios of the scenario space. The performance, design, and scenario spaces are defined according to the criteria space definitions.

[0436] In embodiments, the platform **104** may be configured to explore different scenarios and perform "what if" analysis. The platform may be configured to automatically or semi-automatically explore the robustness of different designs. Trial designs may be evaluated, for example, respective to a range of treatment effects. As depicted in FIG. **29**, a trial design may be evaluated to determine the outcomes of the trial based on whether the treatment effect is optimistic, base, or pessimistic, for example. In some embodiments, the analysis may include changes to assumptions of the trial to determine how a change in assumptions may change the usefulness of the trial.

[0437] In embodiments, the platform may further provide additional sensitivity analysis for designs. Models and designs may include assumptions about behaviors, parameters, and the like of a study. Sensitivity analysis may be used to determine behavior or trial designs in view of perturbations and variations in the model assumptions and/or parameters. Sensitivity analysis may be used to determine the robustness of designs. In some embodiments, the robustness of designs provides for a measure of what variations of assumptions a design can tolerate and still provide a useful result.

[0438] In embodiments, designs may be scored or evaluated based on multiple criteria. In some cases, a series of different tests that evaluate a sensitivity, robustness, and/or risk associated with a design may be computed. In some cases, an overall composite score that takes into account the multiple tests that can be computed.

[0439] FIG. **60** shows aspects of sensitivity analysis. In some embodiments, the separation of trial design inputs and scenario inputs, as described herein, may enable efficient sensitivity analysis. In embodiments, a framework for sensitivity analysis may compare how different combinations of design choices and scenarios affect performance criteria. In one embodiment, a vector of scenarios (SV.sub.1 . . . SV.sub.j . . . SV.sub.57) may be arranged against each combination of designs (DV.sub.1 . . . DV.sub.i . . . DV.sub.1120). For each combination of a designs and scenario (SV.sub.i DV.sub.i combination) performance parameters may be determined, such as by simulating the design and scenario combination. In embodiments, for each combination of a design and scenario, a weighted sum of performance parameters may be determined from simulation data. The arrangement of combinations and a weighted sum of performance criteria may provide for a measure of how performance parameters for each design change or are affected by variations in scenarios. Each row of the table shown in FIG. **60**, when populated with simulation data, would show how performance parameters (or a function of the performance parameters) change over the scenarios. Each row of the table may show for which scenarios and/or what values of scenarios results in acceptable levels of performance (such as performance values above a threshold value). In embodiments, a span of acceptable parameter values may be related to the robustness or sensitivity of the design. In embodiments, a span may be the number of scenarios for which a design or a design parameter generates acceptable parameter values. In embodiments, a span may be a range of scenario parameter values a design or a design parameter that generates acceptable parameter values. In embodiments a larger span may be associated with a higher robustness of a design (i.e. the design or design parameter results in an acceptable performance for many scenarios). In embodiments, robustness may be a function of a span and probabilities associated with each scenario (Pr.sub.1 . . . Pr.sub.j . . . Pr.sub.57).

[0440] In embodiments robustness and/or sensitivity of a design and/or design parameters may be determined by determining design and scenario performance parameters as depicted in FIG. **60**. The performance parameters may be evaluated via simulation. In some cases, simulations may be exhaustive such that each design scenario combination may be simulated to determine performance parameters. In some embodiments, only a partial set of designs and/or scenarios may be simulated. Based on the simulation the robustness and/or sensitivity of each design may be determined across all the scenarios or a partial set of the scenarios. The results of the robustness and/or sensitivity analysis may be provided to a user via tables, lists, and/or interactive interfaces such as tornado diagrams described herein. For example, tables and visual interfaces may provide information about the performance of a design over various scenarios. The interfaces may provide information regarding how close the performance of each design was to an acceptable threshold for each scenario or a subset of scenarios. The data may be used to get a more complete view of the risks associated with a design and possibilities to reduce the risks. The data may be used to infer or calculate the robustness, risk, and/or potential costs associated with a design. The data may be used to reduce the risk or and/or potential costs associated with a design. For example, in some cases, probability of some scenarios may be reduced or eliminated with inexpensive or common precautions or risk mitigation techniques. A user or the platform may identify scenarios for which a performance of a design was below a threshold and analyze or prompt the user to analyze possible mitigation techniques. If inexpensive mitigation techniques are possible the some negative scenarios for a design may be removed from robustness evaluations.

[0441] In some embodiments, a Pareto analysis may provide for a measure of robustness for designs. In embodiments, the Pareto analysis may be used to determine Pareto optimal designs. As described herein, Pareto optimal designs may define the Pareto frontier. In embodiments, robustness of Pareto designs may be determined based on the separation between Pareto designs.

[0442] FIG. **61** shows aspects of measuring the robustness of the design based on Pareto analysis. The table FIG. **61** shows data for seven (7) Pareto designs determined for a set of simulated designs for one performance criteria of probability of technical success (PoTS). For each design, a PoTS weight can be determined. The PoTS weight indicates the interval of PoTS for which each design is optimal according to the Pareto analysis. For example, design with DesignID “88” is optimal from a PoTS value of 0.022 to 0.274 (corresponding to 2.2% and 27.4% respectively). The range of optimality for design “88” is, therefore, 0.252 (25.2%). In another example, design with DesignID “96” is optimal from a PoTS value of 0.274 to 0.857 (corresponding to 27.4% and 85.7% respectively). The range of optimality for design “96” is, therefore, 0.583 (58.3%). The ranges of optimality of the performance parameter are shown in the graph of the figure. The size of the bar in the graph indicates the range for the performance parameter that each design is optimal for. The designs with the largest ranges of optimality (the most robust designs), such as designs with Design IDs “88” and “96”, may make good candidates for recommendation by the system. These designs with the largest range of optimality provide the designs that are typically most likely to be selected by a user, such as a decision-maker selecting the study. For example, in the case of the design corresponding to Design ID “96”, if two or more decision-makers had different weight preferences for PoTS, as long as their preferences were between 0.274 and 0.857, they would all prefer design “96” above all other designs. In the selection of the designs to recommend, unless there are other factors that would dictate a bias towards the importance of one or more criteria, selecting the most robust designs is often a good starting point for analysis and design recommendation. In some cases, Pareto analysis of simulations may result in a large number P-designs for initial consideration. In some cases, initial suggestions of P-designs may be limited to the most robust P-designs.

[0443] In embodiments, robustness and/or sensitivity may be defined with respect to types of scenarios. In embodiments, scenarios may be categorized based on properties of the scenarios such as their probabilities. In one example, scenarios may be categorized into four (4) types of scenarios: Optimistic, Base, Pessimistic, Very pessimistic. In embodiments, a performance score for a design or design parameters may be determined for each scenario. The scores for each scenario may be used to determine a composite score for each type of scenario (by computing an average for example). A composite score may provide a measure of robustness. The score may provide a measure of a performance for a design for scenarios that are likely to happen, unlikely to happen, and the like. Robustness may be determined based on the number of scenario categories for which a design exhibits acceptable performance. For example, designs that have acceptable performance for scenarios that are only likely to happen may not be considered robust, while designs that have acceptable performance for scenarios that likely to happen and unlikely to happen may be considered robust.

[0444] Referring to FIG. **1**, the analysis facility **108** of the platform **104** may include robustness and sensitivity analysis. The analysis facility **108** may include circuits, components, and algorithms for enabling robustness analysis. The analysis facility **108** may receive simulation data from the simulation facility **110** and analyze the simulated data to identify robustness of designs. The identified designs may be recommended to a user.

[0445] FIG. **62** shows aspects of an apparatus for determining robustness of designs. In embodiments, the apparatus may include a robustness analysis circuit **6216** which may be part of the analysis facility **108** of the platform **104**. In embodiments, the apparatus may include an output processing circuit **6206** structured to interpret/obtain design data **6202** of a clinical trial design. In some embodiments the design data **6202** may be outputs of simulation data of trial designs. The design data may include simulation data for designs for various scenarios. The output processing circuit **6206** may transform the design data **6202** into a format suitable for use by the various circuits in the apparatus. The apparatus of FIG. **62** may further include an evaluation circuit **6208** structured to receive processed design data from the output processing circuit **6206**. The evaluation circuit **6208** may identify robustness **6220** and/or robust designs **6218** based on analysis of performance for designs for different scenarios. In some embodiments, the robustness analysis circuit **6216** may include a Pareto robustness determining circuit **6210**. The Pareto robustness determining circuit **6210** may determine Pareto designs from the design data **6202** and determine robustness for the Pareto designs based on the separations of the Pareto designs. The robustness and/or sensitivity of the designs may be compiled into a graphical interface such as a tornado diagram using the graphic generation circuit **6212** and may be provided to a user with the graphic provisioning circuit **6214**.

[0446] As shown in FIG. **63**, a method for determining robustness of designs may include receiving outputs of a plurality of design simulations for a plurality of scenarios **6302**. The method may further include evaluating the outputs to determine changes in performance for the designs over the plurality of scenarios **6304**. The method may also include providing a visual depiction of a tornado diagram to visualize the differences **6306**.

[0447] As shown in FIG. **64**, a method for determining robustness of designs may include receiving outputs of a plurality of trial design simulations for a plurality of scenarios **6402**. The method may further include evaluating the outputs to determine Pareto designs **6404**. The method may also include evaluating the range of optimality for each Pareto design **6406** and determining a score for each Pareto design based at least in part on the range of optimality **6408**. The method may include recommending Pareto designs above a threshold score **6410**.

[0448] In some embodiments, one or more optimization algorithms may be used to explore the global design space or a localized subspace of possible designs. Simulated annealing algorithms may be used to explore a subspace of possible designs. In some embodiments, simulated annealing may be used to explore the design space around an initial selected trial design to determine if there are any additional design options near the selected design that provide an improvement to one or more criteria, e.g., **6204** (FIG. **62**), or parameters. Simulated annealing may reduce the number of designs that are simulated while providing high confidence that optimum or near optimum designs are determined.

[0449] In embodiments, design simulations may be non-exhaustive and the platform may simulate a partial set of possible design options. When a partial set of possible design options for a design criteria is simulated best/optimal designs may be missed. When only partial set of design options has been simulated, designs of interest (such as designs with the best and/or optimal performance for the set of simulated designs) may be identified (such as by a user or by other components of the platform), simulated annealing may be used to search for additional designs that may have similar or better performance than the designs of interest. In embodiments, when only a partial set of design options has been simulated, regions of interest (such as regions of the performance space that are identified as having designs of interest) may be identified (such as by a user or by other components of the platform), simulated annealing may be used to search for additional designs that may have similar or better performance than the designs of interest.

[0450] Simulating annealing of trial designs may involve an initial starting design and iterations that consider neighboring design options. Adaptive logic may be used to move the system between different neighboring design options. Adaptive logic may control which parameters of the design options are modified, how much they are modified, conditions for taking different paths, conditions for retreating towards the initial design, conditions for cooling schedules, and the like. Adaptive logic may predict which parameter modification may results in an improvement in performance compared to the initial design. In embodiments, predictions may be based on historical data. Previous simulation data may be used to generate ML and/or AI models to predict the effects of changes of design on performance. For each modification from the initial design, the design modification may be simulated to determine the performance of the design to determine if the modification resulted in an improved design option. Changes in performance may be used by the control logic to determine the path of exploration and other parameters of simulated annealing.

[0451] Referring to FIG. **1**, the search/exploration component **130** of the simulation facility **110** of the platform **104** may include components for simulated annealing. The search/exploration component **130** may include circuits, components, and algorithms for enabling simulated annealing. The search exploration component **130** may interact with the models **126** and engines **128** components to explore design space. In embodiments the analysis facility **108** may provide analysis data to simulated annealing components to identify designs or regions of interest. The search/explorations component **130** may use simulated annealing to determine designs around designs of interest and/or in or around regions of interest and simulate the designs. The analysis facility **108** may provide analysis of the simulated designs to determine parameters (such as cooling cycles, parameter changes, directions, and the like) for simulated annealing.

[0452] In embodiments, simulated annealing may be used in a workflow where initial design simulations are selected to provide a coarse representation/overview of the performance space of the design options. The coarse representation may be used to identify designs or regions of the performance space, scenario space, and/or design space of interest. The designs or regions of interest may be used as initial starting points for simulated annealing to search for designs near the identified designs or in the regions of interest that have improved performance compared to the initial designs. In some embodiments, initial coarse design simulation may represent 50% or 30% or less of the total design options for a criteria. The use of coarse initial design simulation may reduce initial simulation time and resources. In embodiments, the designs of interest or the regions of interest from the initial simulations may be determined by a user via user interface. In embodiments, the designs of interest or the regions of interest from the initial simulations may be determined by other elements of the system. For example, designs of interest that can be identified using Pareto analysis, convex hull analysis, and the like. Simulated annealing may be used to fill in gaps between initial simulated designs.

[0453] In embodiments, simulated annealing analysis may be configured to fill gaps in a convex hull within a CHP cluster. Simulated annealing may be configured to reduce simulation runs required by the Cartesian product approach. Simulation may start with a coarse cartesian grid (or replications of trials of random samples of designs randomly, possibly stratified) as input and incrementally develop P-designs and CH-designs that are identical or close to the P-designs and CH-designs of the full Cartesian sample using simulated annealing.

[0454] Simulated annealing may be configured to find designs that are optimal for given weights or a design that is nearest in performance to specified desired criteria. In some embodiments, the simulated annealing may use a weighted sum of squares or of absolute differences as the distance from the desired point to iterate to a design if there is a feasible design in a specified elliptical or box neighborhood around the point. The simulated annealing may be configured to use starting points that are designs closest to designs that are in the criteria space. In embodiments, the simulated annealing algorithm/engine may explore the design space around a criteria by exploring the effects of altering parameters of a design. Simulated annealing may be configured to explore all the parameters of a design or preferentially manipulate or explore a subset of the parameters. In some embodiments, users may specify preferences with respect to which parameters to prioritize for the exploration using simulated annealing. In some cases, the user may specify which directions the simulated annealing should explore the design space. The constraints may be based on which areas of the design space already have many designs, for example. In embodiments, historical data related to simulated annealing search may be used to prioritize one or more design parameters for the search using the algorithm.

[0455] In embodiments, inputs to simulated annealing may include a weight vector for criteria, an objective function specification (e.g., normal vector for CHFs), design variable ranges (discretized) numeric or categorical, design simulation engines (with control of a number of simulations and in future feedback of intermediate results as engine decreases replications at inferior designs to exploit simulation efficiency), engines for design simulations or other engines equipped with interfacing wrappers, set of starting designs from which simulated annealing will iteratively attempt to improve using probabilistic search. Inputs may further include cooling schedules with defaults, constraints on design variables (e.g., upper and lower bounds, rules of inadmissible combinations and the like). In embodiments, outputs may include parameters and criteria values for best design found, best design for each start, visualization of paths, cooling schedules, visualization through parallel designs interface, and the like. The output of the simulated annealing analysis may be used to update the set of CH designs and P-designs. The simulated annealing analysis may be configured and/or modified using one or more interactive interfaces (such as from feedback from card interface, heatmap interface, tornado diagram interface).

[0456] In some embodiments, a simulated annealing algorithm/engine may be configured for multicriteria objectives where no weights for performance criteria are specified and the algorithm/ending may search for Pareto points directly. In some embodiments, the simulated annealing algorithm/engine may start a search with P-designs and/or siblings of P-designs. In embodiments, the simulated annealing algorithm/engine may be parallelized. Parallelization may be configured based on convex hull facets and/or different data sets which can be computed in parallel. In embodiments, the simulated annealing algorithm/engine may include bounds and/or improvement cut-off criteria in the search. In embodiments, the simulated annealing algorithm/engine may use a flexible grid structure and may use different step sizes when exploring the design space. In embodiments, the step/grid size may be initially coarse (relatively large steps) and set to finer logic (relatively smaller steps) as the design space is explored. In embodiments, search algorithms/engines may include genetic and/or integer programming algorithms/engines. In some embodiments, smart Monte Carlo methods (including as described herein) may be further used to reduce the number of simulated designs.

[0457] FIG. **65** shows aspects of an apparatus for determining designs using simulated annealing. In embodiments, the simulated annealing component **6502** may be part of the simulation facility **110** of the platform **104**. The simulated annealing analysis component **6502** may receive data for simulated designs **6508** and models **6510**. The simulated design may identify designs of interest or regions of interest that may be used as a starting point for simulated annealing analysis. The parameter selection circuit **6506** of the simulated annealing analysis component **6502** may identify parameters of a design that is neighboring or close to the design of interest or is in the region of interest. In embodiments, parameter selection may be defined by a user from user input **6516** and/or based on input from other components of the platform. Parameter selection circuit **6506** may determine designs parameters from an objective function **6518**, cooling schedule definitions **6514**, and other data. Objective function **6518** may include data from the analysis facility **108** and may provide data regarding locations of Pareto design, CH designs, facets of convex hull, normals of facets, distance between CH designs and Pareto designs, and the like. Parameter selection circuit **6506** may identify feasible designs from the design space **6512** that have the identified parameters. The parameter selection circuit **6506** may verify that the parameters of the design to be evaluated are feasible under defined criteria based on the design space **6512** data. Once the design to be simulated is defined according to the parameter selection circuit **6506** the design definition may be provided to engines component **128** of the simulation facility **110** for simulation and the performance data **6520** of the simulated design may be received after simulation. The adaptive control circuit **6526** may evaluate the performance data **6520** to determine the next direction, step size, set of parameters to manipulate, and the like. The adaptive control circuit **6526** may identify trends and correlations between changes in parameters of designs and the resulting performance parameters of the design. The trends and correlations may be used to by the parameter selection circuit **6506** to identify new design options, e.g., **6522**, to evaluate. The adaptive control circuit **6526** may further interact with the cooling circuit **6504** to determine if the selection of parameters should return to a previous state. The simulated annealing analysis component **6502** may provide search data **6524** and data related to paths and changes in parameters that may be analyzed and/or visualized by users. The search data **6524** may be used to change or update objective functions **6518**, cooling schedule **6514** and other settings related to the simulated annealing analysis component **6502**.

[0458] FIG. **66** shows an example flowchart for simulated annealing which may be implemented by the simulated annealing component **6502**. Simulated annealing may start with a definition of parameters **6602** and/or determination of adjacent combinations **6604** for a design to be simulated. The definition of parameters may include receiving design parameters **6602** or determining parameter variations to a design to identify a new adjacent design **6604**. The parameters of the design to be simulated may be tested for exclusion criteria **6606**. In some cases, the parameters may generate an invalid combination for a design for a criteria of the study. If the design is excluded **6610**, the exclusion may be recorded in an exclusion log **6608** and a new set of parameters may be determined **6602**, **6604**. If the design is not excluded, the design may be searched in a database **6612** of previously simulated designs (such as from previous design studies). If the design is found in the database **6614**, the data for the design may be retrieved and added to the log **6614** and new parameters may for a new design may be determined **6602**, **6604**. If the design is not found in the database, the design may be simulated **6618** and the performance of the design may be evaluated **6620**. Based on the performance, new designs may be selected **6602**, **6604** and the processes repeated.

[0459] As shown in FIG. **67**, a method evaluating designs using simulated annealing may include identifying an initial design **6702**. The method may further include varying the parameter of the initial design to generate parameters for a second design **6704**. The method may include simulating the second design **6706** and analyzing the simulation data to determine parameters for a third design **6708**.

[0460] As shown in FIG. **68**, a method for evaluating designs using simulated annealing may include obtaining trial design simulations **6802**. The method may further include identifying an initial design from the trial design simulations **6804**. The initial design may be an optimum design with respect to the trial design simulation. The method may include predicting performance for variation of the initial design **6806**. Predictions may be based on historical data such as previous simulations. AI and ML algorithms may be used to determine how changes in parameters may affect the performance of a design. Based on the predictions, parameters for a new design may be identified **6808**. The new design may be a design that has favorable predictions such as an improvement in one or more performance parameter values compared to the initial design. The method may include simulating the new design **6810** and identifying a second new design for simulation **6812**. The second new design may be identified based on the simulation results. For example, if the simulation results matched the predictions the second new design may be on the same trajectory from the initial design as the new design.

[0461] In embodiments simulated annealing includes consideration and analysis of performance, design, scenario, and criteria spaces. Simulated annealing analysis searches for designs that show improvements in the performance space. Searching comprises generating variation in the design parameters (design space) and scenarios (scenario space) parameters of an initial design. The performance, design, and scenario spaces are defined according to the criteria space definitions.

[0462] Referring to FIG. **69**, embodiments of the present disclosure may employ Delaunay triangulation, or other interpolation methods, e.g., clustering, to reduce the number of simulated clinical trial designs. In particular, the number of initial simulations may be non-exhaustive and Delaunay triangulation may be used to determine what additional designs should be simulated and/or which areas of the design space should be explored (such as with simulated annealing). For example, an embodiment of a method that uses Delaunay triangulation may start with a number of initial clinical trial designs for which the design parameters and/or performance parameters are known, either through simulation or historical data. The method may construct a piecewise linear criterion surface via Delaunay triangulation, wherein each point on the surface, minus the initial designs, represents interpolated criteria for possible designs. Thus, the criteria for a clinical trial design may be determined (estimated) before the design is simulated.

[0463] Accordingly, the time required to perform simulated annealing may be decreased by testing variations of a clinical trial design without having to simulate the variations by locating the variations on the surface. Interpolation may be computed using the barycentric coordinates of a point within its enclosing simplex. The surface may be used to generate visualizations of the weighted criteria functions over the design space. The visualizations may include a weighted criteria surface generated via the weighted sum of the individual criteria surfaces, which may provide for rapid estimation of the design value for a large set of criteria weights. Embodiments may use linear programming or network formulation as the “simplex finder” for a given design point. The surface may also be used to determine most promising and least promising directions or parameter variations in simulated annealing therefore reducing the number of simulations. Use of the criterion surface may provide for the early detection that a clinical trial design is not likely to be a Pareto design and, therefore, simulation of the clinical trial design may be skipped.

[0464] In particular, embodiments of the current disclosure may use a simulated annealing engine to leverage the criteria values from past clinical trial designs that have been simulated for a scenario vector to estimate design performance under an adjacent scenario. As such, some embodiments may take advantage of the fact that: 1) the edges in a Delaunay triangulation contain all shortest paths between any two design points; and/or **2**) minimum spanning trees of all subsets of the design points are subgraphs of the Delaunay triangulation.

[0465] For example, consider a set of clinical trial designs that have been simulated and have known performance parameter values. The clinical trial designs may be treated as a scatter of points in the K dimensional design space of design vectors (e.g., K=5). Each clinical trial design may be associated with its performance parameter vector of dimension J (e.g., J=3). A Delaunay triangulation of these clinical trial design vectors may be constructed, wherein the surface of any criterion at any point is the interpolation of the criterion values of the K Delaunay simplex vertices containing the point. The interpolation may be computed using the barycentric coordinates of the point within its enclosing simplex. The weighted criteria surface is then the weighted sum of the individual criteria surfaces. As will be appreciated, this approach may provide for rapid estimation of a design's values for a large set of performance parameter weights. As will be further appreciated, Delaunay triangulation also has the advantage of creating simplexes that are not “long and skinny” so that vertices are “reasonably” close to any interior point. This is particularly true where, as in some embodiments of the present disclosure, the design points belong to a rectangular grid. Embodiments of the present disclosure may utilize linear programming or network formulation as the “simplex finder” for a given design point. A cache of recent simplexes since, apart from visualization may then be used to quickly approximate the criterion value.

[0466] Accordingly, as shown in FIG. **69**, a method **6900**, in accordance with the current disclosure, may include obtaining a first plurality of clinical trial designs with determined performance parameters **6910**; and generating a criterion surface **6912**, also referred to herein as a performance surface, based at least in part on the first plurality of clinical trial designs.

[0467] As discussed herein, the points on the performance surface represent interpolated performance parameters for a second plurality of clinical trial designs (which may not have been simulated, as described herein). One or more clinical trial designs may then be evaluated based at least in part on the performance surface **6914**. In certain aspects, the performance surface may be based at least in part on Delaunay triangulation, though other methods of interpolating a surface may be used. In certain aspects, evaluating may include simulated annealing **6916**. The method **6900** may further include generating a visualization based at least in part on the criterion surface **6918**. In embodiments, the visualization may be of weighted criteria functions over the corresponding design space. In embodiments, generating the performance surface may include interpolation based at least in part on the barycentric coordinates of a point **6920**. In embodiments, the evaluating may further include determining that a clinical trial design of the second plurality is not a Pareto design **6922**.

[0468] Turning to FIG. **70**, an apparatus **7000** for implementing one or more aspects of the method **6900** is shown. The apparatus **7000** may form part of one or more computing devices in the platform **104**, to include the computing resources **150**. The apparatus **7000** may include a design processing circuit **7010** structured to interpret clinical trial design data **7012** corresponding to a first plurality of clinical trial designs with determined performance parameters. The apparatus **7000** may further include a surface circuit **7014** structured to generate a performance surface data object **7016** based at least in part on the clinical trial design data **7012**. The performance surface data object **7016** may include data points representing interpolated performance parameters for a second plurality of clinical trial designs. The apparatus **7000** may further include a performance surface provisioning circuit **7020** structured to transmit the performance surface data object **7016**.

[0469] Referring now to FIG. **71**, a non-limiting embodiment of the recommendation component/system **7100** (also referred to herein as recommendation system architecture) is shown. In embodiments, the recommendation component **7100** may be, and/or be part of, the recommendation component **122** (FIG. **1**). In other embodiments, the recommendation component **7100** may be a separate system from the recommendation component **122**. The recommendation component **7100** may be configured to identify and provide one or more clinical trial designs for recommendation to a user via an interface, e.g., interface of a user device **102**. In some embodiments, the recommendation component **7100** may receive feedback from a user via the interface of a user device **102** for evaluating recommended designs and revise or update recommendations based on the feedback. As shown in FIG. **71**, the recommendation component **7100** may include a recommendation database **7110**, a simulation database **7112**, and/or a recommendation algorithm/engine **7114**.

[0470] The trial simulation database **7112** may form part of the data facilities **138** and be a large repository of previous, current, and/or selected clinical trial design simulations. The trial simulation database **7112** may include simulations, as described herein, merged from different databases, groups, users, and the like. The trial simulation database **7112** may include data related to each simulation, such as engines used to run the simulation, date, time, and/or the like. In embodiments, the trial simulation database **7112** may include input data such as: id number, version, scenario id, design id, user id associated with a clinical trial design, the running status, number of interim analyses, time units, performance of events observed, treatment arm information, treatment control name, and/or the like. In embodiments, the trial simulation database **7112** may include output data such as accrual duration, average power, events data, net present value, insufficient count data, follow-up time data, expected net present value, probability of efficiency, probability of favorability, probability of futility, probability of success, study cost, study duration, time required, discounted study cost, total sales, a score, a total score, and/or the like. The inputs and/or outputs may be organized in a hierarchy that includes labels and/or other identifiers that label the items as pertaining to scenarios, clinical trial designs, primary criteria, secondary criteria, stimulation control, and the like. The trial simulation database **7112** may include temporal data for each simulation and may include data related to the beginning phase of a clinical trial design, the middle of a clinical trial design, progress data of virtual patients, and/or the like. In some cases, the trial simulation database **7112** may include raw simulation data from each simulation run. In some cases, the simulation database **7112** may include summary records associated with each clinical trial design simulation and include averages, endpoints, overall statistics, and/or the like. The trial simulation database **7112** may include data that relates each clinical trial simulation to the design space, scenario space, criteria space, and/or performance space, as described herein.

[0471] The recommendation database **7110** may include a subset of the trial simulation database **7112** that has been analyzed or flagged to be applicable to design criteria.

[0472] The recommendation engine **7114** may include and/or interact with one or more components and/or algorithms/engines, e.g., a Pareto engine **7118**, a convex hull engine **7120** and/or any other engines/components described herein, for simulation, global optimization, visualization, analysis of clinical trial designs, control, and/or the like. For example, the recommendation engine **7114** may interact with, e.g., exchange data with and/or invoke procedure calls to, the simulation facility **110** (FIG. **1**). For example, embodiments of the recommendation engine **7114** may utilize a simulated annealing component/algorithm/engine **7116** which may be provided by the search/exploration component **130** (FIG. **1**) of the simulation facility **110**. In embodiments, the recommendation engine **7114** may include and/or interact with a primary algorithm **4510**, as described herein, that controls and/or monitors the workflow of the algorithms and/or engines **7114**, **7116**, **7118**, and/or **7120**.

[0473] In embodiments, the Pareto algorithm/engine **7118** and/or the convex hull algorithm/engine **7120** may be run or executed sequentially such that the output of the Pareto algorithm/engine **7118** may be an input to the convex hull algorithm/engine **7120**. In this scenario, the Pareto engine **7118** may be used to first identify Pareto designs (also referred to herein as "P-designs") from the design space (which may be a subset of the design space), and the convex hull algorithm **7120** may further separate the P-designs and identify convex hull designs (also referred to herein as "CH-designs"), which may be a subset of the P-designs. In embodiments, the convex hull engine **7120** may be the first executed engine and may identify a set of CH-designs from the design space, wherein the Pareto engine **7118** may be used to further identify P-designs from the set of CH-designs. In embodiments, the convex hull engine **7120** may be configured to quickly update the identified CH-designs when new designs are introduced as inputs to the convex hull engine **7120**. The set of identified CH-designs may be augmented incrementally by the Pareto engine **7118** as new designs are identified/simulated and added to the design space.

[0474] In embodiments, the Pareto engine **7118** may be executed without the convex hull engine **7120**, wherein the outputs of the Pareto algorithm/engine **7118** may be used for design recommendations. In some embodiments, the convex hull engine **7120** may be executed without executing the Pareto engine **7118**, wherein the outputs of the convex hull engine **7120** may be used for design recommendations.

[0475] In embodiments, the recommendation engine **7114** may be configured to provide a user with a limited number of recommended designs. The recommendation engine **7114** may provide recommendations that are a subset of the P-designs or the CH-designs. In some cases, the recommendation engine **7114** may be configured to limit the number of designs recommended to between about five (5) and about nine (9) designs. Recommended designs may be presented in small sets (such as between about five (5) and about nine (9) designs), allowing a user to compare the designs in the set. The set of recommended designs may be interactively augmented or updated based on user input or feedback. For example, the recommendation algorithm **7114** may present a set of initial recommended designs and ask a user to select a favorite design. Based on the favorite design, the recommendation engine **7114** may augment a next set of recommended designs. For example, based on the selection of one design, the engine **7114** may further present siblings of the selected design and/or designs that are dominated by the design.

[0476] Referring now to FIGS. **72** and **73**, in embodiments, the recommendation engine **7114** may determine clinical trial designs **7210** to recommend (also referred to herein as "a set of recommended designs" or "recommended designs") to the user by processing a set of simulated designs **7212**, which may be retrieved from the database **7112**. Processing of the simulated designs **7212** may involve use one or more algorithms/engines, such as the Pareto engine **7118** and/or convex hull engine **7120**. For example, in one configuration, the set of clinical trial designs **7212** may be first processed using the Pareto engine **7118** to identify a set of Pareto designs **7214** (P-designs) and/or a set of dominated designs **7216**. As represented in FIG. **73** by the inverse triangle, in embodiments, the set of Pareto designs **7214** may be much less than the set of all designs **7212**, e.g., 10× or 100×smaller, the set of convex hull designs **7218** may be smaller than the set of Pareto designs **7214**, and the set of recommended designs **7210** may be smaller than the set of convex hull designs **7218**. For example, the set of Pareto designs **7214** may be further processed using the convex hull engine **7120** to identify, from the set of P-designs **7214**, convex hull designs **7218**, wherein the convex hull designs **7218** are, generally, Pareto designs **7214** that can be reached by weighting criteria as described herein. In embodiments, non-reachable pareto designs **7222** may not be considered for use by the convex hull engine **7120** and/or recommendation.

[0477] Referring to FIG. **74**, in embodiments, the design recommendation engine **7114** may generate one or more outputs **7410**, including a list or a set of the recommended designs **7210**. The list of recommended designs **7210** may be provided with criterion values **7412**, scenario parameters **7414**, and/or trial design parameters **7416**. A non-limiting example of a list of recommended designs is shown in FIG. **75**. As shown, the list may include design ID, power, costs, and/or duration for each listed design. The term "power", as used herein with respect to a clinical trial design may represent a measure of one or more properties and/or statistics of the clinical trial, e.g., statistical power. For example, power may provide an indication of how many patients are required to avoid a type I (false positive) or type II (false negative) error.

[0478] Inputs **7418** to the recommendation engine **7114** may include the clinical trial design results **7212**, wherein the engine **7114** generates the Pareto **7214** and convex hull **7218** designs via the corresponding engines **7118** and **7120**. In some embodiments, however, the Pareto designs **7214** and/or the convex hull designs **7218** may be fed to the engine **7114** as inputs **7418**. The inputs **7418** may also include any other type of output from the Pareto **7118** and/or convex hull **7120** engines (facets, normal, etc.). In embodiments, the inputs **7418** to the recommendation engine **7114** may also include the set or a subset of all the designs simulated **7212** in addition to the P-designs **7214** and/or CH-designs **7218**. Inputs **7418** may also include user settings **7420** and/or parameters **7422**, such as the number of recommendations the recommendation engine **7114** should provide. The recommendation engine **7114** may receive user selections and other inputs **7418** that may provide guidance to the engine **7114** as to which designs are preferred by the user or which other designs the user wants to explore.

[0479] In embodiments, the algorithm/engine **7114** may generate or output visualizations and/or interfaces (collectively shown as **7424**) to compare two or more recommended designs **7210**. Non-limiting examples of the visualizations **7424** are depicted in FIGS. **76** and **77** and may be configured for performing sensitivity analysis on the recommended designs **7210**, as described herein. Visualizations **7424** may also include other types of graphs and/or other visual representations that depict preference weights regions (polygons in three (3) criteria models), barycentric coordinate graphics, and/or the like. As shown in FIG. **76**, visualizations may depict relationships between recommended designs **7210** with respect to weightings (W1—power and W2—costs) for performance criteria. As will be understood, the numbered polygons in FIG. **76** represent the range of weighting values for each of the recommended designs **7210**, which may be optimal. As shown in **77**, a visualization may depict the relationship of recommended designs, e.g., sixteen (16) different designs (numbered “1-6”, “8-10”, “13”, “15”, “19” “54”, “63”, “69”, and “120”), with respect to weightings **7710** for performance criteria. Polygons may be used to represent the range of weighting values for each of the recommended designs which may be optimal.

[0480] The recommendation engine **7114** may also output lists or sets of designs, referred to herein as “related designs” **7426** (FIG. **74**), that are close to the recommended designs **7210** in the criterion space (which may or may not be P-designs or CH-designs). Related designs **7426** may be determined using various distance measures. For example, one distance measure may be related to the steps needed for a simulated annealing algorithm **7116** (FIG. **71**) to go from one design to another. In embodiments, the recommendation engine **7114** may provide recommendations for designs **7210** (based on the Pareto **7118** and/or the convex hull **7120** engine outputs) and allow a user to compare and analyze the recommended designs **7210** (sensitivity analysis, weigh graphs, etc.). The recommendation engine **7114** may provide lists of twin or sibling designs **7428** (FIG. **74**) that are related to a selected design and show/highlight different types of designs that are available or close to a selected/recommended design.

[0481] In embodiments, design siblings **7428**, and/or other different clinical trial designs that have similar performance criteria, may have different complexity. In some embodiments, types of clinical trial designs may be arranged and/or marked according to the complexity, ratings, historical preference, and/or the like. In some cases, clinical trial designs may be arranged in a hierarchy according to a preference such that, for example, designs that have lower complexity for a performance criteria are provided first. For example, in a case where multiple clinical trial designs have the same or nearly the same performance criteria, the multiple clinical trial designs may be ordered based on the properties of the designs when providing recommendations.

[0482] In embodiments, the recommendation algorithm/engine **7114** may include logic to reduce the set of CH-designs **7218** by a user-specified number by dropping CH-designs within the set **7218** with the objective of minimizing the maximum reduction of criteria values over the weight space. The recommendation engine **7114** may include logic to expand the CH-design set **7218** by choosing subsets of Pareto designs **7214** that are closest to the convex hull facet of the CHF cluster (facets may be Delaunay triangulations as described herein). The recommendation engine **7114** may include logic to fill gaps between recommended designs **7210**. For example, Pareto designs **7214** in CHF clusters may be selected to fill large gaps (e.g., large facets and/or distances from a recommended design and a target point on the facet according to different metrics (e.g., multiple of criteria value differences (ε.sub.1, ε.sub.2, 3, . . .))). The clusters may also be based on default and/or user-defined parameters, and/or average overall weights in a facet of the distance from a target point. The recommendation engine **7114** may include logic to calculate distances in design space to search for designs that are siblings, e.g., close in criterion space but distant in design.

[0483] In some embodiments, the recommendation engine **7114** may provide initial recommendations that cover all possible weightings of performance criteria. In such embodiments, the recommended designs **7210** may serve as anchor designs that facilitate further exploration of the simulated designs. Anchor designs may serve as initial points for design searches, e.g., simulated annealing, as described herein. The recommended designs **7210** may be designs that best approximated the performance (with respect to performance criteria) of the CH-designs **7218** and/or P-designs **7214**. In embodiments, one or more cluster designs **7220** (FIG. **72**) may be associated with each of the CH-designs **7218**. The cluster designs **7220** may be generated by the

Pareto engine **7118**. In embodiments, the cluster designs **7220** may be used to provide rapid recommendations when more than a threshold number, e.g., twenty-four (24), of recommended clinical trial designs **7210** are desired, and/or when designs in a certain range of weights are desired. In embodiments, the cluster designs **7220** may include all of the Pareto designs **7214**.

[0484] As will be understood, embodiments of the recommendation engine **7114** may present different types of designs within the recommended set of designs **720** that are similar in performance criteria. In certain aspects, the different types of designs may have similar performance criteria but different design parameters that may be more favorable for certain situations.

[0485] As will be further understood, in some embodiments, simulations of designs may not be exhaustive, i.e., the set of initial designs **7212** may be incomplete. For example, not every possible combination of clinical trial designs may be initially simulated, and/or a partial set of all clinical trial design combinations may be simulated and processed using one or more of the Pareto, convex hull, and recommendation algorithms/engines. In such cases, when a recommended design **7210** is provided, it may be true that a better, i.e., more optimal, design for the desired performance criteria exists in the space. In some cases, when a design is recommended **7212**, the recommendation engine **7114** (and/or primary algorithm **4510**, may further explore if there are designs that have better or similar performance to the recommended designs **7210** that have not been simulated. In embodiments, the simulated annealing algorithm/engine **7116** may be used to explore the design space around recommended **7210** and/or selected designs.

[0486] Accordingly, turning now to FIG. **78**, a non-limiting example of a method **7800** for recommending clinical trial designs in accordance with the current disclosure is shown. The method **7800** may include obtaining clinical trial design simulation results for a set of clinical trial designs **7810**, and determining a set of Pareto designs **7812** based at least in part on the clinical trial design simulation results and one or more performance parameters of the kind described herein. The method **7800** may further include determining a set of convex hull designs **7814** based at least in part on the clinical trial design simulation results **7212** and/or the Pareto designs **7214**. The method **7800** may further include determining a set of recommended designs **7816** based at least in part on the set of Pareto designs **7214** and/or the set of convex hull designs **7218**. In embodiments, the method **7800** may further include transmitting the set of recommended designs **7818**.

[0487] Referring to FIG. **79**, in embodiments, the method **7800** may further include filtering clinical trial designs which are dominated by Pareto designs **7910**. The method **7800** may further include filtering clinical trial designs which are dominated by convex hull designs **7912**. In embodiments, determining the recommended designs **7210** may include determining that at least one of the recommended designs **7210** is within an epsilon-distance from at least one of the Pareto designs **7914**. In embodiments, determining the recommended designs **7210** may include determining that at least one of the recommended designs is within an epsilon-distance from at least one of the convex hull designs **7916**. In embodiments, the method **7800** may further include identifying different design types in the set of Pareto designs **7918**. As shown in FIGS. **78** and **79**, the Pareto designs **7214** may be determined prior to determination the set of convex hull designs. In such embodiments, the convex hull designs **7218** may be derived from the Pareto designs **7214** such that each of the set of convex hull designs **7218** is one of the Pareto designs **7214**, and such that at least one of the recommended designs **7210** is a convex hull design **7218**. As shown in FIG. **80**, in embodiments, the convex hull designs **7218** may be determined prior to determination of the Pareto designs. In such embodiments, the Pareto designs **7214** may be derived from convex hull designs **7218** such that each of the set of Pareto designs **7214** is a convex hull design **7218**, and such that at least one of the recommended design **7810** is a convex hull design **7218**.

[0488] Returning back to FIG. **79**, the method **7800** may include identifying **7922** a number of clinical trial designs in the Pareto designs **7214**, where the convex hull designs **7218** are determined **7814** when the number is greater-than-or-equal to a threshold **7924**.

[0489] Referring now to FIG. **81**, an apparatus **8100** for implementing the method **7800** is shown. The apparatus **8100** may include a results processing circuit **8110**, a Pareto evaluation circuit **8112**, a convex hull evaluation circuit **8114**, a recommendation evaluation circuit **8116**, and/or a recommendation evaluation provisioning circuit **8118**. The results processing circuit **8110** is structured to interpret/obtain **7810** the clinical trial design simulation results **7212**. The Pareto evaluation circuit **8112** is structured to determine **7812** the Pareto designs **7214** based at least in part on the clinical trial design simulation results **7212** and one or more performance criteria, as described herein. The convex hull evaluation circuit **8114** is structured to determine **7814** the convex hull designs **7218**. The recommendation evaluation circuit **8116** is structured to determine **7816** the recommended designs **7210**. The recommendation provisioning circuit **8118** is structured to transmit **7818** the recommended designs **7210**. The apparatus **8100** may further include one or more filtering circuits, collectively represented by **8120**, that perform filtering of the clinical trial designs **7212**, Pareto designs **7214**, and/or convex hull designs **7218**, as described herein.
[0490] Referring now to FIG. **82**, a non-limiting example of a simulation queue **8210** for management and optimization of clinical trial designs **8212** is provided. The queue **8210** and/or corresponding methods described herein for operating the queue **8210**, may implemented by the simulation facility **110**, analysis facility **108**, and/or other components of the platform **104** (FIG. **1**). As shown in FIG. **82**, the queue **8210** may have an entrance **8214**, where yet to be simulated clinical trial designs **8212** are accepted, and an exit **8216**, where the next to be simulated clinical trial design **8212** is pulled from.
[0491] In embodiments, simulations of clinical trial designs **8212** may be executed according to input queues, e.g., queue **8210**, of individual simulation runs **8212**, as described herein. Queues may be organized based on factors associated with the simulation runs, expected outputs of the simulation runs, and/or relationships between simulation runs. Non-limiting examples of such factors may include similarity, priority, costs, and/or complexity. The relationships may be discovered/identified using machine learning, e.g., artificial intelligence. For example, the simulation runs in a queue may be organized based on time required to run the simulations. In another example, the simulation runs in the queues may be organized to process the most promising designs first, thus facilitating quick access to most the promising designs.
[0492] Most promising designs may be identified from historical data and/or machine learning. A most promising design may be a clinical trial design that has a moderate-to-high chance, e.g., greater than 50%, of being a global optimal for a particular set of performance criteria. Historical data may be acquired from one or more data sources in the data facility **138** (FIG. **1**). In one example, simulation runs in the queues may be organized based on user identified parameters. In one instance, simulation runs in the queues may be populated to provide an initial non-exhaustive sampling of the design space to provide of an overview of the performance of the clinical trial designs. The initial results may be used to populate queues for designs that are near designs that are in the desirable areas of the performance space. Simulated annealing, which may be provided by the search/exploration component **130** (FIG. **1**) may be used to populate the queues with simulation runs for designs that are near initial simulated designs that are determined to be promising. The order of simulation runs in the queues may be revised based on results from initial simulations. Queues may also be organized to prioritize simulation runs to provide real-time results.
[0493] In certain aspects, queues, e.g., queue **8214**, may be organized based on time and/or costs. For example, results of a first simulation run may be needed before results of a second simulation run. Additionally, a simulation run may be given a lower priority in a queue, and/or scheduled, so that it runs on a processing system during off-peak hours, thus, lowering costs. Queues may also be organized to execute simulation runs across different hosting providers, e.g., across multiple cloud computing systems. For example, higher priority simulation runs may be queued to run on a first cloud computing system, where the hosting provider charges a premium price for fast results, and lower priority simulation runs may be queued to run on a second cloud computing system, where

the hosting provider charges a non-premium price for slower results. In certain aspects, queues may be organized by customer and/or across customers. For example, simulation runs for a first customer may be prioritized over simulation runs of a second customer. Queues may also be organized based on workload and/or work type. Queues may also be organized to assign simulation runs to either a binary computing system or a quantum computing system. For example, simulation runs that fall into the bounded error, quantum, polynomial time class, but outside of P, may be assigned to a quantum computing system, while P class problems may be assigned to a binary computing system. Artificial intelligence, e.g., machine learning, may also be used to organize queues, to include populating and distributing simulation runs. For example, in embodiments, a neural network training set may include a variety of clinical trial designs and whether they were previously selected as being a global optimum design for a particular scenario. Using such a scenario, the neural network may learn to identify promising clinical trial designs and prioritize them in one or more queues. In embodiments queue organization may be based at least in part on metadata associated with the models and/or engines. Metadata may include data regarding what engines, run times, resources, and the like are necessary for simulation.

[0494] While FIG. **82** depicts a single queue **8210**, embodiments of the current disclosure may include multiple queues executing on multiple machines, e.g., computing resources **150** (FIG. **1**).

[0495] Illustrated in FIG. **83** is a method **8300** for management and optimization of clinical trial designs. The method **8300** may include determining simulation runs for a trial design study **8310**. The method **8300** may further include selecting a subset of the simulation runs **8312**. The method **8300** may further include populating a simulation queue with the subset of the simulation runs **8314**. The method may further include executing the subset of simulation runs according to the simulation queue **8316**.

[0496] Illustrated in FIG. **84** is an apparatus **8400** for management and optimization of clinical trial designs. The apparatus **8400** includes a trial design processing circuit **8410** structured to interpret trial design study data **8412**. The apparatus **8400** includes a first evaluation circuit **8414** structured to execute simulation runs **8416** of clinical trial designs defined, in part, by the trial design study data **8412**. The apparatus **8400** includes a ranking circuit **8418** structured to, in response to executing the simulation runs **8416**, rank the simulation runs **8416** according to expected performance, i.e., generate rankings **8420** for the simulation runs **8416**. In certain aspects, the expected performance data may be based on data derived from a database of simulated designs. The apparatus **8400** includes a simulation populating circuit **8422** structured to populate a simulation queue **8210** according to the simulation run rankings **8420**. The apparatus **8400** includes a second evaluation circuit **8426** structured to execute simulation runs from the simulation queue **8210**. In embodiments, the rankings **8420** may be revised based at least in part on the outputs of simulated runs.

[0497] As described herein, simulations of trial designs may use simulation engines. Accordingly, referring now to FIG. **85**, a marketplace **8510** for simulation engines **8512** is shown. The marketplace **8510** may form part of the engines component **128** (FIG. **1**) and/or computing resources **150** (FIG. **1**), or the marketplace **8510** may be a stand-alone system that communicates with the platform **104** via one or more application programming interfaces (APIs). The marketplace **8510** may serve as a repository/library which users can browse and/or search for engines suited to a particular need/scenario. Engines **8512** may be selected based on different criteria including, cost, run time, complexity of model, outputs of model, etc. As explained in greater detail herein, selected engines **8512** may be incorporated into the platform **104**, e.g., via the engine component **128**, for subsequent use in clinical trial design simulations, as described herein. For example, in embodiments, the simulation facility **110** (FIG. **1**) may use two or more different engines **8512** from the marketplace **8510**.

[0498] Entities, e.g., third party and/or in-house developers, may create simulation engines **8512** for use with different design types, design complexity, and/or the like. The created engines **8512** may then be uploaded into the marketplace **8510** via a web interface, an application programming interface, a File Transfer Protocol (FTP) interface or other suitable technology for transferring data and/or software files. The marketplace **8510** may include one or more filters which a user can use to limit and/or control which engines **8512** are displayed based on one or more properties. For example, a user may only want to view engines are configured for a particular clinical trial type (engines **8514**, **8516**, and **8518**) and/or may only want to view engines that have been authored by a trusted developer (engines **8520**, **8522**, **8524**). For example, trial type X, e.g., a cluster randomized design, may require a different type of engine than trial type Y, e.g., an adaptive randomization design.

[0499] Turning to FIG. **86**, a non-limiting example of a simulation engine **8610** is shown. In embodiments, the simulation engine **8610** may include a header section **8612** and a main body **8614**. The main body **8614** may include one or more modules for performing a clinical trial simulation, or aspects thereof. The header section **8612** may include one or more definitions **8616** that identify the various inputs used by one or more modules of the main body **8614**. One or more of the definitions **8616** may define an expected output of the engine **8610**. One or more definitions **8616** may define the developer of the engine **8610** and/or a version number of the engine **8610**.

[0500] Upon being selected, the header section **8612** may be registered with an engine registry of the platform **104**, e.g., the engine component **128**. Registration of an engine **8610** may include the registry interrogating the header section **8612** to determine one or more required inputs and/or expected outputs of the engine **8610**. Registration of an engine **8610** may make the engine **8610** available as a selectable option in one or more of the interfaces of the platform **104**, such as in the advisors **114**. Registration of the engine **8610** may also include the registry determining one or more values for the inputs to the engine **8610** based on known settings and/or values for various components of the platform **104**. For example, an input of an engine **8610** specifying how many trial designs can be simulated concurrently by the engine **8610** may be set to a particular value based on known available memory and/or processing resources the platform **104** can make available to the engine **8610**.

[0501] Turning to FIG. **87**, the header section **8612**, to include the definitions **8616**, may be used by one or more of the interfaces of the platform **104**, as described herein and represented generally by **8710**, to populate one or more fields **8712**. The fields **8712** may include dialogue boxes, text fields, input fields, and/or other suitable widgets for conveying one or more of: current values/settings for inputs to the engine **8610**; requested values/setting for inputs to the engine **8610**; recommended value/settings for inputs to the engine **8610**; and/or other information regarding the engine **8610**.

[0502] In embodiments, inputs to the engine **8610** defined by the user may be saved for later use, which may include system audits and/or replication of past outputs. For example, a simulation may track the version number and/or inputs of each engine used in the simulation such that the simulation may be reproduced. Versions of each engine and inputs associated with each engine (such as a seed value) may be recorded, stored and/or associated with each trial design, including for purposes of audit or replication.

[0503] Moving to FIG. **88**, a method **8800** for using a simulation engine marketplace is shown. The method **8800** includes identifying, in the marketplace, a simulation engine for simulating a clinical trial design **8810**. The method **8800** further includes importing specifications, e.g., definitions **8616** (FIG. **86**), of the simulation engine **8812**, and populating a user interface based on the specification **8814**.

[0504] FIG. **89** depicts another method **8900** for using a simulation engine marketplace. The method **8900** includes selecting a simulation engine from a marketplace **8910**, the simulation engine for simulating a clinical trial design. The method **8900** further includes determining inputs to the simulation engine **8912** and executing a simulation of the clinical trial design using the simulation engine with the inputs **8914**. The method **8900** may include saving the inputs **8916**.

[0505] FIG. **90** depicts an apparatus **9000** for using a simulation engine marketplace. The apparatus

9000 includes a user input processing circuit **9010** structured to interpret user input data **9012**. The apparatus **9000** includes a simulation selection circuit **9014** structured to determine a simulation engine **8512** based at least in part on the user input data **9012**. The apparatus **9000** further includes an engine input selection circuit **9018** structured to determine inputs **9020** to the simulation engine **8512** based at least in part on the user input data **9012**. The apparatus **9000** further includes an evaluation circuit **9022** structured to execute/conduct a simulation using the determined simulation engine **8512** and determined inputs **9020**. In embodiments, the apparatus **9000** may further include a recording circuit **9024** structured to save the determined inputs **9020** and the determined simulation engine **8512** to a memory device, e.g., data component **138** (FIG. **1**).

[0506] Embodiments of the current disclosure may provide for one or more methods and apparatuses for evaluating seemingly disparate simulation engines so that a user can determine the most effective and/or efficient engine(s) to use for a particular simulation. As described herein, simulations may use different design models **126** (FIG. **1**) and/or simulation engines **128** (FIG. **1**). In embodiments, the simulation facility **110** (FIG. **1**) may use various engines to simulate different design types, including different design types within one overall clinical trial design simulation. Non-limiting examples of differences in engines and/or engine types include: different underlying purposes, e.g., convex hull analysis vs. simulated annealing, etc.; different creators, e.g., in-house development teams, vendors, suppliers, etc.; versioning, e.g., an update to an existing engine of “version 1.0” to “version 1.5”, etc.; and/or other variations.

[0507] As will be understood, different engines may not be uniform in how they evaluate performance criteria. For example, engines created by different entities may make different assumptions and/or use different logic flows to determine performance criteria for a given simulation. Evaluation of simulated designs often requires that the determined performance of an engine can be correctly and/or practically compared against the determined performance of other engines. As such, embodiments of the current disclosure provide for benchmarking of engines so that their outputs can be normalized to reduce and/or eliminate variations and/or scale the outputs. Reducing variations between engines, in turn, provides for engines to be accurately compared against one another. In embodiments, benchmarking may include simulating one or more designs using various engines. Benchmarking may also include varying one or more parameters common across several different engines/design models and monitoring for corresponding variations/changes in performance criteria, e.g., engine outputs. Based on the changes, a normalizing factor for one or more engines may be determined. Benchmarking may also include providing a set of inputs with a corresponding set of expected outputs, feeding the inputs to one or more engines to generate actual outputs, and comparing the actual outputs to the expected outputs.

[0508] Accordingly, referring now to FIG. **91**, a block diagram of a process **9100** for benchmarking and/or normalizing simulation engines, in accordance with an embodiment of the current disclosure, is shown. The process **9100** may provide a plurality of inputs **9110** and **9112** to a plurality of clinical trial design simulation engines **9114** and **9116**. The clinical trial design engines **9114** and **9116** may then generate first outputs **9118** and **9120** based on the inputs **9110** and **9112**. Variations **9122** and **9124** of the inputs **9110** and **9112**, respectively, may be generated and provided to the engines **9114** and **9116** so that second outputs **9126** and **9128** are generated. In embodiments, the variations **9122** and/or **9124** may include single item changes, e.g., a single parameter value, from their corresponding inputs **4510** and/or **9112**. In embodiments, the variations **9122** and **9124** may be structured to test specific functions of the engines **9114** and **9116**. For example, the only difference between variation **9122** and input **9110** may be a value for an expect cost of a clinical trial design. Non-limiting examples of variations may also include difference in number of expected recruited patients, expected drug costs, expected administrative costs, site availability, drug availability, duration of the trial, and/or any other type of performance criteria and/or parameter for simulating a clinical trial design.

[0509] The set of outputs **9118**, **9120**, **9126** and/or **9128** may then be evaluated to determine one or more normalization factors **9130**. In embodiments, the normalization factors **9130** may be based on delta values **9132** and **9134** generated by comparing one or more of the outputs to each other. For example, in embodiments, the outputs **9118** and **9126** of an engine **9114** may be compared to generate delta value **9132**, wherein the delta value **9132** may represent effects that varying the input **9110** had on engine **9114**. In embodiments, output **9118** could be compared to outputs **9126**, **9120**, and **9128** to determine delta value **9134**, wherein the delta value **9134** may reflect differences between how engines **9114** and **9116** handles variance to the inputs **9110** and **9112**.

[0510] In embodiments, the normalization factors **9130** may provide for a common metric by which to measure the performance of one or more of the plurality of engines **9114** and **9116** against each other. In certain aspects, the normalization factors **9130** may be multiplied against one or more of the outputs **9118**, **9120**, **9126**, and/or **9128**. In embodiments, the normalization factors **9130** may differ with respect to differences between the inputs **9110** and **9112** and their corresponding variations **9122** and **9124**.

[0511] In embodiments, a first clinical trial design simulation engine **9114** of the plurality may be structured to simulate a first clinical trial design that is of a different type than a second clinical trial design which a second clinical trial design simulation engine **9116** of the plurality is structured to simulate. For example, engine **9114** may be structured to simulate trial designs comparing two different drugs to each other, while engine **9116** may be structured to simulate trial designs for evaluating non-drug related therapies. In embodiments, a first clinical trial design simulation engine **9114** of the plurality may be of a different version of a second clinical trial design simulation engine **9116** of the plurality. For example, engine **9116** may be an updated version of the engine **9114**, wherein **9116** may utilize different logic and/or other programmatic changes. In embodiments, a first clinical trial design simulation engine **9114** of the plurality may have been generated by a first entity and a second clinical trial design simulation engine **9116** of the plurality may have been generated by a second entity of the plurality distinct from the first entity. For example, engine **9114** may be structured to simulate the same type of clinical trial designs for which engine **9116** is structured to simulate, but engine **9114** may have been built by an in-house development team while engine **9116** may have been built by a user of the platform, third-party contractor or separate company. In embodiments, the outputs **9118**, **9120**, **9126**, and/or **9128** may include metadata. Non-limiting examples of metadata may include version number of the engine used, authorship of the engine used, creation/simulation date of the output, and/or other types of properties.

[0512] In embodiments, the delta values **9132** and/or **9134** may represent output variability between one or more of the engines **9114** and **9116** for similar inputs, e.g., input **9110**, or between the same engine **9114** across an input **9110** and the corresponding variation **9122**. In embodiments, the delta values **9132** and **9134** and/or the normalization factors **9130** may be used, in part, to determine valid ranges for the output values of an engine **9114** and **9116**. The valid ranges, in turn, may be used to determine whether an engine is providing faulty information, e.g., the engine may have incorrect logic and/or coding errors.

[0513] Illustrated in FIG. **92** is a method **9200** for benchmarking and/or normalizing clinical trial design simulation engines. The method **9200** includes providing inputs to a plurality of clinical trial design simulation engines **9210**. The method **9200** includes receiving first outputs of the plurality of clinical trial design simulation engines in response to the inputs **9212**. The method **9200** includes providing variations of the inputs to the plurality of clinical trial design simulation engines **9214**. The method **9200** further includes receiving second outputs of the plurality of clinical trial design simulation engines in response to the variations **9216**. The method **9200** includes evaluating the first and the second outputs to determine delta values **9218**. The method **9200** includes determining, based in part on the delta values, a plurality of normalization factors for the plurality of clinical trial design simulation engines **9220**.

[0514] In embodiments, engine variability may be confined to small number of parameters or values. For example, variations in engine versions (such as from one version to another) may be confined to minor algorithm changes related to corner cases, extreme values or the like. In some cases, various versions of engines may perform exactly the same except for a small range of values at extreme ends or specific values. Engines may be evaluated for exact ranges of inputs and/or outputs for which engines are comparable, ranges of inputs and/or outputs for which engines differences exhibit acceptable error, and range of inputs and/or outputs for which engines are not comparable. Configuration data may be used to indicate for which values and/or ranges of values engines are comparable. Data that is in the comparable range may be marked as comparable. Data in other ranges may be flagged as not comparable or marked with an estimated error for user review. In some cases, a user may specify threshold for acceptable error values.

[0515] Referring to FIG. **93**, an apparatus **9300** for benchmarking and/or normalizing clinical trial design simulation engines is shown. The apparatus **9300** includes an output processing circuit **9310** structured to interpret output data **9312** from a plurality of clinical trial design simulation engines, e.g., **9114** and **9116** (FIG. **91**). Output data **9312** may correspond to one or more of output data **9118**, **9120**, **9126**, and/or **9128** (FIG. **91**). The apparatus **9300** includes a comparison circuit **9314** structured to compare the interpreted output data **9312** to expected output data **9316**. Expected output data **9316** may include previously calculated outputs for the engines **9114** and/or **9116** and/or outputs, calculated using engines outside of the plurality of engines **9114** and **9116**, for the inputs **4510** and/or **9112** (FIG. **91**), e.g., an agreed upon benchmark standard. The apparatus **9300** includes a normalization circuit **9318** structured to determine a plurality of normalization factors **9130** for the plurality of clinical trial design simulation engines **9114** and **9116**. The apparatus **9300** further includes a normalization provisioning circuit **9322** structured to transmit the plurality of normalization factors **9130**.

[0516] Referring now to FIG. **94**, in addition to optimizing a design for a single clinical trial, embodiments of the platform **104** (FIG. **1**) may provide for optimization of clinical trial designs across a plurality/set of clinical trials **9410** and/or aspects of the clinical trials. As will be appreciated, optimization over a set of related clinical trials may result in better overall performance for the set, as compared to optimizing each element, aspect, or clinical trial in the set individually and combining the results. For example, two clinical trial designs A and B may impact each other such that conducting clinical trials A and B concurrently is more efficient, with respect to a given performance criteria, than conducting A and B at different times. As another example, conducting clinical trials A and B, whether successively or concurrently, may be more efficient, with respect to a given performance criteria, than conducting one of clinical trial A or clinical trial B without conducting the other.

[0517] Improving the performance of a set may, in turn, improve the effectiveness and/or cost efficiencies of the related clinical trials.

[0518] As shown in FIG. **94**, two or more of the clinical trials, e.g., clinical trial A **9412**, clinical trial B **9414**, and/or clinical trial C **9416** may be related to each other through one or more associations **9418**. Non-limiting examples of associations **9418** include: trial sites **9420**; an order of execution and/or dependencies **9422**; shared resources **9424**; clinical trial phases **9426**; test subjects **9428**, and/or other aspects of design space, scenario space and performance space. Trial sites **9420** may include any facility that participates in and/or performs a service related to execution of a clinical trial and/or any other type of facility, as described herein, with respect to the term “site” and/or “clinical trial site”. An order of execution **9422** and/or dependency may include the sequencing of the conduction/execution of one or more clinical trials. For example, clinical trial A **9412** may execute before clinical trial B **9414** which may execute before clinical trial C **9416**. An order of execution **9422** may also specify that two more clinical trials execute concurrently, e.g., have overlapping time periods. For example, clinical trial A **9412** may execute concurrently, e.g., at the same time, as clinical trial B **9414**. Non-limiting examples of shared resources **9424** may include administrative personnel, medical practitioners, and/or drug availability/supply. Clinical trial phases **9426** may include phases 0-4, which may be performed sequentially. In embodiments, the platform **104** may simulate all, or a large percentage, of the feasible clinical trial designs/variations for each of clinical trials (and corresponding phases) and determine the optimal or near optimal combination of trial variations for each phase. Test subjects **9428** may include a drug and/or treatment that is the subject/purpose of a clinical trial **9410**. In embodiments, the set of clinical trials **9410** may include trials that are performed in parallel but are related to different aspects of the same drug/treatment or related drugs/treatments.

[0519] In embodiments, a specification **9430**, e.g., a data file (to include one or more records in a relational and/or object database) and/or written document, may record and/or define the one or more associations **9418**. The specification **9430** may be stored in one or more databases within the data facility **138** (FIG. **1**) where it may be retrieved from and/or updated as needed.

[0520] As will be explained in greater detail below, one or more clinical trial designs **9432**, **9434**, **9436**, **9440**, **9442**, **9444**, **9448**, **9450** and **9452** (collectively referred to as **9456**) may be generated for each of the clinical trials **9410** based at least in part on the specification **9430** and/or associations **9418**. For example, three (3) clinical trial designs **9432**, **9434**, and **9436** (collectively referred to herein as **9438**) may be generated for clinical trial A **9412**, three (3) clinical trial designs **9440**, **9442**, and **9444** (collectively referred to herein as **9446**) may be generated for clinical trial B **9414**, and three (3) clinical trial designs **9448**, **9450**, and **9452** (collectively referred to herein as **9454**) may be generated for clinical trial C **9416**. While the foregoing example includes three (3) clinical trials each having three (3) corresponding clinical trial designs, it will be understood that any number of two or more (>2) clinical trials **9410** may be used with any number of corresponding clinical trial designs **9456**.

[0521] Turning to FIG. **95**, a permutation set **9510** may be determined from the clinical trial designs **9456** (FIG. **94**). The permutation set **9510** may be a collection of the possible combinations of the clinical trial designs **9456**. In embodiments, each item in the permutation set **9510** may include at least one clinical trial design from each of the subgroups **9438**, **9446**, and/or **9454** corresponding to the clinical trials **9412**, **9414**, and **9416**. In the case of three (3) clinical trials, as shown in FIG. **94**, each of the combinations in the permutation set **9510** may associate a clinical trial design from group **9438** (derived from clinical trial A **9412**) with two other clinical trial designs, one from group **9446** (derived from clinical trial B **9414**) and one from group **9454** (derived from clinical trial C **9416**). For example, as shown in FIG. **95**, a first item **9512** of the permutation set **9510** may include design A**1 9432**, design B**1 9440**, and design C**1 9448**. A second item **9414** of the permutation set **9510** may include design A**1 9432**, design B**1 9440**, and design C**2 9450**. A third item **9516** of the permutation set **9510** may include design A**1 9432**, design B**1 9440**, and design C**3 9452**. A fourth item **9518** of the permutation set **9510** may include design A**1 9432**, design B**2 9442**, and design C**1 9448**. As will be understood, the permutations may continue so that the set **9510** contains all possible permutations/combinations as represented by the final item **9020**. In embodiments, the permutation set **9510** may include only a subset of the possible permutations/combinations. In embodiments, the permutation set **9510** may include variations of a permutation/combination based on the one or more associations **9418** (FIG. **94**). For example, where the order of the clinical trials in item **9512** from left to right represents the execution order of the clinical trials, the permutation set **9510** could include variations of item **9412**, e.g., clinical trial design C**1 9448**, clinical trial design B**1 9440**, and clinical trial design A**1 9432**, representing a case where trial C**1 9448** executes before trial B**1 9440** which executes before trial A**1 9432**.

[0522] Combined performance criteria **9526** may be generated for each item of the permutation set **9510** where the combined performance criteria represents the collective performance criteria of the clinical trials within the item. For example, as shown in FIG. **95**, combined performance criteria **9522** may be generated for item **9512**, combined performance criteria **9523** may be generated for item **9514** and so on until all items have a corresponding combined performance criteria, as represented by combined performance criteria **9524** and corresponding item **9520**. In embodiments, the platform **104** may simulate all, or a large percentage, of the feasible trial options for each of the parallel trials to determine the optimal or near optimal combination of trial variations. In some cases, optimization of clinical trials, as disclosed herein, may also include other aspects of trials such as patient recruitment and clinical trial resources (including drug supply). Simulations of trials may include determinations of requirements for drug supply and other aspects.

[0523] Analysis of the combined performance criteria **9526** may provide for determination of which set/permutation/combination of designs is the optimal combination to use for the set of clinical trials **9410**.

[0524] Accordingly, turning to FIG. **96**, a method **9600** for optimization of clinical trial designs across a plurality/set of clinical trials **9410** (FIG. **94**) and/or aspects of the clinical trials is shown. The method **9600** includes obtaining a specification **9610**. The specification **9430** (FIG. **94**) may define one or more associations **9418** (FIG. **94**) between two or more clinical trials **9410**. The method **9600** further includes determining clinical trial designs for each of the two or more clinical trials **9612**. In embodiments, the clinical trial designs may be based at least in part on the specification **9430** and/or the associations **9418**. The method **9600** further includes generating a permutation set of the clinical trial designs **9614**. The method **9600** further includes determining combined performance criteria for each item of the permutation set **9616**. The method **9600** may further include recommending one or more items of the permutation set **9618**. The recommendation may be based at least in part on the combined performance criteria **9526** (FIG. **95**).

[0525] Moving to FIG. **97**, in embodiments, the method **9600** may include applying a first filter to the permutation set **9710**. In embodiments, the first filter may be based at least in part on a Pareto analysis, as described herein. For example, a combination Pareto set may be generated by applying a Pareto analysis to the permutation set **9510**, wherein the combination Pareto set is a subset of the permutation set **9510**. In such embodiments, the recommended items from the permutation set may be members of the combination Pareto set.

[0526] In embodiments, the method **9600** may include applying a second filter to the permutation set **9712** and/or the combination Pareto set. In embodiments, the second filter may be based at least in part on a convex hull analysis, as described herein. In such embodiments, the second filter may be applied to the combination Pareto set wherein the recommended items of the permutation set are on a convex hull of the combination Pareto set.

[0527] Illustrated in FIG. **98** is an apparatus **9800** for implementing the method **9600**. The apparatus **9800** includes a specification receiving circuit **9810** to obtain and/or interpret specification data **9812** corresponding to a specification **9430** (FIG. **94**). In embodiments, the specification may be based at least in part on a globally optimum clinical trial design determined in accordance with the systems and methods described herein. The apparatus **9800** further includes a variation determining circuit **9814** structured to determine clinical trial designs **9456**. Determination of the clinical trial designs **9456** may be based at least in part on the specification data **9812**. The apparatus **9800** further includes a permutation circuit **9816** structured to generate a permutation set **9510** of combinations of the clinical trial designs **9456**. The apparatus **9800** further includes an evaluation circuit **9818** structured to determine combined performance criteria **9526** for each item of the permutation set **9510**. The apparatus **9800** may further include a recommendation circuit **9820** structured to recommend one or more of the permutation set, e.g., select a recommended permutation **9830**. The recommendation **9830** may be based at least in part on the combined performance criteria **9526**.

[0528] In embodiments, the apparatus **9800** may include a first filtering circuit **9822** structured to filter the permutation set **9510**. The first filter **9822** may be based at least in part on a Pareto analysis and generate a combination Pareto set **9824**, as discussed herein. In such embodiments, the recommendation circuit **9820** may be further structured to select the recommendation **9830** from the combination Pareto set **9824**.

[0529] In embodiments, the apparatus **9800** may include a second filtering circuit **9826**. The second filtering circuit **9826** may be based at least in part on a convex hull analysis. In embodiments, the second filtering circuit may filter the combination Pareto set **9824**. In such embodiments, the recommendation circuit **9820** may be further structured to select the recommendation **9830** from the set of points within the combination Pareto set that fall on the convex hull **9828**. Embodiments of the apparatus **9800** may include additional circuits that may perform other types of analysis, e.g., simulated annealing, Monte Carlo, and/or the like.

[0530] As will be appreciated, by generating permutations based on associations **9418**, as described herein, embodiments of the disclosure may determine optimized combinations and/or execution orderings for two or more clinical trials. For example, it may be the case that clinical trial A and clinical trial C can execute at the same facility at the same time with the same administrative staff, while clinical trial B needs to execute after clinical trial C due to dependencies. Embodiments of the current disclosure may also determine whether certain portions/subparts of two or more clinical trials should be executed together (either in time and/or location) or separately (either in time and/or location). In other words, some embodiments of the current disclosure may provide for an overall ordering and/or sequencing of multiple clinical trials, to include ordering of portions/subparts of the clinical trials. Further, filtering the permutation set, as described herein, may reduce the number of non-optimal combinations that need to be considered, thus reducing the amount of time to determine the optimal combination.

[0531] In embodiments, the platform's **104** (FIG. **1**) infrastructure, e.g., components **106**, **108**, **110**, **112**, **138**, and/or **150**, includes engines **128**, models **126** and/or the underlying algorithms, and may be used to optimize clinical designs for robustness against variations in prior probability assessments. In other words, instead of determining optimal clinical trial designs for a given set of scenarios and/or design parameters, some embodiments of the current disclosure may provide for determining robustness for a particular clinical trial design.

[0532] As such, embodiments of the platform **104** may operate in a forward mode of operation and/or an inverse mode of operation. In “forward” operation mode, the platform **104** may be used to provide design recommendations for fixed scenario probabilities over a user selected range of criteria weights, as disclosed herein. In “inverse” operation mode (also referred to herein as “backwards” operation mode), however, the platform **104** may be used to assess the impact of departures from the assumed probabilities of the scenarios (e.g., a departure modeled by multinomial distribution with n=1). In embodiments, the inverse operation mode may be used to compute design performance on multiple criteria for a vector of criteria weights, which may be fixed, while varying multinomial probability vectors. This may be done using algorithms for the forward operation mode by interchanging the role of the multinomial probabilities and the weights. As will be appreciated, this interchanging of roles is possible, in part, due to the mathematical models of the forward and backward modes of operation being duals of each other, in the sense that fixing either the weights or the scenario probabilities typically leads to the same linear model structure for the design performance value.

[0533] A measure of the robustness, also referred to herein as a “robustness value”, of a clinical trial design may correspond to a size of the range of scenario probabilities for which the design is optimal. In embodiments, this range is convex, thus providing for the application of Pareto analysis/optimality, convex hull analysis, and/or simulated annealing. In embodiments, the dimension of the vector of the multinomial distribution for scenarios may be reduced by exploiting uniformity of probabilities over subsets of scenarios (e.g., using three (3) or five (5) ordered categories of likelihood) and/or functional relations between scenario probabilities. This may result in reductions in the number of multinomial vectors and speeds up computations.

[0534] In embodiments, if a user, e.g., **102** (FIG. **1**) provides a prior (e.g., a Dirichlet distribution) over the multinomial probability vector for scenarios the inverse mode of operation computes the posterior distribution for the weighted criterion vector to provide summary measures of robustness such as one or more of the posterior means, standard deviation, and/or credible intervals. As will be appreciated, in embodiments, the forward and inverse modes of operation can be reversed in sequence if there is certainty around weights for criteria and optimal robustness to scenario assumptions is of concern.

[0535] Accordingly, illustrated in FIG. **99**, a method **9900** for determining robustness of a clinical trial design. The method **9900** may provide for operation of the platform **104** in an “inverse” mode of operation, as described herein. As such, the method **9900** includes obtaining a clinical trial design **9910**. In embodiments, the clinical trial design may have been generated in accordance with the “forward” mode of operation of the platform **104**, as described herein. The method **9900** further includes determining a space of scenario probability variations for the clinical trial design **9912**, and evaluating the space of scenario probability variations to determine a robustness of the clinical trial design **9914**.

[0536] Turning to FIG. **100**, another method **10000** for determining robustness of a clinical trial design is shown. The method **10000** may provide for operation of the platform **104** in an “inverse” mode of operation, as described herein. As such, the method **10000** includes obtaining a clinical trial design **10010**. In embodiments, the clinical trial design may have been generated in accordance with the “forward” mode of operation of the platform **104**, as described herein. The method **10000** may include weighting one or more design criteria for the clinical trial design **10012**. The method **10000** may include reducing a dimensionality of the space of scenario probability variations **10018** by evaluating relations between two or more scenarios within the space **10020**. The method **10000** further includes determining a space of scenario probability variations for the clinical trial design **10014**. In embodiments, determining the space of scenario probability variations **10014** is based at least in part on the one or more weighted design criteria. In embodiments, the weights of the design criteria may be fixed. The method further includes evaluating the space of scenario probability variations to determine a robustness of the clinical trial design **10016**. In embodiments, evaluating the space of scenario probabilities **10016** includes conducting a Pareto analysis **10022** and/or a convex hull analysis **10024**.

[0537] Illustrated in FIG. **101** is an apparatus **10100** for determining robustness of a clinical trial design is shown. The apparatus **10100** may form part of the platform **104** and provide for operation of the platform **104** in an “inverse” mode of operation, as described herein. As such, the apparatus **10100** includes a specification processing circuit **10110** structured to interpret clinical trial design data **10112** corresponding to a clinical trial design. In embodiments, the clinical trial design data may have been generated in accordance with the “forward” mode of operation of the platform **104**, as described herein. The apparatus **10100** further includes a space determining circuit **10114** structured to determine, based at least in part on the clinical trial design data **10112**, a space of scenario probability variations **10116** for the clinical trial design. The apparatus **10100** further includes an evaluation circuit **10118** structured to determine, based at least in part on the space of scenario probability variations **10116**, a robustness value **10120** of the clinical trial design. The apparatus **10100** further includes a robustness provisioning **10122** circuit structured to transmit the robustness value **10120**.

[0538] In embodiments, the forward and inverse modes of operations can be executed sequentially over a plurality of iterations. In some examples, designs may be evaluated in the forward mode of operation to evaluate designs. Designs may be evaluated for different performance parameter weights to determine one or more designs of interest for the weights. The designs of interest for the determined weights may be further evaluated to determine the robustness of the designs for scenario. For each design, the platform may be operated in reverse mode for each design of interest to determine the robustness of each design. In some cases, the robustness results may reveal that the design of interest has unsatisfactory robustness. In response to unsatisfactory robustness the platform may be operated in forward mode to find new designs of interest. In some cases, the operation of platform in the forward mode may be modified based on the robustness results. Modifications may include changing weighting of performance criteria, changing design criteria, changing scenario criteria, and the like. Forward mode of operation may be used to find new designs of interest and the platform may be again operated in reverse mode to identify robustness of the new designs of interest. The cycles of forward and reverse operation may be repeated until design with acceptable robustness and performance are found.

[0539] Referring to FIG. **102**, a method **10200** for updating a clinical trial is shown. Since recommendation of globally optimal designs, as disclosed herein, are generally predictive, it is possible that one or more parameters used to determine a globally optimum design for a clinical trial may deviate from what actually occurs during conduction/execution of the trial, i.e., while the trial is underway. For example, a globally optimum design may have been determined based on a scenario where no major worldwide health emergencies occur during the duration of the clinical trial, when, in actuality, a global pandemic emerges shortly after the start of a clinical trial based on the globally optimum design. In such a case, the original globally optimum design may no longer be the optimum design. Updating of a clinical trial, as described herein, may occur multiple times through the course/duration of the clinical trial. In some embodiments, updating of the clinical trial, as described herein, may be performed on a continuous basis throughout the duration of the clinical trial.

[0540] Accordingly, the method **10200** includes obtaining a first simulation output for a first set of clinical trial designs for the clinical trial **10210**. The first simulation output includes first performance parameters, as disclosed herein, associated with each design in the first set of clinical trial designs for a first set of criteria. The method **10200** further includes determining, from the first set of criteria, a first optimality criteria for evaluating the first set of clinical trial designs **10212**. The method **10200** further includes determining, within the first set of clinical trial designs, a first globally optimum design based at least in part on the first optimality criteria and the first performance parameters **10214**. The clinical trial may then be configured based at least in part on the first globally optimum design, e.g., the clinical trial may be made to conform to the globally optimum design.

[0541] As further shown in FIG. **102**, the method **10200** may include conducting/executing the clinical trial based at least in part on the first globally optimum design **10216**. Conduction of the clinical trial may be defined by a start/beginning **10218** of the clinical trial and a stop/end **10220** of the clinical trial. In embodiments, the start **10218** may be the occurrence of the first patient recruitment. In embodiments, the start **10218** may be the occurrence of the first interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. In embodiments, the start **10218** may be the first occurrence of a patient receiving a treatment (including receiving a drug). In embodiments, the stop **10220** may be the last occurrence of patient receiving a treatment (including receiving a drug). In embodiments, the stop **10220** may be the occurrence of the last interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. The time between the start **10218** and the stop **10220** may constitute the duration of the clinical trial as that term is user herein. In embodiments, conduction of the clinical trial may include commencement of any portion and/or process of the clinical trial whether performed in succession and/or intermittently.

[0542] After the start **10218** of the clinical trial, but before the stop **10220**, the globally optimum design may be reassessed. As such, the method **10200** includes obtaining, during conduction of the clinical trial, a second simulation output for a second set of clinical trial designs for the clinical trial **10222**. The second simulation output includes second performance parameters associated with each design in the second set of clinical trial designs for a second set of criteria. In embodiments, the second simulation output may be different than the first simulation output. For example, the second simulation output may be from another evaluation of the clinical trial designs. In embodiments, the second simulation output may be the same as the first simulation output. For example, the first simulation output may be reused. In embodiments, the second performance parameters may be different than the first performance parameters. For example, the second performance parameters may include more or fewer parameters than the first performance parameters. In embodiments, the second performance parameters may be the same as the first performance parameters. In embodiments, the second set of designs may be the same or different than the first set of designs. For example, the second set of designs may include additional designs and/or have removed designs as compared to the first set of designs. In embodiments, the second set of criteria may be the same or different than the first set of criteria. For example, constraints on the clinical trial may have changed since the start **10218**.

[0543] The method **10200** further includes determining, from the second set of criteria, a second optimality criteria for evaluating the second set of clinical trial designs **10224**. In embodiments, the second optimally criteria may be the same or different from the first optimally criteria. For example, a user may have previously determined the globally optimum design with respect to shortest duration and wish to do so again for the second globally optimum design. As another example, a user may have previously determined the globally optimum design with respect to shortest duration and may now wish to determine the globally optimum design with respect to costs.

[0544] The method **10200** further includes determining, within the second set of clinical trial designs, a second globally optimum design **10226**. Determination of the second globally optimum design may be based at least in part on the second optimality criteria and the second performance parameters. The method **10200** may further include adjusting the clinical trial based at least in part on the second globally optimum design **10228**. Adjustment of the clinical trial may include conforming the clinical trial to the second globally optimum design.

[0545] Illustrated in FIG. **103** is another method **10300** for updating a clinical trial. In particular, method **10300** identifies a globally optimum design for a clinical trial after the start **10312** of the clinical trial, but before the end **10314** of the clinical trial, where an initial globally optimum design may not have been determined, or was not determined by an entity performing method **10300**. Accordingly, the method **10300** includes obtaining, during conduction of the clinical trial **10316**, a simulation output for a set of clinical trial designs for the clinical trial **10218**. The simulation output includes performance parameters associated with each design in the set of clinical trial designs for a set of criteria. The method **10300** further includes determining, from the set of criteria, an optimality criteria for evaluating the first set of clinical trial designs **10320**. The method **10300** further includes determining, within the set of clinical trial designs, a globally optimum design based at least in part on the optimality criteria and the performance parameters **10322**. The method **10300** may further include recommending the globally optimum design **10324**. Recommendation may include transmitting the globally optimum design to an entity performing the clinical trial. The recommended globally optimum design may be the first time a globally optimum design was calculated/determined for the clinical trial, or the globally optimum design may be an update to a previously calculated/determined globally optimum design. In embodiments, the method **10300** may not include recommending the globally optimum design, but rather may include adjusting the clinical trial based at least in part on the globally optimum design **10326**. It is to be understood, however, that embodiments of the method **10300** may not include adjusting the clinical trial based at least in part on the globally optimum design. In embodiments, the method **10300** may include both recommending and adjusting the clinical trial based at least in part on the globally optimum design.

[0546] In addition to the design of a clinical trial, the success of the clinical trial often depends on the ability to recruit a satisfactory number of patients, also referred to herein as “subjects”, suitable to participate in the clinical trial. The number of suitable patients available to be recruited for a clinical trial is, in turn, typically a function of the sites selected for the clinical trial, also referred to herein as a “site selection”.

[0547] In some cases, a wrong choice in the selection of sites for a clinical trial may reduce the usefulness of the trial even if the trial is executed without error. In some cases, a wrong choice in the selection of sites for a clinical trial may inhibit and/or prevent completion of the clinical trial, e.g., not enough suitable patients are recruited to satisfy applicable guidelines and/or industry requirements. In some cases, different choices in site selection for a clinical trial may result in very different costs, completion times, and/or other performance parameters for the clinical trial.

[0548] The selection of sites for a clinical trial may include considerations and tradeoffs between hundreds or even thousands of site selections, also referred to herein as site selection options, e.g., different groupings/sets of selected sites. For example, different site selection options, often have different values for performance criteria, e.g., the type of clinical trial being conducted, the minimum and/or maximum number of suitable patients available to be recruited, the time required to complete the clinical trial, the costs associated with conducting the clinical trial, and/or the like. Traditionally, site selection for clinical trials has been based on heuristics and experienced professionals to determine a set of parameters likely to result in a site selection that produces a successful clinical trial. However, traditional approaches are not capable of evaluating more than a handful of site selection options and corresponding tradeoffs. As a result, traditional approaches to site selection often miss site selection options that may result in better performance. As the cost of a clinical trial may exceed tens of millions or even hundreds of millions of dollars and/or may take years to complete, small differences in the performance between site selections for a clinical trial may result in large impacts on the overall cost and/or time associated with the clinical trial.

[0549] The complexity of site selection often requires aspects of statistical expertise, clinical design expertise, and software expertise, which may not be available in many organizations. As such, many organizations fallback on the use of generic site selection methodologies due to their inability to find optimal or near-optimal site selections for a particular clinical trial.

[0550] Accordingly, embodiments of the current disclosure may provide for a site selection platform, systems, and methods for evaluation and/or comparison of site selection options for a clinical trial. In embodiments, evaluation and/or comparison may include a large number of site selection options. In some embodiments, the platform, systems, and methods described herein may be used to evaluate hundreds, thousands, or even millions of site selection options for a clinical trial and may be used to find the optimal or near-optimal site selection for a trial.

[0551] The site selection platform may be used for site selection. In embodiments, a site selection platform may support a team, as described herein, in collaborating and surfacing all the inputs that are key to consider for preparing and selecting an optimal site selection. The site selection platform may use cloud and distributed computing so the team can simulate hundreds of millions of site selection variants/options across all those inputs. The site selection platform may present the team with prioritized options and visualizations to enable the interrogation of the drivers of value.

[0552] A site selection platform may enable a team to quickly identify optimal site selections and the factors that most strongly drive performance factors, strategic goals, and the like. A site selection platform, as described herein, may leverage emerging technologies to provide options for advanced simulations, distributed computing, visualizations, and the like. The site selection platform may leverage methodological knowledge, analysis of the business value of different design choices, and/or analysis of regulatory risk and operational complexity to determine optimum or near optimum site selections. The site selection platform may determine optimum or near optimum site selections by leveraging a novel workflow, speed and/or computing innovations, and/or powerful visualizations for study analysis and optimization.

[0553] A site selection platform may improve how data and processes are used to make better decisions on site selections. Improvements may result from recognizing which innovative options might significantly increase goals. Improvements may be obtained by communicating the benefits of specific site selections in a way that that intuitively allows a variety of team members to understand a particular site selection and/or possible options for the site selection of a clinical trial. A site selection platform may support a team in collaborating and surfacing all the inputs that are key to consider for preparing and selecting an optimal site selection. The site selection platform may present the team with prioritized options and insightful visualizations to enable interrogation of the drivers of value.

[0554] FIG. **104** shows an embodiment of a platform/system for evaluation and comparison of site selections for a clinical trial. The platform **10404** may form part of the platform **104** (FIG. **1**) or the platform **10404** may be stand-alone from the platform **104**. In embodiments, the platform **10404** may communicate with the platform **104** via one or more application programming interfaces (APIs). The platform **10404** may provide for a system for providing users with facilities and methods for determining, evaluating, and/or comparing site selections. The facilities described herein may be deployed in part or in whole through a machine that executes computer software, modules, program codes, and/or instructions on one or more processors, as described herein, which may be part of or external to the platform **10404**. Users may utilize the platform **10404** to identify site selections for criteria, evaluate the site selections, compare site selections, determine optimal site selections, and the like.

[0555] A user may interact with the platform **10404** through one or more user devices **10402** (e.g., computer, laptop computer, mobile computing device, and the like). The platform **10404** may be implemented and/or leverage one or more computing resources **10450** such as a cloud computing service **10452**, servers **10454**, software as a service (SaaS), infrastructure as a service (IaaS), platform as a service (PaaS), desktop as a Service (DaaS), managed software as a service (MSaaS), mobile backend as a service (MBaaS), information technology management as a service (ITMaaS), and the like. The platform **10404** may be provided or licensed on a subscription basis and centrally hosted (e.g., accessed by users using a client (for example, a thin client) via a web browser or other application, accessed through or by mobile devices, and the like). In embodiments, elements of the platform **10404** may be implemented to operate on various platforms and operating systems. In embodiments, interfaces for the user device **10402** through which the users may interact with the platform may be served to the user device **10402** through a webpage provided by a server of the platform **10404**, an application, and the like.

[0556] The platform **10404** may include one or more facilities such as a configuration facility **10406**, simulation facility **10410**, analysis facility **10408**, interfaces facility **10412**, data facility **10438**, and computation resources **10450**.

[0557] The configuration facility **10406** may include advisors **10414**, which may include one or more wizards, tools, algorithms, recommenders, configuration elements, questioners, and the like. Advisors may be used to receive data and/or define or develop space definitions **10416**.

[0558] Space definitions **10416** may include aspects of site selection criteria space **10510** (FIG. **105**). Site selection criteria space may define values, ranges of values, types, ranges of types, and the like that may define general required characteristics of a site selection, as required by a clinical trial. Non-limiting examples of site selection criteria include: maximum and/or minimum duration of the clinical trial, maximum and/or minimum costs of the clinical trial, a minimum and/or maximum number of required patients to complete the trial, and/or the like. In embodiments, site selection criteria space may also include critical dates (the start, stop, duration, and/or milestones of a clinical trial), required protocols, geographic distribution of patients, demographics of patients, and/or the like.

[0559] Space definitions **10416** may include aspects of site selection space **2412** (FIG. **105**). Site selection space **2412** may include the set of parameters and values of the parameters that define different options and variations of sites for implementation of clinical trials. Non-limiting examples of site selection space may include expected patient recruitment, expected patient dropout rate, geographical locations, patient demographics, expected costs, and/or the like. The site selection space may include all possible permutations of the parameters. For example, one site selection may be configured with different expected patient recruitment and different patent dropout rates. The site selection space may include all possible permutations of the different expected costs of the clinical trial for all the different expected patient dropout rates. The site selection space may include all the permutations of all the parameters associated with a site selection. The site selection space may include millions of possible site selection variations. A site selection platform may evaluate all permutations of parameters of the site selection space. A site selection platform may evaluate a partial set of permutations of parameters of the site selection space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically defined, such as according to the site selection criteria parameters.

[0560] Space definitions **10416** may include aspects of site selection scenario space **2414** (FIG. **105**). Site selection scenario space may include the set of parameters and values of the parameters that define different options and variations of scenarios associated with site selections. Site selection scenario space may define the parameters of the environment associated with one or more sites. Non-limiting examples of site selection scenario space include: expected weather conditions, expected pandemics; expected economic conditions; expected resource availability, to include administrative personnel; and/or the like. The site selection scenario space may include all possible permutations of the parameters. For example, one scenario may be configured with a range of values for average patient age and a range of values for average weather conditions, e.g., how will varying weather conditions affect the ability of patients of varying age to participate in a clinical trial. The site selection scenario space may include all the permutations of all the parameters associated with scenarios. The site selection scenario space may include millions of possible scenario variations. A site selection platform may evaluate all permutations of parameters of the site selection scenario space. A site selection platform may evaluate a partial set of permutations of parameters of the site selection scenario space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically or semi-automatically defined, such as according to the site selection criteria parameters.

[0561] Space definitions **10416** may include aspects of site selection performance space **2416** (FIG. **105**). Site selection performance space may include the set of parameters and values of the parameters that define the evaluation criteria for a site selection. Parameters may include: predicted patient recruitment (as estimated by simulation), net present value (NPV), expected NPV, incremental NPV, study cost, incremental study cost, study budget, incremental study budget, time to complete, incremental time to complete, time to market, incremental time to market, clinical utility, incremental clinical utility, probability of regulatory acceptance, incremental probability of regulatory acceptance, probability of success, incremental probability of success, statistical power, incremental statistical power, number of patients, incremental number of patients, number of sites, incremental number of sites, study complexity, incremental study complexity, operational complexity, incremental operational complexity, dose selected, incremental dose selected, statistical design, incremental statistical design, peak revenue, revenue at year five (5), other revenue numbers, incremental revenue, market introduction, whether market introduction beats competition entry, number of treatment arms, hypothesis superiority/equivalence/non-inferiority, other choices around statistical design, treatment effect, hazard ratio, and other choices around estimating the characteristics of the patient population, response, and safety profile, screening criteria, dropout rate, and other choices around modeling/estimating the characteristics and behaviors of the patient population and other factors that impact how the study evolves and its likelihood of achieving its goals (how slowly/quickly patients enroll, etc.), site payments and other choices around operational aspects of the study that can impact how the study evolves and its likelihood of achieving its goals, cost per patient, cost per site, or other cost factors, selections made in other projects (across users within customer companies or organizations and across all users of the platform), priorities set by the customer company or organization, and/or other user-defined filters based on available inputs and outputs of the platform or in the systems and methods described herein. In embodiments, any of the parameters and variables described herein may be incremental parameters and variables. Site selections may be evaluated and compared against all of the parameters of the performance space or a subset of the parameters of the performance space. A set of site selections, e.g., one or more groups each including one or more possible sites, may be evaluated for one or more of the performance parameters. The performance parameters and the values of the performance parameters of site selection and/or clinical trial design define the performance space of the set of site selections.

[0562] The configuration facility **10406** may include a combinations component **10418**. The combinations component **10418** may automatically or semi-automatically define the design space and/or scenario space that may be evaluated by the platform **10404**.

[0563] The simulation facility **10410** of the platform **10404** may, based on the space definitions from the configuration facility **10406**, evaluate the site selections. The simulation facility **10410** may include models **10426**. As used herein with respect to site selection, a model includes the combination of parameters and the values that describe a site selection and/or corresponding clinical trial designs and the scenario under which the site selection is evaluated. Models **10426** may include hundreds or even thousands of models. Models **10426** may include deviation specifications for one or more of the parameters of the models. A deviation specification may define a range of values, a distribution of values, and/or a function of values for one or more parameters of a model. The deviation specifications may be based on expected or previously measured distributions or variations in design parameters.

[0564] The simulation facility **10410** may include engines **10428**. As used herein, engines may relate to the codification of a site selection and/or corresponding clinical trial design that can receive model parameters and run a simulation to generate an output. The output of the engines **10428** may be a predicted behavior for a site selection for one or more corresponding clinical trial designs and/or one or more scenarios and/or conditions. Engines **10428** may evaluate a site selection with analytical methods, mathematical methods, numerical methods, simulation, and/or the like. Evaluating a site selection may include a simulation run to determine performance of the site selection. Evaluating a site selection may include using a Monte Carlo approach to simulate a site selection for different values according to the deviation specifications and using statistical methods to determine the performance of the site selection from a simulation run.

[0565] The simulation facility **10410** may include search/exploration component **10430**. The search/exploration component may facilitate modification of model parameters for simulation. The search/exploration component **10430** may adaptively modify or generate models for simulations based on simulation results of other models/site selections and/or based on triggers and data from other facilities of the platform **10404**.

[0566] The analysis facility **10408** may be configured to analyze simulation results of site selections. The analysis facility **10408** may include a filtering component **10420**. The filtering component **10420** may be configured to use one or more numerical and/or analytical methods to evaluate and compare the performance of evaluated site selections. The filtering component may identify optimal or near-optimal site selections for one or more performance parameters. The filtering component may search the performance space and identify a set of optimal and/or near optimal site selections for one or more performance parameters.

[0567] The analysis facility **10408** may include a recommendation component **10422**. The recommendation component **10422** may provide site selection recommendations. The site selection recommendations may be based on optimal or near-optimal site selections determined by the filtering component **10420**. Recommendations may be adaptive based on settings, feedback, selections, triggers, and the like from the user, and/or other facilities in the platform **10404**.

[0568] The analysis facility **10408** may include an augmenting component, **10424**. The augmenting component may supplement simulation results with real-world data.

[0569] The interfaces facility **10412** may be configured to provide visualizations and interfaces for comparing, searching, and evaluating simulated site selections. Visualization component **10432** may provide for one or more interfaces to visualize the performance of site selections and facilitate comparison of site selections by a user. The feedback analysis component **10434** may track user actions associated with the interfaces and visualizations to determine patterns and/or preferences for site selections. The tradeoff advisor component **10436** may analyze and provide data and guidance for evaluating tradeoffs between two more site selections.

[0570] The platform **10404** may include and/or provide access to one or more data facilities **10438**. Data in the data facilities may include design histories **10440**, simulation data **10442**, site data **10444**, resource data **10446**, population data **10448**, and the like.

[0571] FIG. **105** shows aspects of an embodiment of a process for site selection. The process may include four or more stages. Facilities of the platform **10404** may be configured to implement the stages of the process. The stages of the process may include a configure stage **10502**. The configure stage **10502** may define one or more of the spaces associated with the site selection. The configure stage **10502** may define one or more of site selection criteria space **10510**, site selection design space **10512**, site selection scenario space **10514**, and/or site selection performance space **10516** (FIG. **105**), and **10616** (FIG. **106**). The configure stage **10502** may utilize one or more advisors, wizards, algorithms, and the like for defining the spaces. In some embodiments, the different spaces associated with the configuration stage **10502** may be defined by different members of a team based on the expertise of the members. In some cases, members of a team may have different specializations. For example, some members may specialize in scenarios, while others may specialize in site selection and/or design definitions. Separating the inputs may allow different team members to independently optimize and improve specific models without affecting other inputs. In some embodiments, the inputs may be separated into two or more types based on convenience, expertise, flexibility, and the like.

[0572] The stages of the process may include an evaluate stage **10504**. The evaluate stage **10504** may configure models **10518** for evaluation using simulation **10520** and analytical methods **10524**. The stage may include various methods of enhancing computation and simulation using parallelization and resource management **10522**.

[0573] The stages of the process may include an augment stage **10506**. The augment stage **10506** may add real-world data to the simulation data. Financial data **10526**, regulatory data **10528**, revenue data **10530**, and the like may be added to the and used to augment data from simulations.

[0574] The stages of the process may include an explore and analyze stage **10508**. The explore and analyze stage **10508** may include filtering methods and algorithms **10532** for identifying optimal site selections. The stage may include generating and interacting with visualizations **10534** and tradeoff analysis tools **10536** to compare and select site selections.

[0575] In embodiments, the platform **10404** (FIG. **104**) may be configured for identification and confirmation of optimal site selections for a clinical trial. Optimality of site selection may be in relation to site selection criteria, e.g., a parameter within site selection criteria space **10510** (FIGS. **105** and **106**). For example, embodiments of the current disclosure may provide for the determination of a site selection for a clinical trial as being the most likely site selection to result in the highest number of diabetic patients being recruited to participate in the clinical trial. Site selection criteria may be determined in relation to the site selection performance space **10516** (FIGS. **105** and **106**). Optimality of the site selection criteria may be in relation to one or more site selection performance parameters, e.g., a parameter within site selection performance space **2414**, and the values thereof. An optimal site selection may be a site selection that achieves a most desirable value for one or more specific site selection performance parameters. A most desirable value may depend on the site selection performance parameter and may be different for each site selection performance parameter. In some cases, the most desirable value may be the highest value of a site selection performance parameter. In some cases, the most desirable value may be the lowest value of a site selection performance parameter. In some cases, the most desirable value may be a range of values, a specific value, a function of values, and the like. For example, in some cases an optimal site selection with respect to a cost site selection performance parameter may be a site selection that has the lowest cost and achieves the goals of the clinical trial. As another example, an optimal site selection with respect to a time site selection performance parameter may be a site selection that has the highest NPV and achieves the goals of the clinical trial.

[0576] In embodiments, an optimum site selection is a site selection that achieves most desirable values for two or more specific site selection performance parameters. In the case of optimality for multiple site selection performance parameters, optimality may require a tradeoff between the parameter values. For example, a site selection that has a lower cost may have a low NPV and therefore may not be desirable. The optimality of a site selection may be based on a function of site selection performance parameters. In some cases, a function may be a weighted sum of the site selection performance parameters. A function, or a set of functions, may be used to generate an overall score (or a set of scores) and the score may be used to determine the optimality of the site selection. A highest score, a specific score, lowest score, and the like may be considered optimal depending on the function used to compute the score.

[0577] In embodiments, optimality may be evaluated according to Pareto optimality. Pareto optimal site selections may be site selections where no individual site selection performance parameter can be better off without making at least one other individual site selection performance parameter worse off. In some cases, optimality may be determined using convex hull analysis.

[0578] In some cases, one site selection may be globally optimum. In some cases, more than one site selection may be globally optimum. In some cases, no site selections may be globally optimum. In some embodiments, optimality of site selection may be relative to a benchmark. A known site selection, a set of historical site selections, and/or the like may be used as a benchmark. Site selections may be considered optimal if they meet, exceed, and/or are within a threshold distance of the benchmark site selection performance parameters.

[0579] Site selection performance parameters that may be used to determine site selection optimality may be user defined, system defined, algorithmically defined, and/or the like. In some cases, users may specify a subset of site selection performance parameters that should be used to identify optimal site selections. A user may define optimality criteria by defining ranges, values, characteristics, and the like of the parameter values that may be considered desirable and/or optimal. Interactive graphical interfaces may be provided to a user to evaluate different site selections based on one or more optimality criteria. Interactive interfaces may allow a user to explore different site selections by changing scoring methods, weights associated with the criteria, and the like.

[0580] In embodiments, the characteristics of site selection performance parameters for evaluated site selections may be analyzed by the platform to determine if any of the parameters may be less important for optimality. For example, analysis may include evaluation of ranges, variability, and other statistical analysis. If one or more site selection performance parameters for all evaluated site selections is within a desirable range, or the site selection performance parameter is almost equal for all of the evaluated site selections, the site selection performance parameter may be removed and identified as less significant for optimality and, in some cases, may not be factored in when determining optimality. Prior to determining optimality based on site selection performance parameters, the site selection performance parameters and the values of the site selection performance parameters may be grouped, filtered, normalized, and the like.

[0581] Optimality of site selections may be redefined automatically, semi-automatically, in response to user input, and/or the like. The criteria for optimality of site selections may change as site selections are evaluated by the platform. For example, initial optimality criteria may produce no optimal site selections. In response to no optimal site selections being determined, the criteria may be changed (relaxed, increased, decreased, etc.) until at least one site selection is considered optimal. In another example, optimality criteria may change in response to user feedback. Users may evaluate initial site selections found to be optimal and provide feedback (direct feedback and/or indirect feedback that can be derived from user actions and inactions). The feedback from the user may be used to change how optimality is determined, which site selection performance parameters are used to determine optimality, the values of the site selection performance parameters that are considered optimal, and/or the like.

[0582] In some embodiments, site selection performance parameters may be grouped, ordered, and/or organized into one or more hierarchies, groups, and/or sets. Two or more different optimality criteria may be used in parallel to determine multiple sets of optimal site selections under different criteria. Two or more different optimality criteria may be used sequentially to determine optimal site selections. One criteria may first be used to identify a first set of optimal site selections under first criteria. A second set of criteria may then be used on the first set to reduce the set of optimal site selections.

[0583] In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to all possible site selection options. In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to possible site selection options for one or more criteria. In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to a large percentage (such as 80% or more) of possible site selection options for one or more criteria. In embodiments, a site selection may be globally optimum if the optimality of the site selection is within a high confidence level (90% confidence) with respect to possible site selection options for one or more criteria.

[0584] Traditional methods for evaluating site selections cannot determine global optimum site selections since they evaluate one, several, or a small subset of site selection options. Traditional methods do not consider all or almost all of the site selection options and cannot find a global optimum.

[0585] Trial site selections may involve numerous variables, parameters, considerations, tradeoffs, and the like resulting in a very large number of possible variations. A large number of possible variations makes study site selections and optimization using traditional methods difficult. In many cases, traditional methods may fail to explore or consider the complete space of possible trial site selection options and may miss or never consider globally optimal site selections. Using traditional methods, the number of site selection variations that may be explored in a reasonable time is limited. In some cases, only one (1) statistical site selection and only three (3) clinical scenarios may be evaluated. The best site selection study of the limited number of variations may not result in a globally optimal site selection. A locally optimum site selection chosen from a limited number of considered site selections may represent one (1) local maximum but may be far from the globally optimum site selection. When 10,000 or more clinical scenarios are considered, a globally optimum site selection may be distinguished from the many locally optimum site selections. However, consideration of 10,000 clinical scenarios cannot be practically performed using traditional methods as it would require an estimated 50,000 hours or more to complete.

[0586] In embodiments, the platform and methods described herein may evaluate thousands or even millions of site selection options enabling a determination of a global optimum site selection. In many cases, the globally optimum site selection may have significant advantages over locally optimum site selection. In one example, a globally optimum site selection may require less time to complete than other site selections.

[0587] In embodiments optimization of trial site selections may occur sequentially after optimization of trial design. In one embodiment, a globally optimum trial design may be determined using the techniques described herein. After the globally optimum trial design is determined a globally optimum trial site selection may be determined for the determined trial.

[0588] Referring again to FIG. **104**, the platform **10404** may receive and/or determine performance space using the configuration facility **10406**. Performance space may be defined in the space definitions component **10416**. The performance space may be configured based on input from users and/or based on data **10438** such as history data **10440** and/or simulation data **10442**. In embodiments data **10438** may include external data from external data sources and providers. In one instance, performance space may define optimality criteria. Optimality criteria may define site selection performance parameters, performance values, functions, methods, and algorithms for evaluating optimality and/or global optimality of site selections. In one instance optimality criteria may be configured by the user or determined from benchmark site selections from history **10440** and/or simulation **10442** data. In another instance, optimality criteria may be defined from simulation data from the simulation facility **10410**. Optimality of site selections may be determined in the analysis facility **10408**. The filtering component **10420** may be used to determine one or more sets of globally optimum site selections from the site selections evaluated by the simulation facility **10410**.

[0589] FIG. **106** shows aspects of an apparatus/optimality analysis component **10602** for determining global optimality of site selections. In embodiments, the optimality analysis component **10602** may be part of the analysis facility **10408** of the platform **10404**. The optimality analysis component **10602** may receive data from simulated site selections **10612** and determine one or more sets of optimal site selections **10622**, **10624**. The optimality analysis component **10602** may include one or more circuits for determining optimality of site selection. In embodiments, the optimality analysis component **10602** may include circuits for determining optimality based on optimality functions **10628**. Optimality functions **10628** may determine optimality of site selections based on different weighting of performance factors of the simulated site selections. In embodiments, the optimality analysis circuit **10602** may include circuits for determining optimality based on benchmark analysis **10604**. A benchmark analysis circuit **10604** may determine optimality of site selections based on a comparison of site selection performance parameter values to one or more benchmark site selections such as from historical data **10614** and/or simulation data **10612**. In embodiments, the optimality analysis circuit **10602** may include circuits for determining optimality using sequential analysis **10608** and/or parallel analysis **10610**. The sequential analysis circuit **10608** and parallel analysis circuit **10610** may use one or more different optimality functions **10628** in parallel or sequentially to determine optimal site selections. In embodiments, the optimality analysis circuit **10602** may include circuits for dynamically modifying optimality criteria **10606**. User inputs **10620**, simulation data **10612**, and/or the determined sets of optimal site selections may be monitored and analyzed to determine modifications to optimality criteria. In embodiments, the optimality analysis circuit **10602** identifies a confidence level **10626** associated with the optimality of sets of optimal site selections. In the case where simulation data **10612** may not include simulations of all site selection options for the criteria space **10618**, the optimality circuit **10602** may determine, based on the simulated site selections, a confidence level that the determined optimal site selections are indeed optimal for a given optimality criteria.

[0590] FIG. **107** shows aspects of an apparatus **10700** for determining global optimality of site selections. In embodiments, the apparatus **10700** may include an optimality analysis circuit **10714** which may be part of the analysis facility **10408** of the platform **10404** (FIG. **104**). In embodiments, the apparatus **10700** may include a data processing circuit **10706** structured to interpret/obtain site selection data **10702** of a clinical trial site selection. In some embodiments the site selection data **10702** may be outputs of simulation data of trial site selections. The output processing circuit **10706** may transform the site selection data **10702** into a format suitable for use by the various circuits in the apparatus. For example, the site selection data **10702** may be received by the data processing circuit **10706** and determine and identify site selection performance parameters in the data. In some embodiments, some site selection performance parameters may be grouped, filtered, converted, normalized, and the like.

[0591] The apparatus **10700** of FIG. **107** may further include an optimality determining circuit **10708** structured to receive processed site selection data from the data processing circuit **10706**. The optimality determining circuit **10708** may identify globally optimum site selections **10712** based on one or more optimality criteria. In some embodiments, the globally optimum site selections **10712** may be provided as an output of the apparatus. In some embodiments, globally optimum site selections **10712** may be further processed by the site selection analysis circuit

10710. The site selection analysis circuit **10710** may analyze the globally optimum site selections **10712**, determine characteristics of the site selections, and receive feedback data **10704** about the site selections. The site selection analysis circuit may, based on the determined characteristics, determine modifications for optimality criteria used in the optimality determining circuit **10708**. Using modified optimality criteria, the optimality determining circuit **10708** may determine a new set of globally optimum site selections **10712**.

[0592] As shown in FIG. **108**, a method **10800** for determining globally optimum site selections may include simulating all site selection options for a site selection criteria **10802**. The method **10800** may further include determining an optimality criteria for evaluating simulated site selections **10804**. Optimality criteria may be a function of one or more performance values for each site selection such as a weighted sum of the values, a comparison of the values, and the like. The method **10800** may include searching for globally optimum site selections in the simulated site selections using the determined optimality criteria **10806**. The globally optimum site selections may be recommended to one or more users **10808**.

[0593] As shown in FIG. **109**, a method **10900** for determining globally optimum site selections may include simulating site selection options for a site selection criteria **10902**. The method **10900** may further include determining a first optimality criteria for evaluating simulated site selections **10904**. The method **10900** may further include determining a second optimality criteria for evaluating simulated site selection(s) **10906**. The method **10900** may include determining a first set of optimum site selections using the first optimality criteria, the first set may be determined from the simulated site selections **10908**. The method **10900** may further include determining a second set of optimum site selections using the second optimality criteria, the second set may be determined from the first set of site selections **10910**. The globally optimum site selections may be recommended to one or more users **10912**.

[0594] As shown in FIG. **110**, a method **11000** for determining globally optimum site selections may include simulating site selection options for a site selection criteria **11002**. The method **11000** may further include determining a first optimality criteria for evaluating simulated site selections **11004**. The method **11000** may include determining a first set of optimum site selections using the first optimality criteria, the first set may be determined from the simulated site selections **11006**. The method **11000** may further include identifying characteristics of site selections in the first set of globally optimum site selections **11008**. The method **11000** may further include determining a second optimality criteria for evaluating simulated site selections based on the identified characteristics **11010**. The method **11000** may include determining a second set of globally optimum site selections using the second optimality criteria from the simulated site selections **11012**.

[0595] Illustrated in FIG. **111** is a method **11100** for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure. The method **11100** includes determining a plurality of possible sites for recruiting patients from for a clinical trial **11110**. The method **11100** further includes determining, for each of one or more subgroupings of the plurality of possible sites, a predicted patient recruitment value **11112**. The method **11100** further includes determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes a desired site selection criteria **11114**. In embodiments, determining the predicted patient recruitment value for each of the subgroupings of the plurality of possible sites includes simulating each of the subgroupings **11116**. In embodiments, simulating each of the one or more subgroupings may be based at least in part on use of different types of engines, e.g., engines with different version numbers and/or developed by different entities, e.g., in-house vs third-party vendor. In embodiments, the differences in types of engines may include underlying types of algorithms and/or assumptions, e.g., rounding rules. In embodiments, the method **11100** may further include determining one or more site selection parameters **11118**. In such embodiments, simulating each of the one or more subgroupings **11116** may be based at least in part on the one or more site selection parameters. In embodiments, the one or more site selection parameters may be based at least in part on: a country; a state/province; a county; a city; a zip code; and/or a patient enrollment matriculation number. In embodiments, the method **11100** may further include determining the desired site selection criteria **11120**. In such embodiments, simulating each of the one or more subgroupings **11116** may be based at least in part on the determined site selection criteria. In embodiments, the determined site selection criteria may be based at least in part on: a number of required patients; a start date of the clinical trial; an end date of the clinical trial; and/or a total cost of the clinical trial. In embodiments, determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria **11114** may include and/or be based at least in part on: a convex hull engine; a Pareto engine; a Monte Carlo engine; and/or a simulated annealing engine. In embodiments, determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria **11114** may be based at least in part on a machine learning engine, as described herein. For example, in embodiments, a neural network may be trained to look at past site selections and their outcomes and predict one or more site selection criteria. In embodiments, the neural network may be trained via supervised learning and/or by unsupervised learning, e.g., cost-based policies.

[0596] Turning to FIG. **112**, an apparatus **11200** for determining a site selection to globally optimize patient recruitment for a clinical trial, in accordance with an embodiment of the current disclosure, is shown. The apparatus **11200** may form part of the platform **10404** or it may be stand-alone from the platform **10404** and/or communicate with the platform **10404** via one or more application programming interfaces (APIs). The apparatus **11200** includes a site selection data processing circuit **11210** structured to interpret possible site selection data **11212** identifying a plurality of possible sites for recruiting patients from for a clinical trial. The apparatus **11200** further includes a patient recruitment determination circuit **11214** structured to determine a predicted patient recruitment value **11216** for each of one or more subgroupings of the plurality of possible sites. The apparatus **11200** further includes a site searching circuit **11218** structured to determine which subgrouping **11220** of the plurality of possible sites has a predicted patient recruitment value that globally optimizes a desired site selection criteria **11230**. The apparatus **11200** further includes a site selection provisioning circuit **11222** structured to transmit the subgrouping **11220** of the plurality of possible sites that has the predicted patient recruitment value that globally optimizes the desired site selection criteria. In embodiments, the patient recruitment determination circuit **11214** is further structured to determine the predicted patient recruitment value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In embodiments, simulating each of the one or more subgroupings is based at least in part on use of different types of engines, as described herein. In embodiments, the apparatus **11200** may include a user input circuit **11224** structured to interpret user input data **11226** and a criteria determining circuit **11228** structured to determine the desired site selection criteria **11230** based at least in part on the user input data **11226**. In embodiments, the site searching circuit **11218** may include a convex hull engine; a Pareto engine; a Monte Carlo engine; and/or a simulated annealing engine.

[0597] Referring to FIG. **113**, embodiments of the current disclosure may provide for a design platform **11300** with an interface **11310** for configuring and managing the platform **10404** with respect to optimizing site selection for patient recruitment for a clinical trial. The design platform **11300** may provide for pre-simulation determination of one or more selection parameters, e.g., values within site selection criteria space **10510**, site selection space **10512**, site selection scenario space **10514** and/or site selection performance space **10516**. Some embodiments may provide for adjustment of selection parameters during a simulation. The interface **11310** may include a canvas area **11312** for visualizing/editing/creating selection parameters for use by the platform **10404**

(FIG. **104**). Embodiments of the interface **11310** may be a graphical user interface (GUI) that has one or more input fields **11314** for inputting or selecting selection parameters. The input fields **11314** may be sliders, text boxes, moveable components, and/or other GUI user input widgets. The graphical user interface may also provide for a heat map for selecting possible sites. The heat map may provide for filtering of the possible sites. In embodiments, the platform **11300** may provide, via servers **10454** (FIG. **104**) multiple interfaces, e.g., interfaces **11310**, **11316**, **11318**, for collaborative configuration of the platform **10404** by one or more users. In embodiments, the interfaces **11310**, **11316**, **11318** may be configured differently for different users, e.g., an interface may be tailored to a type of user and/or target audience, e.g., clinical trial experts, novices, and/or other types of users of varying skill levels in clinical trial designs and/or site selection. Tailoring of an interface to a user type may include enabling and/or disabling certain features and/or options on the interface. In embodiments, collaboration between users may involve a first user operating on a first interface **11310** receiving inputs from a second interface **11316** operated by a second user. In embodiments, the interface **11310** may provide for weighting of one or more selection parameters. In embodiments, the interface **11310** may provide for configuration of the simulation component **10410** (FIG. **104**). For example, a user operating the interface **11310** may configure the simulation component **10410** to perform an exhaustive search and/or simulation of site selection options. In embodiments, a user operating the interface **11310** may configure the simulation component **10410** to perform a non-exhaustive search and/or simulation of site selection options. In embodiments, the interface **11310** may provide for a user to configure the platform **10404** to user one or more of a convex hull engine, a Pareto engine, a Monte Carlo engine, and/or simulated annealing engine. In embodiments, the interface **11310** may provide for a user to configure a training set for a machine learning engine to learn how to optimize site selections with respect to patient recruitment, as disclosed herein.

[0598] Turning to FIG. **114**, a method **11400** for collaborative configuration of a site selection platform **10404** for optimization of patient recruitment for a clinical trial is shown. The method **11400** includes displaying a graphical user interface structured to configure a system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria **11410**. The method further includes receiving, via the graphical user interface, one or more user inputs that define one or more selection-parameters used by the system **11412**. The method further includes storing the defined selection-parameters in a memory device **11414**.

[0599] Shown in FIG. **115** is an apparatus **11500** for providing collaborative configuration of a site selection platform **10404** for optimization of patient recruitment for a clinical trial is shown. The apparatus **11500** includes a display generation circuit **11510** structured to generate a graphical user interface **11512** for configuring a system **10404** for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria. The apparatus **11500** further includes a display transmission circuit **11514** structured to transmit the graphical user interface **11512** to an electronic device for display, e.g., **10402** (FIG. **104**). The apparatus **11500** further includes a user interaction circuit **11516** structured to: interpret user inputs **11518** received by the graphical user interface **11512**; and in response to, and based at least in part on, interpreting the user inputs **11518**, define selection parameters **11520** used by the system **10404**. The apparatus **11500** further includes a selection-parameter provisioning circuit **11522** structured to store the defined selection-parameters **11520** in a memory device, e.g., **10438** (FIG. **104**).

[0600] Shown in FIG. **116** is another method **11600** for collaborative configuration of a site selection platform **10404** for optimization of patient recruitment for a clinical trial. The method **11600** includes configuring, via a graphical user interface, a recruitment site selection system via entering one or more user inputs into the graphical user interface that define one or more selection-parameters **11610**. The method **11600** further includes determining, via the recruitment site selection system, which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria **11612**. The method further includes transmitting data identifying the determined subgrouping **11614**.

[0601] Referring to FIG. **117**, embodiments of the disclosure may provide for a platform/system **11700** with an interface **11710**, e.g., a wizard, for guiding a user through configuring a site grouping/selection system/platform **10404** (FIG. **104**) for optimizing site selection for patient recruitment for a clinical trial. In embodiments, the interface **11710** may be generated by a server **10454** (FIG. **104**). The interface **11710** may be command line based or graphical user interfaced based. The interface **11710** may generate a plurality of prompts **11712** that assist in obtaining initial selection parameters, e.g., criteria, from users to determine parameters for site selection criteria space **10510**, site selection space **10512**, site selection scenario space **10514**, and/or site selection performance space **10516**. The plurality of prompts **11712** may ask for a variety of static inputs or ranges. The inputs may include the type of engine **10428** to use in the simulation **10410**. The inputs may also include the type of search algorithm **10430** used. The inputs may include the type of sensitivity analysis algorithms or tools that are preferred. The inputs may include the type of clinical trial. The interface **11710** may recommend one or more site groupings/selections based on the type of clinical trial. The recommended site groupings/selections may serve as a starting base for further modification by a user. Artificial intelligence/machine learning approaches may be used to generate the prompts **11712** and/or suggestions for the user through the configuration process. As will be appreciated, the suggestions and/or guiding by the interface **11710** may allow a user to avoid (or reduce) spending time and resources (including computing resources and the costs of those resources) on sub-optimal simulations.

[0602] In an embodiment, a method for guiding a user through configuring a site grouping/selection system/platform for optimizing site selection for patient recruitment for a clinical trial is provided. The method includes generating an interactive interface. The method further includes presenting, via the interactive interface, a plurality of prompts to a user structured to configure a site selection system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria. The method further includes for each of the plurality of prompts, receiving a responsive user input, and configuring the site selection system based at least in part on the responsive user inputs.

[0603] In another embodiment, a system for guiding a user through configuring a site grouping/selection system/platform for optimizing site selection for patient recruitment for a clinical trial is provided. The system includes a server structured to determine which subgrouping of a plurality of possible sites for recruiting patients from for a clinical trial globally optimizes a desired criteria. The system further includes an electronic device, e.g., **10402**, structured to: display an interactive interface that presents a plurality of prompts to a user for configuring the server; for each of the plurality of prompts, receive a responsive user input; and configure the server based at least in part on the responsive user inputs.

[0604] In another embodiment, a non-transitory computer readable medium storing instructions is provided. The stored instructions, when loaded into at least one processor, adapt the at least one processor to: generate an interactive interface; and present, via the interactive interface, a plurality of prompts to a user. The plurality of prompts are structured to configure a site selection system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria. The stored instructions further adapt the at least one processor to, for reach of the plurality of prompts, receive a responsive user input; and configure the site selection system based at least in part on the responsive user inputs.

[0605] Embodiments of the current disclosure may provide for prediction of an initial site grouping/selection with respect to patient recruitment of a clinical trial. In embodiments, the initial site selection may be structured to maximize (globally optimize) one or more desired criteria, e.g., one or more parameters within site selection criteria space **10510**, site selection space **10512**, site selection scenario space **10514**, and/or site selection performance space **10516**, based on historical data. For example, in embodiments, a predicted initial site selection may correspond to maximizing a number of patients with a particular medical condition. In other embodiments, the predicted initial site selection may correspond to maximizing the number of recruited patients who are likely to complete the clinical trial.

[0606] In embodiments, the historical data may include data from previously conducted clinical trials and/or it may include data from prior simulated clinical trials. In embodiments, the data may be stored in data facility **10438** and/or be generated by the simulation component **10410** and/or the analysis components **10408**. Data from past trials may be used to directly predict aspects of sites. Data from past trials may be used as a guide to determine parameters of the trials that were successful since in many cases, past indicators of success may translate to future success. For example, sites identified as having a high historical recruitment rate may generally be expected to have high recruitment rate for a future study. However, in some cases, depending on the parameter, a high success rate in historical data may translate to a negative or less favorable prediction for the current site selection. For example, a site as having a historical high recruitment for patients with a rare disease may translate to a prediction for low recruitment of the same type of patients for a new study. In some cases, depending on the therapeutic tested, a waiting period for the patients involved in the previous study may be required before they are allowed to participate in a new study making the patients unavailable for a new study. Therefore, an indication of high success in historical data may indicate that the patients will not available and may indicate a low performance for a planned study in the site. In embodiments, models for site selection may be evaluated for negative and positive associations between historical performance and expected current performance.

[0607] The prediction may be generated prior to receiving user input or after receiving some user input e.g., via user device **10402**. The predicted initial site grouping/selection may be displayed in a graphical user interface, e.g., interface component **10412**, for adjustment by a user. The predicted initial site grouping/selection may be the grouping/selection actually used in the clinical trial, or it may serve as a starting point which the user can configure/tweak as desired. The predicted initial site grouping/selection may be the global optimal, with respect to the desired site selection criteria; or it may be close to the global optimal, wherein a user can tweak it, i.e., make adjustments, to be the global optimal. The initial prediction may reduce the amount of time to find the global optimum by providing the user (or computer) with a good starting point based on knowledge gained from historical data. Simulated annealing, e.g., via the search/exploration modules/engines **10430**, may be applied to the initial prediction to test the surrounding subgroupings. Artificial intelligence may be used to analyze the historical data based on known desired criteria for the clinical trial. For example, in embodiments, a neural network may be trained on historical data to identify patterns in site selections that result in particular values for one or more site selection criteria. The neural network may then process site selection data, i.e., data regarding possible sites for a clinical trial, and then generate a predicted initial site selection.

[0608] Accordingly, referring to FIG. **118**, a method **11800** for prediction of an initial site grouping/selection with respect to patient recruitment of a clinical trial is shown. The method **11800** includes accessing past trial site selection data stored in a database **11810**. The method **11800** further includes predicting, based at least in part on the past trial site selection data, the initial site selection **11812**. In embodiments, predicting the initial site selection may be based at least in part on artificial intelligence, as disclosed herein. The initial site selection may correspond to a global optimization of a desired site selection criteria. The method **11800** further includes evaluating the initial site selection with respect to being the global optimization (with respect to the desired site selection criteria) **11814**. Such evaluation may be based at least in part on a convex hull engine, a Pareto engine, a Monte Carlo engine, or a simulated annealing engine, as disclosed herein. The method **11800** may further include displaying the initial site selection in a graphical user interface **11816**. In embodiments, the desired site selection criteria may include a number of required patients; a start date of the clinical trial; an end date of the clinical trial; and/or a total cost of the clinical trial. In embodiments, the desired site selection criteria may be based at least in part on a patient recruitment related number, e.g., a minimum and/or maximum number of patients required to be recruited by the clinical trial guidelines, a minimum number of patients required to complete the clinical trial, and/or the like. In embodiments, the method **11800** further includes adjusting the initial site selection via the graphical user interface **11818**. In embodiments, the method **11800** may further include interpreting one or more user inputs, wherein the prediction of the initial site selection is based at least in part on the one or more user inputs **11820**. In embodiments, the method **11800** may further include simulating the initial site selection to determine performance criteria **11822**. In embodiments, the method **11800** may further include conducting a sensitivity analysis of the initial site selection **11824**, e.g., via analysis component **10408**.

[0609] Illustrated in FIG. **119** is an apparatus **11900** for prediction of an initial site grouping/selection with respect to patient recruitment of a clinical trial. The apparatus **11900** includes a past trial data processing circuit **11910** structured to interpret past trial site selection data **11912**. The apparatus **11900** further includes a patient recruitment prediction circuit **11914** structured to generate, based at least in part on the past trial site selection data **11912**, initial site selection data **11916** for recruiting patients for a clinical trial. The initial site selection data corresponds to a global optimization of a desired site selection criteria. The apparatus **11900** further includes a patient recruitment evaluation circuit **11918** structured to evaluate the initial site selection data with respect to the global optimization. The apparatus **11900** further includes a prediction provisioning circuit **11920** structured to transmit the initial site selection data **11916**.

[0610] Embodiments of the current disclosure may also provide for a method for using the initial site selection. The method may include receiving an initial site selection for recruiting patients for a clinical trial; and conducting a clinical trial based as least in part on the initial site selection. The initial site selection may correspond to a global optimization of a desired criteria, wherein the initial site selection was predicted from past trial site selection data. For example, a first entity may generate initial site selection data and send it to a second entity that conducts a clinical trial based at least on part on the initial site selection data.

[0611] Referring now to FIG. **120**, embodiments of the current disclosure may provide for a platform/system **12000** that generates an interactive interface **12010**, e.g., a GUI, for exploration/evaluation of spaces related to patient recruitment for a clinical trial, as opposed to merely facilitating selection of proposed sites, for the purpose of globally optimizing site selection for a clinical trial to achieve a desired patient recruitment, e.g., a maximum number of recruited patients. The spaces may include site selection criteria space **10510**, site selection space **10512**, site selection scenario space **10514**, and/or site selection performance space **10516**. In embodiments, generation of the site selections and/or evaluation of the spaces may be based at least in part on convex hull, Pareto frontiers, Monte Carlo, simulated annealing, and/or machine learning, e.g., artificial intelligence, as described herein.

[0612] Exploration/evaluation of the spaces may provide insights to a user regarding known and/or unknown constraints on site selection and/or the impact a particular selection parameter, e.g., a parameter within one of the spaces, may have on patient recruitment.

[0613] Exploration of the spaces may be facilitated via visualizations of the spaces. The visualizations may include, and/or be based at least in part on, heatmaps and/or tornado graphs. The interface **12010** may include a canvas area **12012** for rendering (or rasterizing) the visualizations.

[0614] The interface **12010** may provide for users to adjust one or more selection parameters and/or adjust sites within one or more proposed site selections/groupings and see the effect on the predicted patient recruitment. Adjustment of the selection parameters may be facilitated by one or more interactive widgets **12014**, e.g., text boxes, buttons, sliders, and/or the like. In embodiments, adjustment of the selection parameters may be facilitated via the canvas **12012**. In embodiments, the interface **12010** may allow users to evaluate and compare possible site selections/groupings side-by-side.

[0615] In embodiments, exploration of the spaces may provide for sensitivity analysis. For example, embodiments of the interface **12010** may incorporate simulated annealing engines, as described herein.

[0616] In embodiments, platform/system **12000** may include a server, e.g. server **10454** in the computation resources **10450** of platform **10404**. The server **10454** may generate the interface **12010** as a web application, remote desktop, and/or other suitable architecture for providing the interface **12010** to users and/or user devices **10402**.

[0617] The platform may support collaboration among different users. For example, the server **10454** may generate multiple interfaces **12010**, **12016**, and **12018**. In embodiments, the interfaces **12010**, **12016**, and **12018** may be configured/tailored to different types of user/target audience, e.g., users with different levels of experience and/or knowledge with respect to evaluating site groupings/selection for various criteria. For example, a first interface **12010** for an expert user may have more functionality, e.g., access to more options and/or features, than a second interface **12016** for a novice user.

[0618] Turning to FIG. **121**, a method **12100** for exploring/evaluating spaces related to patient recruitment for a clinical trial is shown. The method **12100** includes generating a graphical user interface structured to provide for interactive exploration of one or more spaces corresponding to one or more selection parameters for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired site selection criteria **12110**. The method **12100** further includes adjusting at least one of the selection parameters via the graphical user interface **12112**. The method **12100** further includes updating the graphical user interface in response to adjusting the at least one selection parameter **12114**. In embodiments, the desired selection criteria may be based at least in part on a patient recruitment related number. In embodiments, generating the graphical user interface occurs prior to simulating, as disclosed herein, any one of the possible sites. In embodiments, generating the graphical user interface occurs after simulation of one or more of the possible sites.

[0619] Illustrated in FIG. **122** is a non-limiting embodiment of an apparatus **12200** for exploring/evaluating spaces related to patient recruitment for a clinical trial. The apparatus **12200** includes a patient recruitment space processing circuit **12210** structured interpret space data **12212** corresponding to one or more spaces, e.g., **10510**, **10512**, **10514**, and/or **10516**, related to subgroupings of possible sites for use in conducting a clinical trial. The apparatus **12200** further includes a graphics circuit **12214** structured to generate interactive interface data **12216** in response to the space data **12212**. The interactive interface data **12216** may correspond to a computerized interface **12010** for globally optimizing a desired site selection criteria. The apparatus **12200** further includes a user input circuit **12218** structured to receive user input data **12220** responsive to the presentation of the interactive interface data **12216**. The apparatus **12200** further includes a patient recruitment space exploration circuit **12222** structured to modify the interactive interface data **12226** in response to the user input data **12220**. The apparatus **12200** further includes an interactive provisioning **12224** circuit structured to transmit the modified interactive interface data **12226**.

[0620] Referring to FIG. **123**, a method **12300** for updating patient recruitment is shown. Since recommendation of globally optimal site selection, as disclosed herein, are generally predictive, it is possible that one or more parameters used to determine a globally optimum site selection for a clinical trial may deviate from what actually occurs during conduction/execution of the trial, i.e., while the trial is underway. For example, a globally optimum site selection may have been determined based on a recruitment scenario where no major worldwide health emergencies occur during the duration of the clinical trial, when, in actuality, a global pandemic emerges shortly after the start of a clinical trial. In such a case, the original globally optimum site selection may no longer be the optimum. Updating of a site selection, as described herein, may occur multiple times through the course/duration of the clinical trial. In some embodiments, updating of the site selection, as described herein, may be performed on a continuous basis throughout the duration of the clinical trial.

[0621] Accordingly, the method **12300** includes obtaining a first simulation output for a first set of site selections for a clinical trial **12310**. The first simulation output includes first site selection performance parameters, as disclosed herein, associated with each design in the first set of site selections for a first set of site selection criteria. The method **12300** further includes determining, from the first set of site selection criteria, a first optimality criteria for evaluating the first set of site selections **12312**. The method **12300** further includes determining, within the first set of site selections, a first globally optimum site selection based at least in part on the first site selection optimality criteria and the first site selection performance parameters **12314**. Optimum site selections may be determined using one or more of Pareto analysis, convex hull analysis, and/or simulated annealing analysis. The site selection may then be configured based at least in part on the first globally optimum site selection, e.g., the site selection may be made to conform to the globally optimum site selection.

[0622] As further shown in FIG. **123**, the method **12300** may include conducting/executing the clinical trial based at least in part on the first globally optimum site selection **12316**. Conduction of the clinical trial may be defined by a start/beginning **12318** of the clinical trial and a stop/end **12320** of the clinical trial. In embodiments, the start **12318** may be the occurrence of the first patient recruitment. In embodiments, the start **12318** may be the occurrence of the first interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. In embodiments, the start **12318** may be the first occurrence of a patient receiving a treatment (including receiving a drug). In embodiments, the stop **12320** may be the last occurrence of patient receiving a treatment (including receiving a drug). In embodiments, the stop **12320** may be the occurrence of the last interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. The time between the start **12318** and the stop **12320** may constitute the duration of the clinical trial as that term is user herein. In embodiments, conduction of the clinical trial may include commencement of any portion and/or process of the clinical trial whether performed in succession and/or intermittently.

[0623] After the start **12318** of the clinical trial, but before the stop **12320**, the globally optimum site selection may be reassessed. As such, the method **12300** includes obtaining, during conduction of the clinical trial, a second simulation output for a second set of site selections for the clinical trial **12322**. The second simulation output includes second site selection performance parameters associated with each design in the second set of site selections for a second set of site selection criteria. In embodiments, the second simulation output may be different than the first simulation output. For example, the second simulation output may be from another evaluation of the site selections. In embodiments, the second simulation output may be the same as the first simulation output. For example, the first simulation output may be reused. In embodiments, the second site selection performance parameters may be different than the first site selection performance parameters. For example, the second site selection performance parameters may include more or fewer parameters than the first site selection performance parameters. In embodiments, the second site selection performance parameters may be the same as the first site selection performance parameters. In embodiments, the second set of site selections may be the same or different than the first set of site selections. For example, the second set of site selections may include additional sites selections and/or have removed site selections as compared to the first set of site selections. In embodiments, the second set of site selection criteria may be the same or different than the first set of site selection criteria. For example, constraints on the clinical trial and/or site selections may have changed since the start **12318**.

[0624] The method **12300** further includes determining, from the second set of site selection criteria, a second site selection optimality criteria for evaluating the second set of site selections

12324. In embodiments, the second site selection optimally criteria may be the same or different from the first site selection optimally criteria. For example, a user may have previously determined the globally optimum site selection with respect to shortest duration and wish to do so again for the second globally optimum site selection. As another example, a user may have previously determined the globally optimum site selection with respect to shortest duration and may now wish to determine the globally optimum site selection with respect to costs.

[0625] The method **12300** further includes determining, within the second set of site selections, a second globally optimum site selection **12326**. Determination of the second globally optimum site selection may be based at least in part on the second site selection optimality criteria and the second site selection performance parameters. The method **12300** may further include adjusting the site selection based at least in part on the second globally optimum site selection **12328**. Adjustment of the site selection may include conforming the site selection to the second globally optimum site selection.

[0626] Illustrated in FIG. **124** is another method **12400** for updating site selections. In particular, method **12400** identifies a globally optimum site selection for a clinical trial after the start **12412** of the clinical trial, but before the end **12414** of the clinical trial, where an initial globally optimum site selection may not have been determined, or was not determined by an entity performing method **12400**. Accordingly, the method **12400** includes obtaining, during conduction of the clinical trial **12416**, a simulation output for a set of site selections for the clinical trial **12418**. The simulation output includes site selection performance parameters associated with each site selection in the set of site selections for a set of site selection criteria. The method **12400** further includes determining, from the set of site selection criteria, a site selection optimality criteria for evaluating the first set of site selections **12420**. The method **12400** further includes determining, within the set of site selections, a globally optimum site selection based at least in part on the site selection optimality criteria and the site selection performance parameters **12422**. The method **12400** may further include recommending the globally optimum site selection **12424**. Recommendation may include transmitting the globally optimum site selections to an entity performing and/or planning the clinical trial. The recommended globally optimum site selections may be the first time a globally optimum site selection was calculated/determined for the clinical trial, or the globally optimum site selection may be an update to a previously calculated/determined globally optimum site selection. In embodiments, the method **12400** may not include recommending the globally optimum site selection, but rather may include adjusting the site selection based at least in part on the globally optimum site selection **12426**. It is to be understood, however, that embodiments of the method **12400** may not include adjusting the site selection trial based at least in part on the globally optimum site selection. In embodiments, the method **12400** may include both recommending and adjusting the site selection based at least in part on the globally optimum site selection.

[0627] In addition to the design of a clinical trial, the success of the clinical trial often depends on the availability of resources needed to conduct the clinical trial, also referred to herein as “resource availability”. Non-limiting examples of trial resources include: drugs/drug supply, medical devices, procedures, administrative personnel, and/or equipment/devices needed to conduct a clinical trial, and/or the like. Resource availability, in turn, is typically a function of a site selection.

[0628] In some cases, a wrong choice in the selection of sites for a clinical trial may reduce resource availability which, in turn, may impact and/or prevent completion of the clinical trial. In some cases, difference in available resources between different site selections may result in very different costs, completion times, and/or other performance parameters for the clinical trial.

[0629] The selection of sites for a clinical trial, with respect to optimizing available resources, may include considerations and tradeoffs between hundreds or even thousands of site selections. For example, different site selection options, often have different values for resource availability, e.g., the sites of a first site selection may be closer to medical supply distribution centers than the sites of a second site selection. Traditionally, consideration of resource availability for clinical trials has been based on heuristics and experienced professionals to determine a set of parameters likely to result in a site selection that produces adequate access to resources. However, traditional approaches are not capable of evaluating more than a handful of site selection options and corresponding tradeoffs. As a result, traditional approaches to resource availability often miss site selection options that may result in greater resources availability. As the cost of a clinical trial may exceed tens of millions or even hundreds of millions of dollars and/or may take years to complete, small differences in resources availability between site selections for a clinical trial may result in large impacts on the overall cost and/or time associated with the clinical trial.

[0630] The complexity of site selection with respect to resource availability often requires aspects of statistical expertise, clinical design expertise, and software expertise, which may not be available in many organizations. As such, many organizations fallback on the use of generic site selection methodologies due to their inability to find optimal or near-optimal site selections with respect to resource availability for a particular clinical trial.

[0631] Accordingly, embodiments of the current disclosure may provide for a resource optimization platform, systems, and methods for evaluation and/or comparison of site selection options with respect to optimizing resource availability for a clinical trial. In embodiments, evaluation and/or comparison may include a large number of site selection options. In some embodiments, the platform, systems, and methods described herein may be used to evaluate hundreds, thousands, or even millions of site selection options for a clinical trial and may be used to find the optimal or near-optimal resource availability for a trial.

[0632] The resource optimization platform may be used for site selection. In embodiments, a resource optimization platform may support a team, as described herein, in collaborating and surfacing all the inputs that are key to consider for preparing and selecting a site selection to optimize available resources. The resource optimization platform may use cloud and distributed computing so the team can simulate hundreds of millions of site selection variants/options across all those inputs. The resource optimization platform may present the team with prioritized options and visualizations to enable the interrogation of the drivers of value. In an embodiment, available clinical trial resources may have an initial distribution across one or more sites. For example, a first site may have forty (40) kg of a drug and a second site may have twenty (20) kg of a drug. In embodiments, the platform may determine a site selection based on the initial distribution of one or more available clinical trial resources. In embodiments, the platform may determine one or more adjustments to the initial distribution to optimize availability of the one or more clinical trial resources and/or site selection. In embodiments, the adjustments to the initial distribution may facilitate a different clinical trial design and/or a different type of clinical trial design that was not previously possible given the initial distribution of the one or more available clinical trial resources. In embodiments, the platform may recommend adjustments to the initial distribution.

[0633] A resource optimization platform may enable a team to quickly identify site selections that optimize available resources and the factors that most strongly drive performance factors, strategic goals, and the like. A resource optimization platform, as described herein, may leverage emerging technologies to provide options for advanced simulations, distributed computing, visualizations, and the like. The resource optimization platform may leverage methodological knowledge, analysis of the business value of different design choices, and/or analysis of regulatory risk and operational complexity to determine optimum or near optimum site selections with respect to resource availability. The resource optimization platform may determine optimum or near optimum site selections by leveraging a novel workflow, speed and/or computing innovations, and/or powerful visualizations for study analysis and optimization.

[0634] A resource optimization platform may improve how data and processes are used to make better decisions on site selections. Improvements may result from recognizing which innovative options might significantly increase goals. Improvements may be obtained by communicating the benefits of specific site selections in a way that that intuitively allows a variety of team members to understand a particular site selection and/or possible options for the site selection of a clinical trial. A resource optimization platform may support a team in collaborating and surfacing all the inputs that are key to consider for preparing and selecting an optimal site selection. The resource optimization platform may present the team with prioritized options and insightful visualizations to enable interrogation of the drivers of value.

[0635] FIG. **125** shows an embodiment of a platform/system for evaluation and comparison of site selections with respect to optimizing resource availability for a clinical trial. The platform **12504** may form part of the platform **104** (FIG. **1**) or the platform **12504** may be stand-alone from the platform **104**. In embodiments, the platform **12504** may communicate with the platform **104** via one or more application programming interfaces (APIs). The platform **12504** may provide for a system for providing users with facilities and methods for determining, evaluating, and/or comparing site selections with respect to resource availability. The facilities described herein may be deployed in part or in whole through a machine that executes computer software, modules, program codes, and/or instructions on one or more processors, as described herein, which may be part of or external to the platform **12504**. Users may utilize the platform **12504** to, with respect to optimization of resource availability for a clinical trial, identify site selections for criteria, evaluate the site selections, compare site selections, determine optimal site selections, and the like.

[0636] A user may interact with the platform **12504** through one or more user devices **12502** (e.g., computer, laptop computer, mobile computing device, and the like). The platform **12504** may be implemented and/or leverage one or more computing resources **12550** such as a cloud computing service **12552**, servers **12554**, software as a service (SaaS), infrastructure as a service (IaaS), platform as a service (PaaS), desktop as a Service (DaaS), managed software as a service (MSaaS), mobile backend as a service (MBaaS), information technology management as a service (ITMaaS), and the like. The platform **12504** may be provided or licensed on a subscription basis and centrally hosted (e.g., accessed by users using a client (for example, a thin client) via a web browser or other application, accessed through or by mobile devices, and the like). In embodiments, elements of the platform **12504** may be implemented to operate on various platforms and operating systems. In embodiments, interfaces for the user device **12502** through which the users may interact with the platform may be served to the user device **12502** through a webpage provided by a server of the platform **12504**, an application, and the like.

[0637] The platform **12504** may include one or more facilities such as a configuration facility **12506**, simulation facility **12510**, analysis facility **12508**, interfaces facility **12512**, data facility **12538**, and computation resources **12550**.

[0638] The configuration facility **12506** may include advisors **12514**, which may include one or more wizards, tools, algorithms, recommenders, configuration elements, questioners, and the like. Advisors may be used to receive data and/or define or develop space definitions **12516**.

[0639] Space definitions **12516** may include aspects of site resource criteria space **12610** (FIG. **126**). Resource criteria space may define values, ranges of values, types, ranges of types, and the like that may define general required characteristics of the resources required by a clinical trial. Non-limiting examples of resource criteria include: maximum and/or minimum numbers of administrative personnel; maximum and/or minimum price points for subject drugs; a minimum and/or maximum number of required patients to complete the trial; maximum and/or minimum price points for equipment, to include equipment purchase and/or lease; and/or the like.

[0640] Space definitions **12516** may include aspects of site resource space **12612** (FIG. **126**). Site resource space **12612** may include the set of parameters and values of the parameters that define different options and variations of resources available at a particular site and/or group of sites for implementation of clinical trials. Non-limiting examples of site resource space may include: expected drug and/or price points; expected access to drugs and/or equipment; expected patient recruitment, expected patient dropout rate; geographical locations; patient demographics; expected availability of administrative and/or medical personnel; and/or the like. The site resource space may include all possible permutations of the parameters. For example, one site selection may be configured with different expected drug costs and different administrative personnel availabilities. The site resource space may include all the permutations of all the parameters associated with the resources available at individual sites and/or site selections. The site resource space may include millions of possible site selection variations. A resource optimization platform may evaluate all permutations of parameters of the site resource space. A resource optimization platform may evaluate a partial set of permutations of parameters of the site resource space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically defined, such as according to the resource criteria parameters.

[0641] Space definitions **12516** may include aspects of site selection resource scenario space **12614** (FIG. **126**). Resource scenario space may include the set of parameters and values of the parameters that define different options and variations of scenarios associated with site selections and resource availability. Resource scenario space may define the parameters of the environment associated with one or more sites. Non-limiting examples of resource selection scenario space include: expected flow through drug and/or equipment supply chains; expected weather conditions, expected pandemics; expected economic conditions; and/or the like. The resource scenario space may include all possible permutations of the parameters. For example, one scenario may be configured with a range of values for average drug costs and a range of values for average weather conditions, e.g., how will varying weather conditions affect the price point and/or availability of a drug. The resource scenario space may include all the permutations of all the parameters associated with scenarios. The resource scenario space may include millions of possible scenario variations. A resource optimization platform may evaluate all permutations of parameters of the resource scenario space. A resource optimization platform may evaluate a partial set of permutations of parameters of the resource scenario space. The partial set of permutations may be defined by a user. The partial set of permutations may be automatically or semi-automatically defined, such as according to the resource criteria parameters.

[0642] Space definitions **12516** may include aspects of site resource performance space **12616** (FIG. **126**). Site resource performance space may include the set of parameters and values of the parameters that define the evaluation criteria for a site selection with respect to resource availability. Parameters may include: net present value (NPV), expected NPV, incremental NPV, study cost, incremental study cost, study budget, incremental study budget, time to complete, incremental time to complete, time to market, incremental time to market, clinical utility, incremental clinical utility, probability of regulatory acceptance, incremental probability of regulatory acceptance, probability of success, incremental probability of success, statistical power, incremental statistical power, number of patients, incremental number of patients, number of sites, incremental number of sites, study complexity, incremental study complexity, operational complexity, incremental operational complexity, dose selected, incremental dose selected, statistical design, incremental statistical design, peak revenue, revenue at year five (5), other revenue numbers, incremental revenue, market introduction, whether market introduction beats competition entry, number of treatment arms, hypothesis superiority/equivalence/non-inferiority, other choices around statistical design, treatment effect, hazard ratio, and other choices around estimating the characteristics of the patient population, response, and safety profile, screening criteria, dropout rate, and other choices around modeling/estimating the characteristics and behaviors of the patient population and other factors that impact how the study evolves and its likelihood of achieving its goals (how slowly/quickly patients enroll, etc.), site payments and other choices around operational aspects of the study that can impact how the study evolves and its likelihood of achieving its goals, cost per patient, cost per site, or other cost factors, selections made in other projects (across users within customer companies or organizations and across all users of the platform), priorities set by the customer company or organization, and/or other user-defined filters based on available inputs and outputs of the platform or in the systems and methods described herein. In embodiments, any of the parameters and variables described herein may be incremental parameters and variables. Site selections may be evaluated and compared against all of the parameters of the performance space or a subset of the parameters of the performance space. A set of site selections, e.g., one or more groups each including one or more possible sites, may be evaluated for one or more of the performance parameters.

[0643] The configuration facility **12506** may include a combinations component **12518**. The combinations component **12518** may automatically or semi-automatically define the resource criteria design and/or resource scenario space that may be evaluated by the platform **12504**.

[0644] The simulation facility **12510** of the platform **12504** may, based on the space definitions from the configuration facility **12506**, evaluate the site selections. The simulation facility **12510** may include models **12526**. As used herein with respect to site selection, a model includes the combination of parameters and the values that describe a site selection and/or corresponding clinical trial designs and the scenario under which the site selection is evaluated with respect to resource availability. Models **12526** may include hundreds or even thousands of models. Models **12526** may include deviation specifications for one or more of the parameters of the models. A deviation specification may define a range of values, a distribution of values, and/or a function of values for one or more parameters of a model. The deviation specifications may be based on expected or previously measured distributions or variations in clinical trial design parameters, site selection parameters, and/or resource availability parameters.

[0645] The simulation facility **12510** may include engines **12528**. As used herein, engines may relate to the codification of a site selection and/or corresponding resource availabilities that can receive model parameters and run a simulation to generate an output. The output of the engines **12528** may be a predicted behavior, e.g., resource availability, for a site selection for one or more corresponding clinical trial designs, one or more scenarios, and/or conditions. Engines **12528** may evaluate a site selection with analytical methods, mathematical methods, numerical methods, simulation, and/or the like. Evaluating a site selection may include a simulation run to determine performance of the site selection. Evaluating a site selection may include using a Monte Carlo approach to simulate a site selection for different values according to the deviation specifications and using statistical methods to determine the performance of the site selection from a simulation run.

[0646] The simulation facility **12510** may include search/exploration component **12530**. The search/exploration component may facilitate modification of model parameters for simulation. The search/exploration component **12530** may adaptively modify or generate models for simulations based on simulation results of other models/site selections and/or based on triggers and data from other facilities of the platform **12504**.

[0647] The analysis facility **12508** may be configured to analyze simulation results of site selections. The analysis facility **12508** may include a filtering component **12520**. The filtering component **12520** may be configured to use one or more numerical and/or analytical methods to evaluate and compare the performance of evaluated site selections. The filtering component may identify optimal or near-optimal site selections for one or more performance parameters. The filtering component may search the performance space and identify a set of optimal and/or near optimal site selections for one or more performance parameters, e.g., availability of resources.

[0648] The analysis facility **12508** may include a recommendation component **12522**. The recommendation component **12522** may provide site selection recommendations. The site selection recommendations may be based on optimal or near-optimal site selections determined by the filtering component **12520**. Recommendations may be adaptive based on settings, feedback, selections, triggers, and the like from the user, and/or other facilities in the platform **12504**.

[0649] The analysis facility **12508** may include an augmenting component, **12524**. The augmenting component may supplement simulation results with real-world data.

[0650] The interfaces facility **12512** may be configured to provide visualizations and interfaces for comparing, searching, and evaluating simulated site selections. Visualization component **12532** may provide for one or more interfaces to visualize the performance of site selections and facilitate comparison of site selections by a user. The feedback analysis component **12534** may track user actions associated with the interfaces and visualizations to determine patterns and/or preferences for site selections. The tradeoff advisor component **12536** may analyze and provide data and guidance for evaluating tradeoffs between two more site selections.

[0651] The platform **12504** may include and/or provide access to one or more data facilities **12538**. Data in the data facilities may include design histories **12540**, simulation data **12542**, site data **12544**, resource data **12546**, population data **12548**, and the like.

[0652] FIG. **126** shows aspects of an embodiment of a process for site selection. The process may include four or more stages. Facilities of the platform **12504** may be configured to implement the stages of the process. The stages of the process may include a configure stage **12602**. The configure stage **12602** may define one or more of the spaces associated with the site selection. The configure stage **12602** may define one or more of site selection criteria space **12610**, site selection design space **12612**, site selection scenario space **12614**, and/or site selection performance space **12616**. The configure stage **12602** may utilize one or more advisors, wizards, algorithms, and the like for defining the spaces. In some embodiments, the different spaces associated with the configuration stage **12602** may be defined by different members of a team based on the expertise of the members. In some cases, members of a team may have different specializations. For example, some members may specialize in scenarios, while others may specialize in site selection and/or design definitions. Separating the inputs may allow different team members to independently optimize and improve specific models without affecting other inputs. In some embodiments, the inputs may be separated into two or more types based on convenience, expertise, flexibility, and the like.

[0653] The stages of the process may include an evaluate stage **12604**. The evaluate stage **12604** may configure models **12618** for evaluation using simulation **12620** and analytical methods **12624**. The stage may include various methods of enhancing computation and simulation using parallelization and resource management **12622**.

[0654] The stages of the process may include an augment stage **12606**. The augment stage **12606** may add real-world data to the simulation data. Financial data **12626**, regulatory data **12628**, revenue data **12630**, and the like may be added to the and used to augment data from simulations.

[0655] The stages of the process may include an explore and analyze stage **12608**. The explore and analyze stage **12608** may include filtering methods and algorithms **12632** for identifying optimal site selections. The stage may include generating and interacting with visualizations **12634** and tradeoff analysis tools **12636** to compare and select site selections.

[0656] In embodiments, the platform **12504** (FIG. **125**) may be configured for identification and confirmation of optimal site selections for a clinical trial. Optimality of site selection may be in relation to site resource criteria, e.g., a parameter within site resource criteria space **12610** (FIGS. **126** and **127**). For example, embodiments of the current disclosure may provide for the determination of a site selection for a clinical trial as being the least likely site selection to experience a drug shortage during the duration of the clinical trial. Site resource criteria may be determined in relation to the site resource performance space **12616** (FIGS. **126** and **127**). Optimality of the site resource criteria, via site selection, may be in relation to one or more site resource performance parameters, e.g., a parameter within site resource performance space **12616**, and the values thereof. An optimal site selection may be a site selection that achieves a most desirable value for one or more specific site resource performance parameters. A most desirable value may depend on the site resource performance parameter and may be different for each site resource performance parameter.

[0657] In some cases, the most desirable value may be the highest value of a site resource performance parameter. In some cases, the most desirable value may be the lowest value of a site resource performance parameter. In some cases, the most desirable value may be a range of values, a specific value, a function of values, and the like. For example, in some cases an optimal site selection with respect to a drug availability site resource performance parameter may be a site selection that has the lowest risk of drug supply interruption and achieves the goals of the clinical trial. As another example, an optimal site selection with respect to an equipment resource performance parameter may be a site selection wherein all sites within the selection have duplicate/redundant equipment, e.g., multiple Magnetic Resonance Imaging (MIR) systems on site.

[0658] In embodiments, an optimum site selection is a site selection that achieves most desirable values for two or more specific site resource performance parameters. In the case of optimality for multiple site resource performance parameters, optimality may require a tradeoff between the parameter values. For example, a site selection that has a lower risk of drug supply interruption may have a low NPV and therefore may not be desirable. The optimality of a site selection may be based on a function of site resource performance parameters. In some cases, a function may be a weighted sum of the site resource performance parameters. A function, or a set of functions, may be used to generate an overall score (or a set of scores) and the score may be used to determine the optimality of the site selection. A highest score, a specific score, lowest score, and the like may be considered optimal depending on the function used to compute the score.

[0659] In embodiments, optimality may be evaluated according to Pareto optimality. Pareto optimal site selections may be site selections where no individual site resource performance parameter can be better off without making at least one other individual site resource performance parameter worse off. In some cases, optimality may be determined using convex hull analysis.

[0660] In some cases, one site selection may be globally optimum. In some cases, more than one site selection may be globally optimum. In some cases, no site selections may be globally optimum. In some embodiments, optimality of site selection may be relative to a benchmark. A known site selection, a set of historical site selections, and/or the like may be used as a benchmark. Site selections may be considered optimal if they meet, exceed, and/or are within a threshold distance of the benchmark site resource performance parameters.

[0661] Site resource performance parameters that may be used to determine site selection optimality may be user defined, system defined, algorithmically defined, and/or the like. In some cases, users may specify a subset of site resource performance parameters that should be used to identify optimal site selections. A user may define optimality criteria by defining ranges, values, characteristics, and the like of the parameter values that may be considered desirable and/or optimal. Interactive graphical interfaces may be provided to a user to evaluate different site selections based on one or more optimality criteria. Interactive interfaces may allow a user to explore different site selections by changing scoring methods, weights associated with the criteria, and the like.

[0662] In embodiments, the characteristics of site resource performance parameters for evaluated site selections may be analyzed by the platform to determine if any of the parameters may be less important for optimality. For example, analysis may include evaluation of ranges, variability, and other statistical analysis. If one or more site resource performance parameters for all evaluated site selections is within a desirable range, or the site resource performance parameter is almost equal for all of the evaluated site selections, the site resource performance parameter may be removed and identified as less significant for optimality and, in some cases, may not be factored in when determining optimality. Prior to determining optimality based on site resource performance parameters, the site resource performance parameters and the values of the site resource performance parameters may be grouped, filtered, normalized, and the like.

[0663] Optimality of site selections may be redefined automatically, semi-automatically, in response to user input, and/or the like. The criteria for optimality of site selections may change as site selections are evaluated by the platform. For example, initial optimality criteria may produce no optimal site selections. In response to no optimal site selections being determined, the criteria may be changed (relaxed, increased, decreased, etc.) until at least one site selection is considered optimal. In another example, optimality criteria may change in response to user feedback. Users may evaluate initial site selections found to be optimal and provide feedback (direct feedback and/or indirect feedback that can be derived from user actions and inactions). The feedback from the user may be used to change how optimality is determined, which site resource performance parameters are used to determine optimality, the values of the site resource performance parameters that are considered optimal, and/or the like.

[0664] In some embodiments, site resource performance parameters may be grouped, ordered, and/or organized into one or more hierarchies, groups, and/or sets. Two or more different optimality criteria may be used in parallel to determine multiple sets of optimal site selections under different criteria. Two or more different optimality criteria may be used sequentially to determine optimal site selections. One criteria may first be used to identify a first set of optimal site selections under first criteria. A second set of criteria may then be used on the first set to reduce the set of optimal site selections.

[0665] In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to all possible site selection options. In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to possible site selection options for one or more criteria. In embodiments, a site selection may be globally optimum if the site selection is optimal with respect to a large percentage (such as 80% or more) of possible site selection options for one or more criteria. In embodiments, a site selection may be globally optimum if the optimality of the site selection is within a high confidence level (90% confidence) with respect to possible site selection options for one or more criteria.

[0666] Traditional methods for evaluating site selections cannot determine global optimum site selections since they evaluate one, several, or a small subset of site selection options. Traditional methods do not consider all or almost all of the site selection options and cannot find a global optimum.

[0667] Trial site selection may involve numerous variables, parameters, considerations, tradeoffs, and the like resulting in a very large number of possible variations. A large number of possible variations makes study site selections and optimization using traditional methods difficult. In many cases, traditional methods may fail to explore or consider the complete space of possible site selection options and may miss or never consider globally optimal site selections. Using traditional methods, the number of site selection variations that may be explored in a reasonable time is limited. In some cases, only one (1) statistical site selection and only three (3) clinical scenarios may be evaluated. The best site selection study of the limited number of variations may not result in a globally optimal site selection. A locally optimum site selection chosen from a limited number of considered site selections may represent one (1) local maximum but may be far from the globally optimum site selection. When 10,000 or more clinical scenarios are considered, a globally optimum site selection may be distinguished from the many locally optimum site selections. However, consideration of 10,000 clinical scenarios cannot be practically performed using traditional methods as it would require an estimated 50,000 hours or more to complete.

[0668] In embodiments, the platform and methods described herein may evaluate thousands or even millions of site selection options enabling a determination of a global optimum site selection with respect to availability of resources for a clinical trial. In many cases, the globally optimum site selection may have significant advantages over locally optimum site selection. In one example, a globally optimum site selection may require less time to complete than other site selections.

[0669] In embodiments optimization of trial site selections for resource availability may occur sequentially after optimization of trial design. In one embodiment, a globally optimum trial design may be determined using the techniques described herein. After the globally optimum trial design is determined a globally optimum trial site selection for resource availability may be determined for the determined trial.

[0670] Referring again to FIG. **125**, the platform **12504** may receive and/or determine performance space using the configuration facility **12506**. Performance space may be defined in the space definitions component **12516**. The performance space may be configured based on input from users and/or based on data **12538** such as history data **12540** and/or simulation data **12542**. In embodiments, data **12538** may include external data from external data sources and providers. In one instance, performance space may define optimality criteria. Optimality criteria may define site resource performance parameters, performance values, functions, methods, and algorithms for evaluating optimality and/or global optimality of site selections. In one instance optimality criteria may be configured by the user or determined from benchmark site selections from history **12540** and/or simulation **12542** data. In another instance, optimality criteria may be defined from simulation data from the simulation facility **12510**. Optimality of site selections may be determined in the analysis facility **12508**. The filtering component **12520** may be used to determine one or more sets of globally optimum site selections from the site selections evaluated by the simulation facility **12510**.

[0671] FIG. **127** shows aspects of an apparatus/optimality analysis component **12702** for determining global optimality of site selections with respect to availability of resources for a clinical trial. In embodiments, the optimality analysis component **12702** may be part of the analysis facility **12508** of the platform **12504**. The optimality analysis component **12702** may receive data from simulated site selections **12712** and determine one or more sets of optimal site selections **12722**, **12724**. The optimality analysis component **12702** may include one or more circuits for determining optimality of site selection. In embodiments, the optimality analysis component **12702** may include circuits for determining optimality based on optimality functions **12728**. Optimality functions **12728** may determine optimality of site selections based on different weighting of performance factors of the simulated site selections. In embodiments, the optimality analysis circuit **12702** may include circuits for determining optimality based on benchmark analysis **12704**. A benchmark analysis circuit **12704** may determine optimality of site selections based on a comparison of site resource performance parameter values to one or more benchmark site selections such as from historical data **12714** and/or simulation data **12712**. In embodiments, the optimality analysis circuit **12702** may include circuits for determining optimality using sequential analysis **12708** and/or parallel analysis **12710**. The sequential analysis circuit **12708** and parallel analysis circuit **12710** may use one or more different optimality functions **12728** in parallel or sequentially to determine optimal site selections. In embodiments, the optimality analysis circuit **12702** may include circuits for dynamically modifying optimality criteria **12706**. User inputs **12720**, simulation data **12712**, and/or the determined sets of optimal site selections may be monitored and analyzed to determine modifications to optimality criteria. In embodiments, the optimality analysis circuit **12702** identifies a confidence level **12726** associated with the optimality of sets of optimal site selections. In the case where simulation data **12712** may not include simulations of all site selection options for the criteria space **12610**, the optimality circuit **12702** may determine, based on the simulated site selections, a confidence level that the determined optimal site selections are indeed optimal for a given optimality criteria.

[0672] FIG. **128** shows aspects of an apparatus **12800** for determining global optimality of site selections with respect to availability of resources for a clinical trial. In embodiments, the apparatus **12800** may include an optimality analysis circuit **12814** which may be part of the analysis facility **12508** of the platform **12504** (FIG. **125**). In embodiments, the apparatus **12800** may include a data processing circuit **12806** structured to interpret/obtain site resource data **12802** of a clinical trial site selection. In some embodiments the site resource data **12802** may be outputs of simulation data of trial site selections. The data processing circuit **12806** may transform the site resource data **12802** into a format suitable for use by the various circuits in the apparatus. For example, the site resource data **12802** may be received by the data processing circuit **12806**, which may then determine and identify site resource performance parameters in the data. In some embodiments, some site resource performance parameters may be grouped, filtered, converted, normalized, and the like.

[0673] The apparatus **12800** of FIG. **128** may further include an optimality determining circuit **12808** structured to receive processed site resource data from the data processing circuit **12806**. The optimality determining circuit **12808** may identify globally optimum site selections **12812** based on one or more optimality criteria. In some embodiments, the globally optimum site selections **12812** may be provided as an output of the apparatus **12800**. In some embodiments, globally optimum site selections **12812** may be further processed by the site resource analysis circuit **12810**. The site resource analysis circuit **12810** may analyze the globally optimum site selections **12812**, determine characteristics of the site selections, and receive feedback data **12804** about the site selections. The site resource analysis circuit may, based on the determined characteristics, determine modifications for optimality criteria used in the optimality determining circuit **12808**. Using modified optimality criteria, the optimality determining circuit **12808** may determine a new set of globally optimum site selections **12812**.
[0674] As shown in FIG. **129**, a method **12900** for determining globally optimum site selections with respect to availability of resources for a clinical trial may include simulating all site selection options for a site resource criteria **12902**. The method **12900** may further include determining an optimality criteria for evaluating simulated site selections **12904**. Optimality criteria may be a function of one or more performance values for each site selection such as a weighted sum of the values, a comparison of the values, and the like. The method **12900** may include searching for globally optimum site selection(s) in the simulated site selections using the determined optimality criteria **12906**. The globally optimum site selections may be recommended to one or more users **12908**.
[0675] As shown in FIG. **130**, a method **13000** for determining site selections to globally optimize available resources for a clinical trial may include simulating site selection options for a site resource criteria **13002**. The method **13000** may further include determining a first optimality criteria for evaluating simulated site selections **13004**. The method **13000** may further include determining a second optimality criteria for evaluating simulated site selections **13006**. The method **13000** may include determining a first set of optimum site selections using the first optimality criteria, the first set may be determined from the simulated site selections **13008**. The method **13000** may further include determining a second set of optimum site selections using the second optimality criteria, the second set may be determined from the first set of site selections **13010**. The globally optimum site selections may be recommended to one or more users **13012**.
[0676] As shown in FIG. **131**, a method **13100** for determining a site selection to globally optimize available resources for a clinical trial may include simulating site selection options for a site resource criteria **13102**. The method **13100** may further include determining a first optimality criteria for evaluating simulated site selections **13104**. The method **13100** may include determining a first set of optimum site selections using the first optimality criteria, the first set may be determined from the simulated site selections **13106**. The method **13100** may further include identifying characteristics of site selections in the first set of globally optimum site selections **13108**. The method **13100** may further include determining a second optimality criteria for evaluating simulated site selections based on the identified characteristics **13110**. The method **13100** may include determining a second set of globally optimum site selections using the second optimality criteria from the simulated site selections **13112**.
[0677] Illustrated in FIG. **132** is a method **13200** for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure. The method **13200** includes determining a plurality of possible sites for recruiting patients from for a clinical trial **13210**. The method **13200** further includes determining, for each of one or more subgroupings of the plurality of possible sites, a predicted available resources value **13212**. The method **13200** further includes determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria **13214**. In embodiments, determining the predicted available resources value for

each of the subgroupings of the plurality of possible sites includes simulating each of the subgroupings **13216**. In embodiments, simulating each of the one or more subgroupings may be based at least in part on use of different types of engines, e.g., engines with different version numbers and/or developed by different entities, e.g., in-house vs third-party vendor. In embodiments, the differences in types of engines may include underlying types of algorithms and/or assumptions, e.g., rounding rules. In embodiments, the method **13200** may further include determining one or more site resource parameters **13218**. In such embodiments, simulating each of the one or more subgroupings **13216** may be based at least in part on the one or more site resource parameters. In embodiments, the one or more site resource parameters may be based at least in part on: a supply of a drug; administrative personnel; and/or equipment. In embodiments, the method **13200** may further include determining the desired site resource criteria **13220**. In such embodiments, simulating each of the one or more subgroupings **13216** may be based at least in part on the determined site resource criteria. In embodiments, the determined site resource criteria may be based at least in part on: a supply of a drug; administrative personnel; and/or equipment. In embodiments, determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria **13214** may include and/or be based at least in part on: a convex hull engine; a Pareto engine; a Monte Carlo engine; and/or a simulated annealing engine. In embodiments, determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria **13214** may be based at least in part on a machine learning engine, as described herein. For example, in embodiments, a neural network may be trained to look at past site selections and their outcomes and predict one or more site resource criteria. In embodiments, the neural network may be trained via supervised learning and/or by unsupervised learning, e.g., cost-based policies.

[0678] Turning to FIG. **133**, an apparatus **13300** for determining a site selection to globally optimize available resources for a clinical trial, in accordance with an embodiment of the current disclosure, is shown. The apparatus **13300** may form part of the platform **12504** or it may be stand-alone from the platform **12504** and/or communicate with the platform **12504** via one or more application programming interfaces (APIs). The apparatus **13300** includes a site selection data processing circuit **13310** structured to interpret possible site selection data **13312** identifying a plurality of possible sites for recruiting patients from for a clinical trial. The apparatus **13300** further includes an available resources determination circuit **13314** structured to determine a predicted available resource value **13316** for each of one or more subgroupings of the plurality of possible sites. The apparatus **13300** further includes a site searching circuit **13318** structured to determine which subgrouping **13320** of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria **13330**. The apparatus **13300** further includes a site selection provisioning circuit **13322** structured to transmit the subgrouping **13320** of the plurality of possible sites that has the predicted available resources value that globally optimizes the desired site resource criteria. In embodiments, the available resources determination circuit **13314** is further structured to determine the predicted available resources value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In embodiments, simulating each of the one or more subgroupings is based at least in part on use of different types of engines, as described herein. In embodiments, the apparatus **13300** may include a user input circuit **13324** structured to interpret user input data **13326** and a criteria determining circuit **13328** structured to determine the desired site resource criteria **13330** based at least in part on the user input data **13326**. In embodiments, the site searching circuit **13318** may include a convex hull engine; a Pareto engine; a Monte Carlo engine; and/or a simulated annealing engine.

[0679] Referring to FIG. **134**, embodiments of the current disclosure may provide for a design platform **13400** with an interface **13410** for configuring and managing the platform **12504** with respect to optimizing site selection for availability of resources for a clinical trial. The design platform **13400** may provide for pre-simulation determination of one or more resource selection parameters, e.g., values within resource criteria space **12610**, site resource space **12612**, resource scenario space **12614** and/or site resource performance space **12616**. Some embodiments may provide for adjustment of resource selection parameters during a simulation. The interface **13410** may include a canvas area **13412** for visualizing/editing/creating resource selection parameters for use by the platform **12504** (FIG. **125**). Embodiments of the interface **13410** may be a graphical user interface (GUI) that has one or more input fields **13414** for inputting or selecting resource selection parameters. The input fields **13414** may be sliders, text boxes, moveable components, and/or other GUI user input widgets. The graphical user interface may also provide for a heat map for selecting possible sites. The heat map may provide for filtering of the possible sites. In embodiments, the platform **13400** may provide, via servers **12554** (FIG. **125**) multiple interfaces, e.g., interfaces **13410**, **13416**, **13418**, for collaborative configuration of the platform **12504** by one or more users. In embodiments, the interfaces **13410**, **13416**, **13418** may be configured differently for different users, e.g., an interface may be tailored to a type of user and/or target audience, e.g., clinical trial experts, novices, and/or other types of users of varying skill levels in clinical trial designs and/or site selection. Tailoring of an interface to a user type may include enabling and/or disabling certain features and/or options on the interface. In embodiments, collaboration between users may involve a first user operating on a first interface **13410** receiving inputs from a second interface **13416** operated by a second user. In embodiments, the interface **13410** may provide for weighting of one or more resource selection parameters. In embodiments, the interface **13410** may provide for configuration of the simulation component **12510** (FIG. **125**). For example, a user operating the interface **13410** may configure the simulation component **12510** to perform an exhaustive search and/or simulation of site selection options. In embodiments, a user operating the interface **13410** may configure the simulation component **12510** to perform a non-exhaustive search and/or simulation of site selection options. In embodiments, the interface **13410** may provide for a user to configure the platform **12504** to user one or more of a convex hull engine, a Pareto engine, a Monte Carlo engine, and/or simulated annealing engine. In embodiments, the interface **13410** may provide for a user to configure a training set for a machine learning engine to learn how to optimize site selections with respect to resource availability, as disclosed herein.

[0680] Turning to FIG. **135**, a method **13500** for collaborative configuration of a site selection platform **12504** for optimization of availability of resources for a clinical trial is shown. The method **13500** includes displaying a graphical user interface structured to configure a system for determining which subgrouping, of a plurality of possible sites for a clinical trial, globally optimizes available clinical trial resources **13510**. The method **13500** further includes receiving, via the graphical user interface, one or more user inputs that define one or more resource selection parameters used by the system **13512**. The method **13500** further includes storing the defined resource selection parameters in a memory device **13514**.

[0681] Shown in FIG. **136** is an apparatus **13600** for providing collaborative configuration of a site selection platform **12504** for optimization of availability of resources for a clinical trial is shown. The apparatus **13600** includes a display generation circuit **13610** structured to generate a graphical user interface **13612** for configuring a system **12504** for determining which subgrouping, of a plurality of possible sites for a clinical trial, globally optimizes available clinical trial resources. The apparatus **13600** further includes a display transmission circuit **13614** structured to transmit the graphical user interface **13612** to an electronic device for display, e.g., **12502**. The apparatus **13600** further includes a user interaction circuit **13616** structured to interpret user inputs **13618** received by the graphical user interface **13612**; and in response to, and based at least in part on, interpreting the user inputs **13618**, define resource selection parameters **13620** used by the system **12504**. The selection parameter provisioning circuit **13622** is structured to store the defined selection-parameters **13620** in a memory device, e.g., **12538**.

[0682] Shown in FIG. **137** is another method **13700** for collaborative configuration of a site selection platform **12504** for optimization of availability of resources for a clinical trial. The method **13700** includes configuring, via a graphical user interface, a recruitment site selection system via entering one or more user inputs into the graphical user interface that define one or more selection-parameters **13710**. The method **13700** further includes determining, via the recruitment site selection system, which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes available clinical trial resources **13712**. The method **13700** further includes transmitting data identifying the determined subgrouping **13714**.

[0683] Referring to FIG. **138**, embodiments of the disclosure may provide for a platform/system **13800** with an interface **13810**, e.g., a wizard, for guiding a user through configuring a site grouping/selection system/platform **12504** (FIG. **125**) for optimizing site selection with respect to availability of resources for a clinical trial. In embodiments, the interface **13810** may be generated by a server **12554** (FIG. **125**). The interface **13810** may be command line based or graphical user interfaced based. The interface **13810** may generate a plurality of prompts **13812** that assist in obtaining initial resource selection parameters, e.g., criteria, from users to determine parameters for resource criteria space **12610**, site resource space **12612**, resource scenario space **12614**, and/or site resource performance space **12616**. The plurality of prompts **13812** may ask for a variety of static inputs or ranges. The inputs may include the type of engine **12528** to use in the simulation **12510**. The inputs may also include the type of search algorithm **12530** used. The inputs may include the type of sensitivity analysis algorithms or tools that are preferred. The inputs may include the type of clinical trial. The interface may recommend one or more site groupings/selections based on the type of clinical trial. The recommended site groupings/selections may serve as a starting base for further modification by a user. Artificial intelligence/machine learning approaches may be used to generate the prompts **13812** and/or suggestions for the user through the configuration process. As will be appreciated, the suggestions and/or guiding by the interface **13810** may allow a user to avoid (or reduce) spending time and resources (including computing resources and the costs of those resources) on sub-optimal simulations.

[0684] In an embodiment, a method for guiding a user through configuring a site grouping/selection system/platform for optimizing site selection for resource availability for a clinical trial is provided. The method includes generating an interactive interface. The method further includes presenting, via the interactive interface, a plurality of prompts to a user structured to configure a site selection system **12504** for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired resource criteria, e.g., one or more parameters within resource criteria space **12610**. The method further includes for each of the plurality of prompts, receiving a responsive user input, and configuring the site selection system based at least in part on the responsive user inputs.

[0685] In another embodiment, a system for guiding a user through configuring a site grouping/selection system/platform for optimizing site selection for resource availability for a clinical trial is provided. The system includes a server structured to determine which subgrouping of a plurality of possible sites for recruiting patients from for a clinical trial globally optimizes a desired resource criteria. The system further includes an electronic device, e.g., **12502**, structured to: display an interactive interface that presents a plurality of prompts to a user for configuring the server; for each of the plurality of prompts, receive a responsive user input; and configure the server based at least in part on the responsive user inputs.

[0686] In another embodiment, a non-transitory computer readable medium storing instructions is provided. The stored instructions, when loaded into at least one processor, adapt the at least one processor to: generate an interactive interface; and present, via the interactive interface, a plurality of prompts to a user. The plurality of prompts are structured to configure a site selection system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired resource criteria. The stored instructions further adapt the at least one processor to, for reach of the plurality of prompts, receive a responsive user input; and configure the site selection system based at least in part on the responsive user inputs.

[0687] Embodiments of the current disclosure may provide for prediction of an initial site grouping/selection with respect to resource availability of a clinical trial. In embodiments, the initial site selection may be structured to maximize (globally optimize) access to clinical trial resources and/or other criteria, e.g., one or more parameters within resource criteria space **12610**, site resource space **12612**, resource scenario space **12614**, and/or site resource performance space **12616**. For example, in embodiments, a predicted initial site selection may correspond to minimizing interruptions in supply of a drug used in the clinical trial. In other embodiments, the predicted initial site selection may correspond to maximizing the number of administrative personnel or healthcare providers available to conduct the clinical trial. In yet other embodiments, the predicted initial site selection may correspond to maximizing the availability of medical equipment used in the clinical trial.

[0688] In embodiments, the initial site selection may be based at least in part on historical data. The historical data may include data from previously conducted clinical trials and/or it may include data from prior simulated clinical trials. In embodiments, the data may be stored in data facility **12538** and/or be generated by the simulation component **12510** and/or the analysis components **12508**.

[0689] The prediction may be generated prior to receiving user input or after receiving some user input e.g., via user device **12502**. The predicted initial site grouping/selection may be displayed in a graphical user interface, e.g., interface component **12512**, for adjustment by a user. The predicted initial site grouping/selection may be the grouping/selection actually used in the clinical trial, or it may serve as a starting point which the user can configure/tweak as desired. The predicted initial site grouping/selection may be the global optimal, with respect to the desired resource; or it may be close to the global optimal, wherein a user can tweak, i.e., make adjustments, it to be the global optimal. The initial prediction may reduce the amount of time to find the global optimum by providing the user (or computer) with a good starting point based on knowledge gained from historical data. Simulated annealing, e.g., via the search/exploration modules/engines **12530**, may be applied to the initial prediction to test the surrounding subgroupings. Artificial intelligence may be used to analyze the historical data based on known desired criteria for the clinical trial. For example, in embodiments, a neural network may be trained on historical data to identify patterns in site selections that result in particular values for the availability of a resource at one or more sites. The neural network may then process site selection data, i.e., data regarding possible sites for a clinical trial, and then generate a predicted initial site selection.

[0690] Accordingly, referring to FIG. **139**, a method **13900** for prediction of an initial site grouping/selection for optimizing resource availability for a clinical trial is shown. The method **13900** includes accessing past trial site selection data stored in a database **13910**. The method **13900** further includes predicting, based at least in part on the past trial site selection data, the initial site selection **13912**. In embodiments, predicting the initial site selection may be based at least in part on artificial intelligence, as disclosed herein. The initial site selection corresponds to a global optimization of access to a desired resource for the clinical trial, as disclosed herein. The method **13900** further includes evaluating the initial site selection with respect to being the global optimization **13914**. Such evaluation may be based at least in part on a convex hull engine, a Pareto engine, a Monte Carlo engine, or a simulated annealing engine, as disclosed herein. The method **13900** may further include displaying the initial site selection in a graphical user interface **13916**. In embodiments, the desired resource may be based at least in part on a drug supply, administrative personnel, and/or equipment. In embodiments, the method **13900** further includes adjusting the initial site selection via the graphical user interface **13918**. In embodiments, the method **13900** may further include interpreting one or more user inputs, wherein the prediction of the initial site selection is based at least in part on the one or more user inputs **13920**. In embodiments, the method may further include simulating the initial site selection to determine performance criteria

13922. In embodiments, the method **13900** may further include conducting a sensitivity analysis of the initial site selection **13924**, e.g., via analysis component **12508**.

[0691] Illustrated in FIG. **140** is an apparatus **14000** for prediction of an initial site grouping/selection for optimizing resource availability for a clinical trial. The apparatus **14000** includes a past trial data processing circuit **14010** structured to interpret past trial site selection data **14012**. The apparatus **14000** further includes a resource prediction circuit **14014** structured to generate, based at least in part on the past trial site selection data **14012**, initial site selection data **14016** for a clinical trial. The initial site selection data **14016** may correspond to a global optimization of access to one or more resources for the clinical trial. The apparatus **14000** further includes a resource evaluation circuit **14018** structured to evaluate the initial site selection data **14016** with respect to the global optimization. The apparatus **14000** further includes a prediction provisioning circuit **14020** structured to transmit the initial site selection data **14016**.

[0692] Embodiments of the current disclosure may also provide for a method for using the initial site selection. The method may include receiving an initial site selection for a clinical trial, and conducting a clinical trial based as least in part on the initial site selection. The initial site selection may correspond to a global optimization of access to one or more resources for the clinical trial, wherein the initial site selection was predicted from past trial site selection data. For example, a first entity may generate initial site selection data and send it to a second entity that conducts a clinical trial based at least on part on the initial site selection data.

[0693] Referring now to FIG. **141**, embodiments of the current disclosure may provide for a platform/system **14100** that generates an interactive interface **14110**, e.g., a GUI, for exploration/evaluation of spaces related to availability of resources for a clinical trial, as opposed to merely facilitating selection of proposed sites, for the purpose of globally optimizing site selection for a clinical trial to optimize availability of resources. The spaces may include site resource criteria space **12610**, site resource space **12612**, resource site scenario space **12614**, and/or site resource performance space **12616**. In embodiments, generation of the site selections and/or evaluation of the spaces may be based at least in part on convex hull, Pareto frontiers, Monte Carlo, simulated annealing, and/or machine learning, e.g., artificial intelligence, as described herein.

[0694] Exploration/evaluation of the spaces may provide insights to a user regarding known and/or unknown constraints on site selection and/or the impact a particular selection parameter, e.g., a parameter within one of the spaces, may have on resource availability.

[0695] Exploration of the spaces may be facilitated via visualizations of the spaces. The visualizations may include, and/or be based at least in part on, heatmaps and/or tornado graphs. The interface **14110** may include a canvas area **14112** for rendering (or rasterizing) the visualizations.

[0696] The interface **14110** may provide for users to adjust one or more selection parameters and/or adjust sites within one or more proposed site selections/groupings and see the effect on the predicted resource availability. Adjustment of the selection parameters may be facilitated by one or more interactive widgets **14114**, e.g., text boxes, buttons, sliders, and/or the like. In embodiments, adjustment of the selection parameters may be facilitated via the canvas **14112**. In embodiments, the interface **14110** may allow users to evaluate and compare possible site selections/groupings side-by-side.

[0697] In embodiments, exploration of the spaces may provide for sensitivity analysis. For example, embodiments of the interface **14110** may incorporate simulated annealing engines, as described herein.

[0698] In embodiments, platform/system **14100** may include a server, e.g. server **12554** in the computation resources **12550** of platform **12504**. The server **12554** may generate the interface **14110** as a web application, remote desktop, and/or other suitable architecture for providing the interface **14110** to users and/or user devices **12502**.

[0699] The platform **14100** may support collaboration among different users. For example, the server **12554** may generate multiple interfaces **14110**, **14116**, and **14118**. In embodiments, the interfaces **14110**, **14116**, and **14118** may be configured/tailored to different types of user/target audience, e.g., users with different levels of experience and/or knowledge with respect to evaluating site groupings/selection for various criteria. For example, a first interface **14110** for an expert user may have more functionality, e.g., access to more options and/or features, than a second interface **14116** for a novice user.

[0700] Turning to FIG. **142**, a method **14200** for exploring/evaluating spaces related to resource availability for a clinical trial is shown. The method **14200** includes generating a graphical user interface structured to provide for interactive exploration of one or more spaces corresponding to one or more selection parameters for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes clinical trial resources **14210**. The method **14200** further includes adjusting at least one of the selection parameters via the graphical user interface **14212**. The method **14200** further includes updating the graphical user interface in response to adjusting the at least one selection parameter **14214**. In embodiments, the clinical trial resources may be based at least in part on a supply of a drug, administrative personnel, and/or equipment. In embodiments, generating the graphical user interface occurs prior to simulating, as disclosed herein, any one of the possible sites. In embodiments, generating the graphical user interface occurs after simulation of one or more of the possible sites.

[0701] Illustrated in FIG. **143** is a non-limiting embodiment of an apparatus **14300** for exploring/evaluating spaces related to patient recruitment for a clinical trial. The apparatus **14300** includes a resource space processing circuit **14310** structured interpret space data **14312** corresponding to one or more spaces, e.g., **12610**, **12612**, **12614**, and/or **12616**, related to subgroupings of possible sites for use in conducting a clinical trial. The apparatus **14300** further includes a graphics circuit **14314** structured to generate interactive interface data **14316** in response to the space data **14312**. In embodiments, the interactive interface data **14316** corresponds to a computerized interface **14110** for globally optimizing site selection for clinical trial resource availability. The apparatus **14300** further includes a user input circuit **14318** structured to receive user input data **14320** responsive to the presentation of the interactive interface data **14316**. The apparatus **14300** further includes a resource space exploration circuit **14322** structured to modify the interactive interface data **14326** in response to the user input data **14320**. The apparatus **14300** further includes an interactive provisioning **14324** circuit structured to transmit the modified interactive interface data **14326**.

[0702] Referring to FIG. **144**, a method **14400** for updating site selection according to available resources is shown. Since recommendation of globally optimal site selection, as disclosed herein, are generally predictive, it is possible that one or more parameters used to determine a globally optimum site selection for a clinical trial may deviate from what actually occurs during conduction/execution of the trial, i.e., while the trial is underway. A globally optimum site selection may have been determined based on an initial availability of resources, when, in actuality, a global pandemic emerges shortly after the start of a clinical trial affecting the availability of resources. In such a case, the original globally optimum site selection may no longer be the optimum. Updating of a site selection, as described herein, may occur multiple times through the course/duration of the clinical trial. In some embodiments, updating of the site selection, as described herein, may be performed on a continuous basis throughout the duration of the clinical trial.

[0703] Accordingly, the method **14400** includes obtaining a first simulation output for a first set of site selections for a clinical trial based on the availability of resources **14410**. The first simulation output includes first resource availability, as disclosed herein, associated with each site in the first set of site selections. The method **14400** further includes determining a first resource availability **14412**. The method **14400** further includes determining, within the first set of site selections, a first globally optimum site selection based at least in part on the availability of resources **14414**. Optimum site selections may be determined using one or more of Pareto analysis, convex hull analysis, and/or simulated annealing analysis. The site selection may then be configured based at least in part on the first globally optimum site selection, e.g., the site selection may be made to conform to the globally optimum site selection.

[0704] As further shown in FIG. **144**, the method **14400** may include conducting/executing the clinical trial based at least in part on the first globally optimum site selection **14416**. Conduction of the clinical trial may be defined by a start/beginning **14418** of the clinical trial and a stop/end **14420** of the clinical trial. In embodiments, the start **14418** may be the occurrence of the first patient recruitment. In embodiments, the start **14418** may be the occurrence of the first interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. In embodiments, the start **14418** may be the first occurrence of a patient receiving a treatment (including receiving a drug). In embodiments, the stop **14420** may be the last occurrence of patient receiving a treatment (including receiving a drug). In embodiments, the stop **14420** may be the occurrence of the last interaction between administrative personnel (for the clinical trial) and a patient or recruitment site, in respect of the trial. The time between the start **14418** and the stop **14420** may constitute the duration of the clinical trial as that term is user herein. In embodiments, conduction of the clinical trial may include commencement of any portion and/or process of the clinical trial whether performed in succession and/or intermittently.

[0705] After the start **14418** of the clinical trial, but before the stop **14420**, the globally optimum site selection may be reassessed in view of changes to availability of resources. As such, the method **14400** includes obtaining, during conduction of the clinical trial, a second simulation output for a second set of site selections for the clinical trial based on a second resource availability **14422**. The second simulation output includes second site selection performance parameters associated with each design in the second set of site selections for a second set of site selection criteria. In embodiments, the second simulation output may be different than the first simulation output. For example, the second simulation output may be from another evaluation of the site selections according to a second resource availability. In embodiments, the second simulation output may be the same as the first simulation output. For example, the first simulation output may be reused. In embodiments, the second site selection performance parameters may be different than the first site selection performance parameters. For example, the second site selection performance parameters may include more or fewer parameters than the first site selection performance parameters. In embodiments, the second site selection performance parameters may be the same as the first site selection performance parameters. In embodiments, the second set of site selections may be the same or different than the first set of site selections. For example, the second set of site selections may include additional sites selections and/or have removed site selections as compared to the first set of site selections. In embodiments, the second set of site selection criteria may be the same or different than the first set of site selection criteria. For example, availability of a resource such as a drug for the clinical trial and/or site selections may have changed since the start **14418**.

[0706] The method **14400** further includes determining, within the second set of site selections, a second globally optimum site selection **14426**. Determination of the second globally optimum site selection may be based at least in part on the second resource availability **14424**. The method **14400** may further include adjusting the site selection based at least in part on the second globally optimum site selection **14428**. Adjustment of the site selection may include conforming the site selection to the second globally optimum site selection.

[0707] Illustrated in FIG. **145** is another method **14500** for updating site selections based on resource availability. In particular, method **14500** identifies a globally optimum site selection for a clinical trial for a first resource availability after the start **14512** of the clinical trial, but before the end **14514** of the clinical trial, where an initial globally optimum site selection may not have been determined, or was not determined by an entity performing method **14500**. Accordingly, the method **14500** includes obtaining, during conduction of the clinical trial **12416**, a simulation output for a set of site selections for the clinical trial for a resource availability **14518**. The simulation output includes site selection performance parameters associated with each site selection in the set of site selections for a resource availability. The method **14500** further includes determining, from the set of site selection criteria, a site selection optimality criteria for evaluating the first set of site selections **14520**. The method **14500** further includes determining, within the set of site selections, a globally optimum site selection based at least in part on the site selection optimality criteria and the availability of resources **14522**. The method **14500** may further include recommending the globally optimum site selection for the available resources **14524**. Recommendation may include transmitting the globally optimum site selections to an entity performing and/or planning the clinical trial. The recommended globally optimum site selections may be the first time a globally optimum site selection was calculated/determined for the clinical trial, or the globally optimum site selection may be an update to a previously calculated/determined globally optimum site selection. In embodiments, the method **14500** may not include recommending the globally optimum site selection, but rather may include adjusting the site selection based at least in part on the globally optimum site selection **14526**. It is to be understood, however, that embodiments of the method **14500** may not include adjusting the site selection trial based at least in part on the globally optimum site selection. In embodiments, the method **14500** may include both recommending and adjusting the site selection based at least in part on the globally optimum site selection.

[0708] FIG. **146** shows aspects of another view or organization of a platform **14606** as discussed herein. In one embodiment, entities such as users may interact with the platform **14606** with a user device such as an application in a browser **14604**. The browser application **14604** may receive content from a content management system **14602**. The browser application **14604** may communicate with an authentication module **14610** to authenticate the entity and enable access to the services **14618** and other elements of the platform **14606**. In embodiments, the access and interaction with the platform **14606** may include interaction with the application programming interface **14612** of the platform **14606**. The API interface **14612** may provide an interface to the services **14618** of the platform. The services of the platform may provide services provided by the configuration facility **106**, analysis facility **108**, simulation facility **110**, and/or the interfaces facility **112** shown with respect to the platform configuration of FIG. **1**. The services of the platform **14606** may include services such as an engine registry service **14624**, query service **14626**, subscription service **14628**, simulation service **14630**, project service **14632**, statistical service **14634**, and augmentation service **14636**.

[0709] In embodiments, one or more of the services may interact with other services and interact with the compute component **14638**. The compute component **14638** may include components for executing simulations. The compute component may include one or more components that provide the functionality of the simulation facility **110** of the configuration of the platform shown in FIG. **1**. The compute component **14638** may include queues **14640**, **14642**, **14644** that provide data to and/or receive data from engines **14650**. The queues may sort and manage simulation models for simulation by the simulation engines **14650**. Data from the queues and/or engines **14650** may be stored and received by the data storage and data management components such as a data lake **14651**, storage service **14646**, and databases **14648**.

[0710] In embodiments, the platform **14606** may include one or more cloud services **14616** provided by one or more cloud providers. Cloud services may include code management services **14652**, deployment pipeline services **14654**, container services **14656**, and the like. In embodiments, one or more monitors **14620** may monitor the operation of the platform **14606** and identify errors, faulty components, completions of operations or processing and the like. The monitors **14620** may cause alerts or other notifications for the browser app **14604**. In some embodiments, the platform **14606** may include an application insights **14622** module which may provide performance monitoring and management of applications and components associated with the platform **14606**.

[0711] In embodiments, elements of the platform may include a quantum computer. In embodiments, one or more algorithms and/or methods described herein may be implemented using a quantum computer that may be executing a quantum algorithm. A quantum computer may be a computer that is based on quantum mechanical phenomena such as superposition and entanglement to perform operations on data. A computing system may include a hybrid system that includes a quantum computer and a classical computer. The methods and systems described herein may be deployed such that they are distributed among the classical and quantum computers. A quantum computer may execute one or more quantum algorithms for solving one or more quantum computing tasks, and a classical computer may execute one or more classical algorithms for solving one or more classical computing tasks. In embodiments, parts of the platform may use quantum computing and quantum algorithms to speed up computations for algorithms or parts of algorithms that are difficult for classical computers. In some embodiments, algorithms for quantum search, quantum simulation, quantum annealing, and the like may be used in parts of the platform for implementing aspects of the methods and systems described herein.

[0712] In embodiments, one or more algorithms and/or methods described herein may be implemented with artificial intelligence algorithms such as machine learning algorithms and neural network algorithms. Artificial intelligence algorithms may be used to build mathematical models based on training data to make predictions or decisions. In embodiments, training data may include any one or subset of: interface interactions, simulated annealing inputs and results, pareto analysis inputs and results, convex hull analysis inputs and results, recommendation algorithm inputs and results, orchestrating algorithm inputs and results, design advisor **14614** (FIG. **146**) inputs and trade-off advisor inputs and outputs, and other data received or determined by the platform described herein. In embodiments artificial intelligence may include supervised machine learning, unsupervised machine learning, reinforcement machine learning, and the like. In embodiments artificial intelligence algorithms may be used to identify design optimality, identify optimal designs, identify analysis flow and methods to reduce computation and analysis time, and the like.

[0713] In embodiments, the system and methods described herein may include one or more computing resources such as a cloud computing service. The cloud computing service may provide on demand availability of computer system resources. Computing and/or storage resources may be allocated based on demand, cost, timing requirements, and the like. The computing resources may be distributed across multiple locations. Computing resources may be allocated on demand during operation of the platform. Different stages of operation may require different computing resources. Simulations, for example, may require an increase in computing and storage resources. The amount, locations, and the like of the computing resources may be selected based on timing and cost considerations. High priority design studies may be allocated more resources for example. In embodiments, cloud computing may be used for platform and functions to optimize trial design, site selection, and/or clinical trial resources.

[0714] In embodiments, the system and methods described herein may utilize one or more external data sources. External data sources may include databases of data, federated data sources, government data, real-time data, and the like. In some cases, external data sources may be queried for data from a single source. In some cases, external data may require data harvesting from multiple locations or resources using one or more crawlers, queries, bots, and the like. For example, financial data used for augmenting data in the platform described herein may require querying or multiple resources to determine current costs for sites, doctors, drugs, and the like. External data sources may be updated using data calculated, compiled, or determined by the platform or parts of the platform. Data may be written to multiple locations while using one or more write-back methods to maintain data coherency.

[0715] In embodiments, the system and methods described herein may include authentication and/or provide conditional access. The platform, resources associated with the platform, and the like may require establishing and confirming identities of entities that interact with the platform and associated resources thereof. Entities may be persons and/or other resources. Identities may be associated with account and may track usage for billing and accounting. Identities may be associated with access or capabilities restrictions. Some aspects of the platform may be enabled for some entities associate with specific accounts based on subscription level. Conditional access may be provided to specific algorithms, models, engines, data, analysis interfaces, and the like. Data and communications may be secured with one or more encryption and data security methods for maintaining data security and confidentiality.

[0716] In embodiments, the system and methods described herein may include metadata. Metadata may include descriptive metadata, structural metadata, administrative metadata, reference metadata, and/or statistical metadata. Metadata may be associated with stored data, data as it progresses through the platform, elements of the platform (for example elements that may self-identify and register to the platform). Metadata may be associated with major data structures and elements of the system. Metadata may be associated with and/or accompany data related to the design space, criteria space, performance space and the like. The metadata may provide information about where the data originated, who or what created the data, when the data was created, assumptions and limitations of the data and the like. For example, simulated data may include metadata that relates to the engines and algorithms that were used for the computations. The metadata may identify what version of engines, what random number seeds were used, known limitations and compatibility of the engines and data generated by the engines with other engines and data produced by other engines.

[0717] In embodiments, the system and methods described herein may include reporting functionality. Reporting may include charts, spreadsheets and other tools used to present the results of the optimization process and/or the data fed into the optimization process. Reporting may include heat maps and tornado graphs. Reporting may be generated for user review and analysis. In some cases reporting may be generated for machine analysis. User report and machine reports may include different formatting and amounts of data. Reporting may be system initiated or user initiated. In some cases reporting may be triggered by an event, such as in an analysis. Reporting may include data and documentation for audit or methods, procedures, and the like used by the platform and parts thereof. Reporting may be necessary for compliance and regulatory approval.

[0718] In embodiments, the system and methods described herein include integrations with one or more databases, third party systems, sources of data, marketplaces, computational resources, and the like.

[0719] In embodiments, the systems, methods, and platform described herein may include aspects of application programming interfaces (APIs). APIs may include software interfaces that provide for communications between various components of the overarching clinical trial framework, e.g., backend servers, frontend graphical user interfaces, querying of historical data, available resource data, and the like. APIs may be exposed (such as software hooks) for expanding, controlling, and/or modifying functionality of the platform. APIs may include libraries and frameworks for interacting and integrating third party simulation and analysis systems. Third party simulation engines may consume platform APIs to control or use system resources. In embodiments, the systems, methods, and platform described herein may consume APIs of external or internal software and systems.

[0720] In embodiments, the system and methods described herein may include alerts. The platform or components thereof may include components for generation and transmission of data messages to an end user (human or machine). Alerts may be generated for notifying an end user of analysis results, status of processes (such as simulation, analysis, configuration, and the like), errors (delays in processing, unavailability of platform or external resources, unauthorized access, and the like), time of completions of simulations and/or analysis, and the like. Alerts may be logged for system audit and used for predictions. Alerts may be pushed or pulled to user devices, such as mobile devices and may wake a device from a sleep or low power mode. Alerts may be provided to other platform elements which may be used as a trigger to initiate and/or abort other processes of the platform. For example, simulated annealing analysis may provide alerts when improved designs are observed. The alerts may be provided to a user and used to trigger an update of interfaces that display analyzed designs.

[0721] In embodiments, the system and methods described herein may include collaboration features. Collaboration may include collaboration among users. Components of the various interfaces may provide for users to collaborate with respect to trial design and/or site selection. Collaboration may include: messaging/commenting systems, screen sharing, and/or platforms that merge various elements that are created/edited by different users. Users may be able to post, view, edit and/or download simulation results. Collaboration may include collaboration across sites. Users at different locations may use and collaborate with the same system. Collaboration may include collaboration across time. Settings, analysis, results, and the like may be saved and modified by different users at different times. Changing settings from analysis performed in the past may automatically trigger analysis based on new setting and a comparison against previous results.

[0722] In embodiments, the systems and methods described herein may include design and optimization or various clinical trial types and may include: parallel group design, cluster randomized design, crossover design, titration design, enrichment design, group sequential design, placebo-challenging design, blinder reader designs, single-stage up-and-down phase 1 design, two-stage up-and-down phase 1 design, continual reassessment method phase 1 design, optimal/flexible multiple-stage designs, randomized phase II designs, dose-escalating design, biomarker-adaptive design, adaptive randomization design, pick the winner design.

[0723] In embodiments, the system and methods described herein may include trial design and optimization for different phases of trials. In embodiments, different phases of trials (such as preclinical, phase 0, phase 1, phase 2, phase 3, phase 4) may use different considerations and, in some cases, use different simulation engines, analysis algorithms, interfaces, wizards, and the like. In embodiments, the scenario space, design space, criteria space, and/or performance space may be modified or different based on the phase of the trial and/or type of trial.

[0724] In embodiments, the systems and methods described herein may include consideration and analysis of trial resources. Trial resources may include resources to prepare, conduct, and evaluate a clinical trial. Examples include drugs/drug supply subject to the trial, devices subject to the trial, and/or administrative personnel and/or equipment needed to administer a procedure/drug/device subject to the trial. Resources may include test equipment to analyze and certify results. Availability, cost, time for acquisition and the like of resources may be a factor in performance space, design space, scenario space, and/or criteria space during design and evaluation of clinical trials.

[0725] Computational resources (such as servers and cloud services) used for simulation or analysis during trial design may operate in batch mode or may operate with a time delay between when the resources are requested and when they are available for use. Batch mode and a time delay may reduce responsiveness of an interactive design simulation. In embodiments, a platform may predict when a request for computation resources should be issued such that they are available when needed. Triggers, such as progress in the interface, time of day, amount of data entered, meeting schedules, and the like may be used to predict when simulations or analysis will be ready for execution or computation. In embodiments, machine learning models may be used to predict when computational resources should be requested such that they are ready when simulations are ready for execution. Models may use historical data. Computation resources may be requested ahead of time before they are needed in anticipation of a future request.

[0726] In embodiments, the size of a batch of computation (which may be correlated with the time of computation) may be sized based on predicted computational requirements for the project. Predictions may be based on history of similar projects, users, and the like. In embodiments, the size of a batch may be related to when computation resources are expected to be available, a prediction of when simulations or analysis will be ready for execution or computation and how long the execution or computation is expected to take.

[0727] FIG. **147** shows aspects of an apparatus for determining resource allocation in accordance with an embodiment of the current disclosure. The apparatus may include a resource allocation engine **14706**. The resource allocation engine **14706** may include a resource response data component **14708** configured to identify and/or maintain data related to resource capabilities, costs, allocation delay, computing power and the like. The resource response data component **14708** may include one or more tables or databases that identify available or authorized resources for performing batch computations for simulation, analysis, and other platform tasks. The resource response data component **14708** may be configured to trigger the polling engine **14712** to determine data for computational resources. The polling engine **14712** may be configured to periodically or upon a trigger event, identify a list of available resources, their availability, cost, computational capability, time to availability and the like. The polling engine **14712** may transmit a data request directly to one or more resources to determine their availability. In some cases, the polling engine **14712** may transmit a data request **14716** to a central database to determine data for the resources. The polling engine **14712** may update, with the resource response data, the component with the determined data. The resource allocation engine may receive data related to the design progress **14702** within the platform. The design progress may indicate what data has been entered for a design study, how quickly data is entered, what part of the interface the user is currently interacting with, and the like. The resource allocation engine may receive data related to the study parameters **14704**. The study parameters **14704** may identify how many designs and/or scenarios are being considered for simulation, types of simulations required, the types of computation engines related to the simulations, and the like. The prediction engine **14710**, may, based on the design progress data **14702** and/or study parameter data **14704**, predict when resources will be required and how much of the resources are required for the study. The prediction engine **14710**, may, using resource response data and the required resource predictions determine when the resources should be requested such that they are available when needed. The prediction engine **14710** may factor in the allocation delay, costs of resources, and the like to determine when a request for resources should be made and how many resources should be requested. In some cases, the prediction engine **14710** may determine, based on the predictions, a trigger in the design progress data **14702** that when reached will cause the resource allocation engine to issue a resource request **14714** to allocate resources in anticipation of need.
[0728] In embodiments, the prediction engine may determine when resources should be allocated or determine progress triggers for allocation based on historical data of design progress and time of resource request. In embodiments, one or more machine learning models may be trained on the historical data to train the model to predict when resources will be needed. The prediction when the resources will be needed may then be used to request resources ahead of when they are needed according to the time delay associated with each resource. In some embodiments, additional data such as calendar data, meeting data, and the like may be used to make or supplement the prediction process. Meeting data may indicate that resources may be required for computation during the meeting.
[0729] In embodiments a prediction engine may determine triggers such as a specific location in the interface that indicate that the study is almost ready for simulation and resources should be requested. Triggers may include when specific data is entered, when one or more locations in the interface progression are reached, and the like.
[0730] As shown in FIG. **148**, a method for determining a trigger for requesting computational resources may include monitoring design specification progress **14802** and determining resource allocation parameters **14804**. Resource allocation parameters may include data related to the time delay between when a resource is requested and when the allocation is available for use. The method may further include predicting when computation resources will be required based on the design specification progress **14806**. Predicting may be based on historical data, trained machine learning models, external data, and the like. Based on the predicting, a design specification

progress trigger point may be determined **14808**. The trigger point may be identified to correspond to the time delay associated with obtaining a resource and expected requirement of the resource. The design specification progress may be monitored for the determined trigger and in response to the trigger being observed, the computational resources may be requested such that they are allocated and ready when they are predicted to be needed **14810**.

[0731] In embodiments, computing resources may be allocated in anticipation of collaborative sessions for trial design. For example, embodiments of the current disclosure may detect that one or more users are in, or are about to enter, a collaborative session and spool computing resources. The spooling of computing resources may be based on one or more aspects of the platforms, disclosed herein, that the users are likely to use. In embodiments, where it is detected that one or more uses are about to enter a collaborative session with interactive interfaces, as described herein, one or more computationally expensive but highly interactive interfaces may be spooled up to improve overall responsiveness of the interfaces to the users.

[0732] In certain aspects, allocating of resources may be based on one or more triggers, e.g., a user location in an interface, embodiments of the platform may provide an alert and/or message dialogue box to a user confirming that the user's wishes to proceed with the allocation.

[0733] Embodiments of the current disclosure may provide for a score for comparing simulated designs. The score may be a proxy or an indicator of metrics that may not be directly determined from available or simulated data. The score may be used as a guide to identify interesting or valuable designs during design analysis or exploration. The score may be used as an initial design ranking score. As will be understood, embodiments of the analysis facility **108** (FIG. **1**) may compute the score (herein also referred to as a “proxy score” or a “comparison score”).

[0734] The comparison score may be a score based on one or more score components. The score may be a function of one or more score components. Score components may include one or more simulated, predicted, and/or calculated performance metrics of a design such as cost, time to completion, success, and the like. Score components may include one or more elements of the design space such as properties of a design that are not dependent on simulation and may be related to the type of a design and/or specified by a user. For example, score components may include aspects of design type, dose of drug, frequency of drug, maximum duration, patient inclusion/exclusion criteria, randomization type, and the like.

[0735] The score may be computed based on a weighted sum or other function of a plurality of score components. Score components and/or functions for a score may be configured by a user. A user may configure a score via one or more interfaces or may provide a specification by other means (such as via a specification or configuration file that is accessible by the platform). A user (using an interface, specification files, etc.) may specify or select one or more score components for computing the score, the function used to compute the score, weighting of score components, normalization of score component values, and the like. In some cases, a set of preconfigured scores that have preconfigured score components, weights, functions, and the like may be selected from a list of predefined scores.

[0736] In some cases, score configuration may include an input or a specification of the type of score the user would like to compute. The type may include that the score is a proxy score for NPV, duration, robustness, and the like. Each of the types may be associated with a set of score components. Based on the selection of type and the associated score components for each type, the platform may identify a list of available score components that are related to a computation of the type of score selected. In some cases, not all score components associated with the type of score selected may be available in the simulated data. The available score components for the selected score type may be automatically used to compute the score. In some cases, the available score components may be presented to a user and the user selects one or more of the score components for inclusion in the score.

[0737] In some cases, the score components may be normalized or transformed before the score component is used in the computation of a score. Score components may be normalized according to the type of data (i.e. Boolean, integer, float, string, etc.), number of possible values (i.e. a set of possible values, continuous values), range of values (i.e. difference between maximum and minimum values in the simulation data), and the like. For example, score components that are of a string data type may be normalized to an integer value wherein each string is represented by a different integer value. In another example, score components that are of a string data type may be normalized to a value between 0 and 1. In another example, score component values that are larger than 1 or less than 0 may be normalized such that each score component value is within the range between 0 and 1. Normalization may be configured such that the maximum value of a score component is normalized to the value **1**, the minimum value of a score component is normalized to a value of 0, and all other values of the score component are normalized to a value between 0 and 1 where the normalized value is based on how far the value was from the maximum. For example, a score component x may be normalized to a score component x′ according to x (x−x.sub.min)/(x.sub.max−x.sub.min). In embodiments, normalization may include normalization techniques that include and/or are based on linear scaling, clipping, log-scaling, z-score, and the like. In embodiments, normalization may include normalization techniques including substitution, rounding, mapping, and the like. In some cases, normalization techniques that normalize each score component value to a value between 0 and 1 may be preferable as they can be easier to manipulate and compare numerically.

[0738] A score may be a function of one or more score component values. In one embodiment, a score may be a sum of the values of a plurality of score components. In another embodiment, a score may be a sum of the normalized values of a plurality of score components. In yet another embodiment, a score may be a weighted sum of the normalized values of a plurality of score components. For example, a score s.sub.1 for a design may be computed as a weighted sum of the normalized score components c.sub.1, c.sub.1, . . . , c.sub.n according to s.sub.1=w.sub.1c.sub.1+w.sub.2c.sub.1+ . . . +w.sub.nc.sub.n wherein w.sub.1, w.sub.1, . . . , w.sub.n are weighting values associated with each normalized score component. The weights associated with each score component for the computation of the score may be based on relative importance of the score component. Score components that are more important for a score may be multiplied by a larger weighting value.

[0739] A score may be computed for each simulated design. In some cases a plurality of scores based on different score components, functions, weights, and the like may be computed for each simulated design. The score may be used to filter designs such that only designs that are larger than the score, lower than the score, between some values, and/or the like are shown. The score may be used to rank or order designs such that designs with the highest score are shown first to a user.

[0740] In embodiments, the score may be computed before simulation (a score that is not based on simulation results), during simulation (scores may be computed using one or more simulated score components in real time as simulation results are obtained), and/or after simulation.

[0741] In embodiments, a score computed using normalized score component values may be a relative score. The score may provide a relative value of a design with respect to other designs that are computed according to the same normalization. In some cases, scores may not be absolute and scores from different simulation runs may not be comparable. For example, if a score is normalized with respect to the minimum and maximum score component values of a simulation, the score will not be comparable with a score from a different simulation that has different minimum and maximum score component values.

[0742] In some cases, score values may be stored or associated with the data used to determine the score. A score may be associated or stored with data that identifies which score components were used to compute the score, the values of the score components, the function for computing the score, the normalize score components, normalization function, and/or the like. The associated data may be a vector or array of data that is stored or associated with each score or simulation run and

may be used to determine if scores from different simulation runs are comparable. The associated score data from two different simulation runs for different designs may be compared to determine if the scores are based on the same score function, normalization function, score components, and the like to determine if they can be used to accurately compare designs from different simulations. In some cases, when the scores from different simulation runs are identified as not comparable based on the comparison of the associated data, the mismatch between the associated data may be identified. In some cases, the mismatch between the data may be used to identify functions or methods to recalculate or modify one or more of the scores to make the scores comparable.
[0743] For example, one set of scores for designs simulated in a first simulation run may be based on the same score function, score components, and normalization functions for the score component values as a second set of scores for designs in a second simulation run. The first set of scores and the second of scores may still not be comparable since the minimum and/or maximum values of the score components for the first simulation run and the second simulation may be different which may result in a different normalization of values (such as when the normalization is based on the minimum and maximum values as described herein).
[0744] In one example, identification of the minimum and maximum values for the score components for each simulation run may allow a modification of the scores such that they are based on the minimum and maximum scores of the two simulation runs. In embodiments, the associated data for scores from two or more simulation runs may be compared. The platform may determine if the scores are comparable. If they are not comparable the platform may determine if the associated data includes enough information to transform or renormalize the score component values such that they are comparable.
[0745] FIG. **149** shows aspects of an apparatus for determining a score in accordance with an embodiment of the current disclosure. The apparatus may include a scoring engine component **14908**. The scoring engine component **14908** may be part of the analysis facility **108** of the platform **104**. The scoring engine component **14908** may determine a score for design that may be used to compare the designs. The scoring engine component **14908** may receive one or more simulation data **14902** that may include simulated performance characteristics of designs and the design definitions. The scoring engine component **14908** may receive one or more score selections **14904** that may define which score should be computed, how a score is computed, the type of score that is computed and the like. The score selections **14904** may be defined by user input **14906** or other data input or files that are accessible to the scoring engine **14908**. The scoring engine component **14908** may include a scoring definitions component **14920** that provides definitions or mappings between score selections **14904** and operations, score components, and calculations that are needed to determine a score. The score definitions **14920** may include data that defines what score components should be included for one or more score type calculations.
[0746] The scoring engine component **14908** may include a simulation data analysis component **14912** that may identify score components that are used for computing a score and may determine if and how they should be normalized. The simulation data analysis component **14912** may analyze the range of the data, data type, number of values, and the like to identify the normalization operations for the score components. The normalization component **14910** may be configured to perform normalization operations on the score component values from the simulation data according to the results of the simulation data analysis **14912** component. The normalization component **14910** may perform any number of normalization functions including, substitution, mapping, rounding, clipping, and the like. The calculation module **14914** of the scoring engine **14908** may determine one or more scores of the designs according to the score definition **14920** and normalized data from the normalization component **14910**. The score and associated data **14918** may be stored in a database that is local to the scoring engine **14908**, in other parts of the platform **104** or external to the platform. The score and associated data **14918** may include the score, score definitions used to determine the score, normalization functions used to normalize

values of the score components, results of simulation data analysis (such as min and max values), and/or the like.

[0747] The scoring engine component **14908** may further include a comparison component **14916**. The comparison component **14916** may be configured to receive score and associated data **14918** from one or more simulation runs and determine if the scores are comparable. Scores may be comparable if the scores are based on the same score definitions, calculations, normalization functions, and the like. The comparison component **14916** may compare the scores and associated data from one or more simulation runs and determine if the scores may be modified to make them comparable. In embodiments, the comparison component **14916** may identify differences in the associated data (such as differences in normalization functions) and determine how one or more of the scores or score components may be modified or mapped to new values to make scores comparable. In some cases, the comparison component **14916** may cause one or more of the calculation components **14914**, normalization components **14910**, and/or simulation data components **14912** to recalculate or modify the score based on the determined differences in the associated data between scores.

[0748] As shown in FIG. **150**, a method for determining a score for a design may include obtaining trial design simulation results for a set of trial designs **15002** and receiving a score selection **15004**. The score selection may be a definition of a score, a type of a score, a framework of a score (such as what weights and type information), and the like. Based on the score selection, the score components for the score selection may be identified **15006**. The score components may be identified according to the type of score that the user specified. A lookup table may be used to provide a listing of all score components that are related to a score type. The identifying of step **15006** may include searching the simulation results to find which score components are available. The method may further include determining a normalization function for each score component **15008**. The normalization function may be based on the type of data, ranges of data, and the like as described herein. Each score component may have different normalization functions. In some cases two or more normalization functions may be applied to a score component. The normalization functions may be used to normalize the score components **15010** and the normalized score components may be used to determine a score **15012**. The score may be based on a function of the score components. The function may be a weighted sum of the normalized score components. The weights may be specified by the user or determined based on the type of score. Scored designs may be presented and/or recommended to a user and ranked or filtered according to the score.

[0749] As shown in FIG. **151**, a method for score transformation may include obtaining design scores and associated score data for designs from a plurality of simulation runs **15102**. The simulation runs may be from parallel simulations or simulations at different times. The associated score data may include data as to how the score was computed, normalization functions, score functions, weighting of score components, aspects of the data values (such as ranges, min/max values, etc.) of the score components, and the like. The method may include comparing the associated score data to determine if the scores from the plurality of simulation runs are comparable **15104**. If the associated score data indicates that the scores are based on the same or comparable functions, normalization functions, and the like the scores may be determined as comparable and otherwise determined as not comparable **15106**. When the scores are not comparable, the method may include determining a normalization function for one or more scores to make the scores comparable **15108**. For example, the normalization function may be taken into account the minimum and maximum values for score components across all of the simulation runs and determine a multiplications factor or other function to make the scores comparable. Designs with scores that are comparable may be presented and/or recommended to a user and ranked or filtered according to the score. In embodiments, the proxy score may be computed during one or more collaborative session for design analysis. In such embodiments, the proxy score may be based at least in part on one or more user preferences detected through one or more interactive interfaces.

In embodiments, the proxy score may be generated in part via machine learning, e.g., a neural network. For example, a neural network can be trained to generate a proxy score from one or more design parameters and/or scenario parameters.

[0750] In embodiments, the platform may be configured for collaboration. Collaboration features may be enabled via one or more methods and/or interfaces for design specification, filtering, and selection. Collaboration features may be configured to allow multiple users to work together to determine, develop, analyze, and/or select a trial design. In some embodiments interfaces and methods may be configured such that multiple users may view and interact with design and analysis tools for group evaluation of simulated designs. Collaboration features may be used to facilitate collaboration between users at different locations (or simply users that use separate computers and interfaces) and/or users that are at one location and can view the same interface. Collaboration may occur in one or more collaboration sessions. Collaboration sessions may include sessions where multiple users work on different or the same tasks concurrently. Collaboration sessions may include sessions where multiple users work and collaborate on different tasks sequentially. Collaboration sessions may occur in a continuous time block or may include two or more disjoint or asynchronous time blocks that may occur at different times of the day, different days, and the like.

[0751] In some embodiments, a collaboration session may include one or more users collaborating in real time. A real-time collaboration session may include a session in which multiple users may work together to reach a consensus on one or more aspects of a trial design. The real-time collaboration session may include a session in which users may work together to evaluate and select one or more trial designs based on evaluation of simulated trial designs. The real-time collaboration session may include a session in which users may work together to specify design and evaluation parameters for a simulation for a trial.

[0752] During a collaboration session, the interface may step through one or more tasks for accomplishing the goals of the session. Tasks may be associated with a sequence of different graphical interfaces, a sequence of computations, and/or a combination thereof. The sequences of interfaces and/or computations may be at least partially preconfigured providing for a framework of sequences for accomplishing a task. The framework of sequences may include divergent or a tree like framework allowing users to tailor or dynamically change the sequences based on decisions made during the session, results from previous operations, and the like.

[0753] For example, in one case, a goal of a collaboration session may include selection of one or more trial designs from a set of simulated trial designs. Based on the specified goal, a platform may load or determine a proposed starting point for the session (such as which interface to show) and what interfaces may be shown and/or computations may be performed as a result of selections or actions in the first interface. As an example, the starting point for the session in this example may be a list of top or optimum design as determined from the simulated data using convex hull analysis. The interface may show the top designs along with their parameters. The top designs may be shown with options for selection, further analysis, comparison, and the like. Based on the selections the sequence may be configured to provide additional analysis or comparison of the top designs or provide additional suggested designs (such as twins or siblings of the top designs). The design may further be compared against one another or against the space of all available designs (such as using heatmaps, tornado diagrams, and the like). In one example, the general sequence for the session may include design selection, design comparison, evaluation of twin designs, a drill down of performance parameters, and the like. The sequence of interfaces may be configured to ensure the top designs are considered, as well as alternative designs that are close to selected designs are considered during the session.

[0754] In another example, a sequence of interfaces and/or computations in a session may be configured to surface, in real time, similar designs such as twins, siblings, Pareto designs, and the like to one or more selected or top designs. A user or a group of users may be guided to explore/consider a range of different design types and/or design parameters. Design alternatives (such as different design types, siblings, twins, etc. that may have similar performance to selected designs) may be automatically identified (such as by using one or more Pareto, Convex Hull, and other algorithms) and provided for consideration. Parameters of the alternative design that complement or diverge from previous designs and selections may be emphasized and users may be guided to make evaluations and selections of the alternative parameters.

[0755] In another example, a sequence of interfaces and/or computations in a session may be configured to allow designs to be compared with respect to robustness of the designs. Robustness of the designs may indicate the range of parameters for which designs have acceptable or good performance. Interfaces may be used to indicate design performance over a range of parameters in addition to the best possible performance thereby allowing users to visualize/evaluate and debate the risks associated with the designs.

[0756] In some embodiments, collaboration interfaces in a collaboration session may be tailored or customized based on the type of the user. Users may be provided with a different interface according to their expertise, authority, tasks, roles, and the like. During a collaboration session, the platform may receive or determine the type of user interacting with the platform. A user type may be specified by an administrator or a curator of a project or a session. A user type may be associated with an identity or credentials of a user. In some cases, a user may specify their own role or type. In some cases, the sequence of interfaces or available computations may be different for each user type in a session. For example, during a collaboration session configured with a goal of selecting one or more designs, different user types may be shown different parameters of a design under consideration. The parameters and data shown to the user may depend on the expertise of the user. For example, a user designated as a financial expert may be show parameters that are focused on the cost, time, resources, personnel, and the like associated with the design. Another user that is designated as an expert in patient recruitment may be shown parameters of the designs that focus on the patient requirement and/or assumptions associated with each design. In embodiments, each interface customized for each user type may provide options to search for other designs according to the parameters associated with the user type. In some cases, some users may be provided with interfaces that hide certain aspects, such as aspects that are sensitive or that the user is not authorized to view. In some embodiments, interfaces may be configured such that every group member can view the same interface during a collaboration session.

[0757] In some embodiments, decisions in a collaboration session may be achieved by consensus, voting, and the like. In embodiments, some users or user types may be designed as owners or curators of one or more parameters of the designs. The owners or curators may be specified according to expertise of the user. In some embodiments, consensus on a design decision may require approval by each curator of one or more parameters of the design. In some cases, design parameters may be divided into subsets and different users may be assigned as experts for each subset of parameters. In one example, during a collaboration session, different users may be shown different parameters of a design based on their expertise. The interfaces for each user may show options for approving a design based on the respective parameters, rejecting the design based on the respective parameters, and the like. In one configuration, consensus on a design or a selection of a design during a collaborative session may require approval from each user responsible for a subset of the design parameters. In another example, interfaces for voting on designs may allow a user to collectively agree or disagree on a design by voting. In some cases, votes of users may be weighted based on their expertise, seniority, and the like. In embodiments, the platform may trac each user vote (a binary value such as yes or no, a range of values or rating such as 1-10, or 1-100). The votes may be associated with the user expertise such that the votes may be filtered according to each expertise or type of user. The votes may be associated with a weight (based on seniority, expertise, assigned weight). A vote score for a design may be determined by summing all the votes and/or vote value for each design. In some embodiments, each vote or each vote value may be multiplied by the weight associated with each vote to determine a vote score.

[0758] In another example, a goal of a collaboration session may include selection of one or more trial designs from a set of simulated trial designs. A collaboration session may be configured to divide users into multiple groups of one or more users. Each group may be provided with a sequence of interfaces and computations to evaluate and select one or more designs. Each user or group of users may individually explore and/or be guided to explore and consider different designs. Design selections made by the individuals or subgroups of users may then be evaluated collectively in a joint collaborative session.

[0759] In another example, a goal of a collaboration session may include development of simulation parameters for running a design simulation. Based on the specified goal, a platform may load or determine a proposed starting point for the session (such as which interface to show) and what interfaces may be shown and/or computations may be performed as a result of selections or actions in the first interface. As an example, the starting point for the session in this example may be an interface for specifying design goals and design parameters. The sequence of interfaces may step through the design, scenario, and performance parameters that need to be defined before the simulation is executed. In embodiments, different users may be identified as experts or associated with different parameter types. In some cases one type of users may be shown only parameters for scenarios while another may be shown only parameters for designs.

[0760] As shown in FIG. **152**, a method for determining a collaborative session sequence may include receiving a goal for a collaboration session **15202**. Based on the goal, a framework for a sequence of interfaces and/or computations for the collaboration session may be identified **15204**. The method may further include presenting an initial interface according to the framework **15206**. The method may further include determining the next sequence based user input in the initial interface, according to the framework **15208**.

[0761] As shown in FIG. **153**, a method for generating a collaborative interface may include displaying a graphical user interface structured to evaluate designs by a group of users **15302**. The method may further include identifying expertise parameters for each user in the group of users **15304** and configuring the graphical user interface for each user based at least in part on the expertise parameters **15306**. The method may further include receiving user input from users via the graphical user interface **15308** and scoring designs based on the user input and expertise parameters **15310**.

[0762] FIG. **154** shows aspects of an apparatus for generating a collaborative interface. The apparatus may include a collaborative interface circuit **15408**. The collaborative interface circuit **15408** may generate interfaces **15416**. The collaborative interface circuit **15408** may receive user interaction **15402** from the interfaces **15416**. The collaborative interface circuit **15408** may receive user type definitions **15404** that may be used for interface customization **15414** with the selection parameter provisioning component **15410**. The sequence of the interfaces may be defined by the sequence component **15412** according to the user interactions **15402** with the user interfaces **15416** populated with simulation data **15406**.

[0763] The space of simulated designs can be explored in a systematic way using convex hulls and convex hull peeling. As described herein, convex hulls separate out P-designs that are reachable by linear weighting criteria (CH-designs or CH-points). In many cases, design analysis and recommendation may start with recommendations of CH-designs or designs that are twins, siblings, or are within an epsilon distance to the CH-designs. Designs that are on or near the convex hull are often the most desirable designs (designs that are often ultimately selected for a study). Concentrating recommendations and design analysis on designs on or near the convex hull greatly reduces the number of designs that need to be examined. In some cases only one or two percent of the total simulated designs need to be considered when initial design recommendations provided by the platform are on or near the convex hull. Design recommendations based on convex hull designs may have further benefits such as providing fast evaluation for any weights specified and allowing introduction of constraints that can be used to eliminate unlikely or uninteresting designs and scenarios.

[0764] In embodiments, simulated designs may be explored based on a hierarchy of convex hulls. A hierarchy of convex hulls may be created by determining a convex hull of designs, removing the designs that are on the convex hull, and determining another convex hull of the remaining designs. The "peeling" of convex hulls and determining new convex hulls can be performed iteratively to identify a series of convex hulls in a simulated design space. The designs associated with each convex hull can create a hierarchy of designs.

[0765] FIG. **155** shows a graphical example of a hierarchy of convex hulls. The figure shows four layers (CH_1, CH_2, CH_3, and CH_4) of convex hulls in a two dimensional example. The first convex hull (CH_1) of the designs (represented by points in the graph) may be determined by finding the convex hull of all the designs. The second convex hull (CH_2) may be determined by finding the convex hull of all the design except the designs that are on CH_1. The third convex hull (CH_3) may be determined by finding the convex hull of all the design except the designs that are on CH_1 and CH_2. The fourth convex hull (CH_4) may be determined by finding the convex hull of all the design except the designs that are on CH_1, CH_2, and CH_3, and so on. In the example, the convex hulls are peeled to identify a new convex hull of the remaining design to create a hierarchy of designs according to each convex hull layer. It should be understood that although FIG. **155** shows a convex hull peeling example in two dimensions, a hierarchy of convex hulls may be determined for any number of dimensions for data related to any number of performance parameters.

[0766] Designs from each convex hull may be associated with a level. The designs in each convex hull may be stored and associated with the convex hull level on which they can be found. In general, designs on the first convex hull (first level) may have better performance than designs on following convex hulls (higher levels). In some cases, although a design from a higher lever may have worse performance than a design in a first level convex hull, the design from a higher level may be preferrable for a study due to other considerations such as practicality, familiarity with the design type, regulatory approval delays, and the like. The hierarchy of designs may provide for quick identification of designs that are within a given percentage of the optimum designs (designs that are on the first convex hull). In some embodiments, convex hull levels may be used for recommending designs to a user (such as with the recommendation engine described herein). Initial recommendations may include recommendations from the first convex hull or the first couple of convex hulls. In response to a user request or other triggers, additional recommendations from other levels of convex hulls may be provided to the user. The organization and progressive suggestion of designs from higher level convex hulls provides for a systematic organization of designs for recommendations allowing a user to consider designs ordered by their optimality.

[0767] In some embodiments convex hull levels may be associated with an epsilon distance. Convex hull peeling may include peeling of designs that are on a convex hull and designs that an epsilon distance from the designs on the convex hull. Designs associated with each convex hull level may include designs that are on a convex hull and designs that are epsilon distance away from the designs on a convex hull. Epsilon distance convex hulls level may be defined by first determining designs on the convex hull and epsilon distance designs from the designs on the convex hull. The designs on the first convex hull and epsilon distance away from the designs on the first convex hull may be associated with the first level. The second level designs may be determined by finding designs a convex hull of all the design except the designs that are in the first level. The second level designs may include designs that are on the second convex hull and all the designs that are epsilon distance away from the second convex hull. Additional levels of designs may be determined in a like manner. In embodiments, epsilon distance may be refined based on the number of designs in each level. In some cases, a different epsilon distance may be defined for each level such that each level has the same number of designs, less than predetermined number of designs, at least minimum number of designs, or other metric.

[0768] As shown in FIG. **156**, a method for determining a design hierarchy based on convex hull peeling may include obtaining trial design simulation results for a set of trial designs **15602**. The method may further include determining designs on a first convex hull of the set of trial designs **15604**. In some cases, the method may include identifying designs that are epsilon distance from the designs on the first convex hull **15606** and the designs epsilon distance away from the first convex hull may be identified as first level designs **15608**. In embodiments, the epsilon distance may be adjusted such that the number of designs that in the first level is within a range of values or is less than or more than a threshold value. To determine the second level of designs, the designs identified as being in the first level may be removed from the set of designs **15610** and a second convex hull of the remining designs may be determined **15612**. Optionally, designs that are an epsilon distance from the second convex hull may also be identified **15614**. Designs on the second convex hull and the designs epsilon distance away from the second convex hull may be identified as second level designs **15616**. In embodiments, the epsilon distance may be adjusted such that the number of designs in the second level is within a range of values or is less than or more than a threshold value. In some cases, the epsilon distance may be adjusted such that the number of designs in the second level is the same or within a threshold value to the number of designs in the first level. The process of “peeling” the convex hulls (and optionally designs that are epsilon distance away from the designs on the convex hull) and determining new a convex hull may repeat until a desired number of design levels is obtained. Designs in each level may be presented and/or recommended to a user and ranked or filtered according to their associated level. The platform may use the hierarchy of convex hulls to suggest or identify the best designs (designs that are on the first convex hull) and second-best designs (designs that are on the second convex hull) and so on.

[0769] In some embodiments, a hierarchy of convex hulls and convex hull peeling may be used to reduce the number of simulations in a study. In some cases where scenarios are monotone with respect to criteria, results of simulation of one scenario may be leveraged to reduce the number of designs that need to be simulated to find the convex hull for designs for other scenarios. In one embodiment, an algorithm may iteratively determine a convex hull of designs under a first scenario and simulate the designs for a second scenario. The convex hull of the designs in the second scenario may be determined without simulating all of the designs but only designs that are within the first couple of convex hulls under the first scenario until no improvement to the convex hull of the designs under the second scenario is observed. In some examples, a 4×-8× reduction in simulations needed to find the convex hull for a second scenario can be achieved by leveraging convex hull peeling in simulated designs for a first scenario.

[0770] FIG. **157**(*a-e*) shows a graphical example of how convex hull peeling may be leveraged to reduce the number of simulations needed to find a convex hull for designs for a scenario. In embodiments, some scenarios may be monotone with respect to criteria and can be ordered. In some cases, some scenarios parameters may be known to have a direct correlation to one or more performance parameters of designs. In cases where the scenarios may be ordered with respect to the performance of the designs, convex hulls of simulations for one scenario may be leveraged to reduce the number of simulations needed to find a convex hull for another (worse) scenario. In embodiments, simulations may be performed for designs under a first scenario. In some cases the simulations for designs under the first scenario may be exhaustive. Levels of convex hulls may be determined for the designs using convex hull peeling as described herein. To determine designs that are on a convex hull for a second scenario, only the designs that are on the convex hulls of the first scenario may be simulated.

[0771] FIGS. **157**(*a-e*) shows a progression how convex hulls for designs for one scenario (scenario “67”) may be used to determine which designs should be simulated for a second scenario (scenario “69”) to determine the convex hull designs for the second scenario. It should be noted that the figures, for clarity, do not show all of the simulated designs for the first scenario and only show the designs that are on the convex hull for the first scenario. FIG. **157**(*a*) shows the first iteration of the method. In the first iteration a first convex hull for designs for scenario **67** may be determined (CH_67_1). The designs in the first convex hull may then be simulated to determine their performance under the second scenario (CH_67_1_69) and the convex hull of all the designs simulated for the second scenario may be determined (CH(CH_67_1_69)). After the first iteration, in this example, only designs that are on CH_67_1 are simulated for the second scenario.

[0772] FIG. **157**(*b*) shows the second iteration of the method. In the second iteration, a second convex hull for designs for scenario **67** is determined (CH_67_2). The second convex hull may be determined by convex hull peeling described herein. The designs in the second convex hull may then be simulated to determine their performance under the second scenario (CH_67_2_69) and the convex hull of all the designs simulated for the second scenario may be determined (CH(CH_67_2_69)). In the second iteration, in this example, only the designs that are on CH_67_2 are simulated for the second scenario. In the second iteration, for this example, the convex hull for the second scenario does not change.

[0773] FIG. **157**(*c*) shows the third iteration of the method. In the third iteration, a third convex hull for designs for scenario **67** is determined (CH_67_3). The third convex hull may be determined by convex hull peeling described herein. The designs in the third convex hull may then be simulated to determine their performance under the second scenario (CH_67_3_69) and the convex hull of all the designs simulated for the second scenario may be determined (CH(CH_67_3_69)). In the third iteration, in this example, only the designs that are on CH_67_3 are simulated for the second scenario. In the third iteration, for this example, the convex hull for the second scenario changes compared to the second iterations.

[0774] FIG. **157**(*d*) shows the fourth iteration of the method. In the fourth iteration, a fourth convex hull for designs for scenario **67** is determined (CH_67_4). The fourth convex hull may be determined by convex hull peeling described herein. The designs in the fourth convex hull may then be simulated to determine their performance under the second scenario (CH_67_4_69) and the convex hull of all the designs simulated for the second scenario may be determined (CH(CH_67_4_69)). In the fourth iteration, in this example, only the designs that are on CH_67_4 are simulated for the second scenario. In the fourth iteration, for this example, the convex hull for the second scenario further changes compared to the second iterations.

[0775] The iterations of determining a new convex hull for the first scenario, simulating the designs from the convex hull under the second scenario, and determining the convex hull of all the simulated designs under the second scenario may continue until there is no improvement or change in the convex hull for the second scenario for a threshold number of iterations (such as two or more, or three or more iterations). FIG. **157**(*e*) shows the tenth iteration of the method. In the tenth iteration, a tenth convex hull for designs for scenario **67** is determined (CH_67_10). The tenth convex hull may be determined by convex hull peeling described herein. The designs in the tenth convex hull may then be simulated to determine their performance under the second scenario (CH_67_10_69) and the convex hull of all the designs simulated for the second scenario may be determined (CH(CH_67_10_69)). In the tenth iteration, in this example, only the designs that are on CH_67_10 are simulated for the second scenario. In the tenth iteration, for this example, the convex hull for the second scenario has not changed for more than two iterations and method may stop wherein the convex hull designs for the second scenario are defined by the convex hull of the designs simulated up to and including the tenth iterations (CH(CH_67_10_69)). For this example, the number of designs that required simulation for determining the convex hull for the second scenario corresponds to the number of designs on the first ten convex hulls for the first scenario. The number of designs on the first ten convex hulls is a small percentage of the total number of designs for this example. In many embodiments, simulation for scenarios based on convex hull peeling may results in a reduction of simulation of four to eight times compared to an exhaustive simulation for a scenario.

[0776] A convex hull peeling for finding convex hull for adjacent monotone scenario without simulating full set of designs may take as input a dataset for a first scenario. The dataset for the first scenario may include simulation results for all design for the first scenario and may include design parameters for the designs and a multicriteria vector that identifies the simulated performance of the designs for the first scenario. Input to the algorithm may further include scenario variables for a second scenario. The algorithm may output the designs on the convex hull for the second scenario. The algorithm may start by initializing stopping parameter k to an initial value of 1. In step two of the algorithm, the kth convex hull for the dataset for scenario **1** may be computed using a convex hull algorithm. In step three of the algorithm, each design in the kth convex hull determined in step two may be simulated under the second scenario to calculate its multi-criteria vectors. In step four, the convex hull of the vectors determined in step three may be determined. In step five, the convex hull for the second scenario is compared to the convex hull computed for the second scenario in the k−1 iteration. In step six, the value of k may be incremented and steps two through five of the algorithms may be repeated until the convex hull for the second scenario does not change for at least two iterations.
[0777] As shown in FIG. **158**, a method for determining a convex hull for a scenario using convex hull peeling in another scenario may include initializing an iteration counter k to a value such as the value one **15802**. The method may include computing the kth convex hull for designs simulated for a first scenario **15804**. The designs from the kth convex hull may be simulated for a second scenario **15806** and a convex hull for all the designs simulated for the second scenario may be computed **15808**. The value of k may be incremented **15810** and the method repeated starting at **15804** until no improvement to the convex hull is observed for i iterations **15812** wherein i may be a variable set by a user and may have a value of two or more.
[0778] FIG. **159** shows aspects of an apparatus for convex hull peeling in accordance with an embodiment of the current disclosure. The apparatus may include a peeling engine component **15904**. The peeling engine component may receive simulation data **15902**. The simulation set **15906** component may store and manipulate the simulation data. The convex hull engine **15908** of the peeling engine may determine a convex hull of the simulation data. The simulation set component **15906** remove designs that are found in a convex hull from the simulation data and associate them with design levels **15912**. The epsilon engine **15910** may optionally determine designs that are epsilon distance away from the designs on the convex hull. These designs may be optionally assigned to levels that are associated with each convex hull.
[0779] In embodiments, convex hull peeling may provide for evaluation of a design's robustness. For example, in embodiments, each convex hull level can have its own robustness ranking. In such embodiments, a user may be able to determine the most robust designs in each layer. As will be understood, in embodiments, some layers may have designs with an average robustness higher than an average robustness of other layers. Thus, some embodiments of the current disclosure may focus a user to search for designs within a particular layer having a high robustness. Embodiments of the design recommendation algorithm, as described herein, may evaluate the robustness of each layer and rank one or more of the layers based at least in part on robustness. The recommendation algorithm may be configured to recommend one or more layers, e.g., the top three (3), based on preferences derived from historical data, e.g., past user preferences.
[0780] Turning to FIG. **160**, embodiments of the current disclosure may provide for adaptive replication in clinical trial design simulations and/or other types of simulations described herein. As will be understood, embodiments of the simulation facility **110** (FIG. **1**) may evaluate a clinical trial design by using a fixed number of simulated replications. Adaptive replication, however, may involve dynamically changing the number of simulation replications for a particular design. In embodiments, adaptive rules may terminate replication sampling for designs. As will be explained in greater detail below, such changes may be based on computed standard error or other performance criteria.

[0781] Accordingly, an embodiment system **16000** for providing adaptive replication in clinical trial design simulation is shown. The system **16000** may include a server **16010** having at least one processor and a memory device. The system **16000** may further include an electronic device **16012**, one or more remote servers **16014**, **16016**, **16018**, and/or a database **16020** which may be in electronic communication with the server **16010** and/or each other via a network **16022**. The server **16010** may form part of and/or host one or more of the platforms **104** (FIG. **1**), **10404** (FIG. **104**) and/or **12504** (FIG. **125**), e.g., the simulation facilities **110** (FIG. **1**), **10410** (FIG. **104**) and/or **12510** (FIG. **125**); and/or the computational resources **150** (FIG. **1**), **10450** (FIG. **104**), and/or **12550** (FIG. **125**).
[0782] The server **16010** may be structured to execute a replication process forming part of a clinical trial design simulation that comprises a plurality of replications of a clinical trial design. As will be understood, a replication of a clinical trial design is a simulated instance of a clinical trial design under a given scenario and with a given set of parameters. During the replication process, the server **16010** may determine a performance criteria, e.g., a member of criteria space **318** (FIG. **3**) that defines a characteristic of the clinical trial, e.g., a number of patients who successfully completed the clinical trial. The server **16010** may then adjust the replication process based at least in part on the performance criteria. The adjustment may increase or decrease the number of replications of the clinical trial in the replication process. For example, if the server **16010** determines that there is little variation in the performance criteria of the most recently executed replication as compared to one or more previously executed replications, the server may reduce the number, e.g., the total number, of replications executed/evaluated in the replication process. As will be appreciated, reducing the number of replications in such a manner may reduce the overall time and resources required to complete simulation of the clinical trial design. Conversely, if the server **16010** determines that there is variation (above a desired amount) in the performance criteria of the most recently executed replication as compared to one or more previously executed replications, the server **16010** may increase the number of replications executed/evaluated in the replication process. As will be appreciated, increasing the number of replications in such a manner may improve the accuracy of the simulation. The server **16010** may also make other types of adjustments to the replication process, as described herein.
[0783] The electronic device **16012** may be a user device, e.g., **102** (FIG. **1**), such as a desktop, laptop, smart device, etc. In embodiments, the electronic device **16012** may provide for and/or present an interactive interface, e.g., **112** (FIG. **1**) that presents a plurality of prompts to a user for configuring the clinical trial design. The electronic device **16012** may also receive and display the results of the clinical trial simulation and/or provide notifications to a user regarding any adjustments made to the replication process by the server.
[0784] The database **16020** may form part of a data facility, e.g., **138** (FIG. **1**) and store replication results data, e.g., data generated during execution/evaluation of a replication of a clinical trial design. In embodiments, the database **16020** may store the replication results in a quick search data structure, as described herein, e.g., a SimCube. As such, embodiments of the server **16010** may access the database to retrieve and/or store replication results data.
[0785] The remote servers **16014**, **16016**, and/or **16018** may form part of a collection of computation resources, e.g., **150** (FIG. **1**) which can be accessed by the server **16010** to distribute processing tasks. For example, the server may generate batches of replications of the same replication process and/or of entire clinical trial design simulations for separate processing/evaluation by the remote servers **16014**, **16016**, and/or **16018**. Such batch processing may be accomplished in parallel, e.g., distributed parallel processing of replications, e.g., **100** replications for up to a maximum number, e.g., ten (10), of batches for several designs simultaneously.
[0786] In some embodiments, the number of simulated replications used to evaluate a design may be dynamically determined. The number of simulated replications may be dynamically evaluated

according to results of simulations. In some embodiments simulations for a design may be configured for a fixed number of replications. As the simulations progress, data from the simulations may be analyzed to determine if the number of simulations may be decreased or should be increased. For example, some embodiments may stop replications when the standard error of the score estimate is sufficiently small. Embodiments may also adapt the number of replications to the quality of the design. For example, some embodiments may stop replications when the difference from the lower 99% confidence interval of the best design found so far is higher than a 99% upper confidence interval of the design being replicated. Embodiments may invoke parallel processing to compute replications in batches, e.g., one-hundred (100) replications for up to a maximum number, e.g., (10), of batches for several designs simultaneously. Adaptive rules, e.g., rules that change over time or in response to a set of conditions, may terminate replication sampling for designs.

[0787] Turning to FIG. **161**, an embodiment of an apparatus **16100** for providing adaptive replication in clinical trial design simulation is shown. The apparatus may form part of the **16010** and/or other computing devices described herein. The apparatus **16100** may include a replication circuit **16110**, a results interpretation circuit **16112**, a performance circuit **16114**, an adjustment determining circuit **16116**, and an adjustment circuit **16118**. The replication circuit **16110** may be structured to execute a replication process **16120** that includes a plurality of replications **16122**, as discussed herein. Execution of the replication process **16120** generates corresponding replication results data **16124**. In embodiments, the replication circuit **16110** may be structured to batch the plurality of replications **16122** into a plurality of batches for parallel execution on two or more processors, e.g., remote servers **16014**, **16016**, and/or **16018**.

[0788] The results interpretation circuit **16112** is structured to interpret the replication results data **16124** of at least one of the replications **16122**, and the performance circuit **16114** is structured to determine, based at least in part on the replication results data **16124**, a performance criteria value **16126**. The adjustment determining circuit **16116** is structured to determine, based at least in part on the performance criteria value **16126**, an adjustment value **16128** to the replication process **16120**. The adjustment circuit **16118** is structured to adjust the replication process **16120** based at least in part on the adjustment value **16128**.

[0789] The performance criteria value **16126** may include and/or be based at least in part on a standard error. The adjustment determining circuit **16116** may be further structured to configure the adjustment value **16128** to cease the replication process **16120** when the standard error is below a threshold.

[0790] The performance criteria value **16126** may include and/or be based at least in part on an upper confidence interval of the clinical trial design corresponding to the replication **16122** that generated the replication results data **16124**. In embodiments, the adjustment determining circuit **16116** may be further structured to configure the adjustment value **16128** to cease the replication process **16120** when a difference from a lower confidence interval of another clinical trial design (other than the one corresponding to the replication **16122** which generated the replication results **16124**) is higher than the upper confidence interval.

[0791] In embodiments, the apparatus **16100** may include a results retrieval circuit **16130** structured to retrieve at least some of the replication results data **16124** from a quick search data structure **16132**, which may be stored in a database, e.g., **16020** (FIG. **160**).

[0792] Illustrated in FIG. **162** is a method **16200** for providing adaptive replication in clinical trial design simulation. The method **16200** may be performed by the server **16010** and/or apparatus **16100** and/or another computing device(s) described herein. The method **16200** includes interpreting, via at least one processor, e.g., apparatus **16100** (FIG. **161**), replication results data **16210**. As described herein, the replication results data may form part of a replication process of a clinical trial design simulation, or other type of simulation. The method **16200** further includes determining, via the at least one processor, a performance criteria value based at least in part on the replication results data **16212**. The method **16200** further includes determining, via the at least one processor and based at least in part on the performance criteria value, an adjustment value **16214**. The method **16200** further includes, in response to determining the adjustment value, adjusting, via the at least one processor, the replication process **16216**.

[0793] In embodiments, adjusting the replication process **16216** may include ceasing the replication process when the performance criteria value includes and/or is based at least in part on a standard error that is below a threshold **16218**. In embodiments, adjusting the replication process **16216** may include ceasing the replication process when the performance criteria value includes and/or is based at least in part on an upper confidence interval of the clinical trial design and a difference from a lower confidence interval of another clinical trial design is higher than the upper confidence interval **16220**. In such embodiments, the lower confidence interval and/or the upper confidence interval may be 99%. In embodiments, adjusting the replication process **16216** may include increasing a number of replications in the replication process **16224**. In embodiments, adjusting the replication process **16216** may include decreasing a number of replications in the replication process **16222**. In some embodiments the number of simulated replications used to evaluate a design may be dynamically determined as part of the replication process or it may be determined outside of the replication process. In embodiments, the number of replications may be fixed based on data from previously simulated designs.

[0794] The method **16200** may further include retrieving at least some of the replication results data from a quick search data structure **16226**. The quick search data structure may be a SimCube. In embodiments, the quick search data structure may be stored in a database, e.g., database **16020** (FIG. **160**).

[0795] As will be appreciated, by providing for dynamic changing/adjusting of the number of replications performed as part of a simulation, some embodiments of the present disclosure may reduce the amount of time required to simulate a clinical trial design by reducing the number of replications in situations where continued evaluations produce diminishing returns and by increasing the number of replications in situations where more accuracy is beneficial. In embodiments, the replication process and/or clinical trial simulation may be based at least in part on, or form part if, a simulated annealing analysis. Further, in embodiments, machine learning may be used to determine an adjustment to a replication process. For example, a neural network may be trained to determine, from design and/or scenario criteria, when the number of replications should be increased, decreased, and/or when a replication process should be stopped.

[0796] Referring now to FIG. **163**, embodiments of the current disclosure may provide for enhanced simulated annealing (SA) in clinical trial design simulations and/or other types of simulations. As described elsewhere in this disclosure, embodiments of the simulation facility **110** (FIG. **1**) may evaluate a clinical trial design by using SA. As will be explained in greater detail below, some embodiments of the current disclosure provide for modifications to the SA process that reduce the amount of time and/or computational resources required to complete the analysis. For example, certain embodiments may reduce the number of designs simulated during SA via machine learning based interpolation and/or sampling of designs based on relationships to a convex hull tunnel derived from simulation of the clinical trial designs.

[0797] Accordingly, a system **16300** for providing enhanced SA in clinical trial design simulation is shown. The system **16300** may include a server **16310** having at least one processor and a memory device. The system **16300** may further include an electronic device **16312**, one or more remote servers **16314**, **16316**, **16318**, and/or a database **16320** which may be in electronic communication with the server **16310** and/or each other via a network **16322**. The server **16310** may form part of and/or host one or more of the platforms **104** (FIG. **1**), **10404** (FIG. **104**) and/or **12504** (FIG. **125**), e.g., the simulation facilities **110** (FIG. **1**), **10410** (FIG. **104**) and/or **12510** (FIG. **125**); and/or the computational resources **150** (FIG. **1**), **10450** (FIG. **104**), and/or **12550** (FIG. **125**).

[0798] The server **16310** may be structured to execute a SA process forming part of a clinical trial design simulation. The server **16310** may use machine learning to predict simulation results, as opposed to performing a more traditional simulation, for one or more designs identified during the SA process. For example, the server **16310** may select an initial clinical trial design to serve as the starting point for SA analysis/exploration. The server **16310** may determine the direction in which to move from the initial clinical trial design and then identify a new design in the selected direction. The server **16310** may then use machine learning to predict simulation results and then begin the process over again until termination of the SA path. In certain embodiments, the server **16310** may receive and/or generate data defining a convex hull tunnel for the initially selected clinical trial design. The server may then select designs for inclusion in the SA path based at least in part on relationships between the designs and the convex hull tunnel.

[0799] The electronic device **16312** may be a user device, e.g., **102** (FIG. **1**), such as a desktop, laptop, smart device, etc. In embodiments, the electronic device **16312** may provide for and/or present an interactive interface, e.g., **112** (FIG. **1**) that presents a plurality of prompts to a user for configuring the clinical trial design and/or SA process. The electronic device **16312** may also receive and display the results of the clinical trial simulation, SA process, and/or provide notifications to a user regarding any adjustments made to the SA process by the server **16310**. The database **16320** may form part of a data facility, e.g., **138** (FIG. **1**) and store simulation results data. The remote servers **16314**, **16316**, and/or **16318** may form part of a collection of computation resources, e.g., **150** (FIG. **1**) which can be accessed by the server **16310** to distribute processing tasks.

[0800] Illustrated in FIG. **164** is an embodiment of an apparatus **16400** for providing enhanced simulated annealing. The apparatus **16400** may form part of the server **16310** and/or other computing devices described herein. The apparatus **16400** may include a results interpretation circuit **16410**, a first identification circuit **16412**, a performance prediction circuit **16414**, a second identification circuit **16416**, a results prediction circuit **16418**, and a third identification circuit **16420**. In embodiments, the apparatus **16400** may include a convex hull interpretation circuit **16422**, a results determining circuit **16424**, and/or a transmission circuit **16426**.

[0801] As will be appreciated, embodiments of the apparatus **16400** may include various combinations of the circuit shown in FIG. **164** wherein some circuits are included while others are excluded. For example, an embodiment may include the convex hull interpretation circuit **16422**, the first identification circuit **16412**, the performance prediction circuit **16414**, the second identification circuit **16416**, the results determining circuit **16424**, and the third identification circuit **16420** but not include the results interpretation circuit **16410**, the performance prediction circuit **16414**, the results prediction circuit **16418**, and/or the transmission circuit **16426**. Further, in embodiments, the first identification circuit **16412**, the second identification circuit **16416** and/or the third identification circuit **16420** may be combined into a single identification circuit as indicated by the dashed box **16428**.

[0802] The results interpretation circuit **16410** may be structured to interpret initial simulation results data **16430** for a set of clinical trial designs. The first identification circuit **16412** is structured to identify an initial clinical trial design **16432** based at least in part on the initial simulation results data **16430**. The performance prediction circuit **16414** is structured to predict performance data **16434** for clinical trial designs related to the initial clinical trial design **16432** based at least in part on varying parameters for the initial clinical trial design **16432**. The second identification circuit **16416** is structured to identify a first new clinical trial design **16436** for simulation based on the predicting. The results prediction circuit **16418** is structured to predict, via machine learning, first simulation results data **16438** for the first new clinical trial design **16436**. The third identification circuit **16420** is structured to identify, based at least in part on the first simulation results data **16438**, a second new clinical trial design **16440** for simulation by varying parameters of the first new clinical trial design **16436**.

[0803] The convex hull interpretation circuit **16422** is structured to interpret convex hull tunnel data **16442** corresponding to a convex hull tunnel defined, in part, by the set of clinical trial

designs. The first identification circuit **16412** may be structured to identify the initial clinical trial design **16432** based at least in part on the convex hull tunnel data **16442**. The second identification circuit **16416** may be structured to identify the first new clinical trial design **16436** based on the performance criteria data **16434** and on the convex hull tunnel data **16442**. The results determining circuit **16424** may be structured to determine first simulation results data **16444** for the first new clinical trial design **16436**. The third identification circuit **16420** may be structured to identify, based at least in part on the first simulation results data **16444**, the second new clinical trial design **16440** for simulation by varying parameters of the first new clinical trial design **16436**.
[0804] In embodiments, the machine learning may be based at least in part on a neural network and/or a regression model, e.g., a regression tree. Embodiments of the machine learning may be trained via supervised learning on training sets. Such training sets may include a series of designs with known performance results. Data from the previously calculated neighboring designs may be leveraged to train a neural network via reinforcement learning to predict the value of a design as opposed to simulating the design. The training set may include a subset of values of scenario parameters and the predicted output may be values for the one or more designs.
[0805] Shown in FIG. **165** is a design space **16500** with designs **16510** and **16512**, for which simulation results data is known, and design **16514**, for which simulation results data is unknown. The machine learning may be used to predict the simulation results data of design **16514** from the simulation results data of neighboring designs, e.g., **16512**. As used herein, “neighboring” designs are designs that are close to one another in design space **16500** and/or other spaces, as would be understood by those of skill in the art. For example, designs **16512** are neighboring designs to design **16514**, while designs **16510** are not neighboring designs to design **16514**. As will be understood, in embodiments, feeding simulation results of neighboring designs **16512** into the machine learning model may provide for interpolation of the design **16514**.
[0806] Turning to FIG. **166**, a convex hull tunnel **16600** generated by convex hull peeling (as disclosed herein), is shown. The convex hull tunnel may have an upper bound **16610**, a lower bound **16612**, and a center line **16614**. Designs **16616** may be selected for inclusion in the SA path based on their relationship to the convex hull tunnel **16600**. For example, in embodiments, a penalty function may be used to score and/or rank the designs **16616** based on their distance from the centerline **16614**, lower bound **16612**, and/or upper bound **16610**, for inclusion in a SA path. In embodiments, the penalty function may encourage/promote selection of designs **16616**, for inclusion in a SA path, that are closer to the center line **16614** over designs **16616** that are father away from the center line **16614**. In other words, some embodiments of the disclosure may discourage use of designs **16616**, in a SA path, that are father away from the center line **16614**.
[0807] Referring now to FIG. **167**, a method **16700** for enhanced simulated annealing is shown. The method may be performed by the server **16310** (FIG. **163**) and/or the apparatus **16400** (FIG. **164**). The method **16700** includes interpreting initial simulation results data for a set of clinical trial designs **16710** and identifying an initial clinical trial design based at least in part on the initial simulation results data **16712**. The method **16710** further includes predicting performance data for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design **16714**. The method **16700** further includes identifying a first new clinical trial design for simulation based on the predicting **16716**, and predicting, via machine learning, first simulation results data for the first new clinical trial design **16718**. The method **16700** further includes identifying, based at least in part on the first simulation results data, a second new clinical trial design for simulation by varying parameters of the first new clinical trial design **16720**. In embodiments, the method **16700** may further include interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by the set of clinical trial designs **16722**. In such embodiments, identifying the first new clinical trial design for simulation **16716** may be further based at least in part on the convex hull tunnel data.
[0808] Illustrated in FIG. **168** is another method **16800** for enhanced simulated annealing. The

method may be performed by the server **16310** (FIG. **163**) and/or the apparatus **16400** (FIG. **164**). The method **16800** includes interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by a set of clinical trial designs **16810**, and identifying an initial clinical trial design based at least in part on the convex hull tunnel data **16812**. The method **16800** further includes predicting performance for clinical trial designs based at least in part on varying parameters for the initial clinical trial design **16814**, and identifying a first new clinical trial design for simulation based on the predicting and on the convex hull tunnel data **16816**. The method **16800** further includes determining first simulation results for the first new clinical trial design **16818**, and identifying, based at least in part on the first simulation results, a second new clinical trial design for simulation by varying parameters of the first new clinical trial design **16820**. In embodiments, determining first simulation results for the first new clinical trial design **16818** may include predicting the first simulation results via machine learning **16822**. In embodiments, the method **16800** may further include interpreting initial simulation results data **16824**.

[0809] Illustrated in FIG. **169** is yet another method **16900** for enhanced simulated annealing. The method **16900** includes interpreting initial simulation results data for a set of clinical trial designs **16910**, and identifying, based at least in part on the initial simulation results data, a clinical trial design for simulation **16912**. The method **16910** further includes predicting, via machine learning and based at least in part on the initial simulation results data, simulation results data for the clinical trial design **16914**; and transmitting the simulation results data **16916**.

[0810] In embodiments, one or more of the method of enhanced simulated annealing described herein may be form part of (or work in conjunction with) the recommendation engine/algorithm. For example, embodiments of the recommendation engine may use enhanced simulated annealing to find candidate designs for recommendation. In embodiments, enhanced simulated annealing may be used to dynamically update one or more parameters of a design, which may be in real-time. For example, one or more parameters of a design corresponding to an ongoing trial may analyzed and/or adjusted based on results from an enhanced simulated annealing analysis. In embodiments, the one or more parameters may be updated while the trial is being conducted, i.e., during the trial. In embodiments, enhanced simulated annealing may be used to determine changes in the outcome of an ongoing trial resulting from potential adjustments to the corresponding design.

[0811] Referring now to FIG. **170**, a system **17000** for design exploration and search is shown. The design exploration and search may be based at least in part on data structures referred to herein as “quick search data structures”, e.g., “design libraries”. The quick search data structures may enable efficient mapping and/or comparison within a design space and criteria space. The data structures may be configured to enable comparing designs across multiple variables, (e.g., finding “similar designs” for a plurality of criteria). Embodiments of the quick search data structures may have geometries that localize designs resulting in similar criteria, i.e., different designs that result in the same outputs are located next to (or near) each other. Designs may be populated into the quick search data structures after being simulated. Thus, if a design is selected at a later point to be simulated, the quick search data structure can be checked prior to simulation of the design to see if the data for the design already exists. A design does not need to be simulated if it is already in the quick search data structure. Thus, a first simulated annealing (or other design space exploration approach) may cause a first set of designs to be simulated and populated into a quick search data structure. At a later point in time, a second simulated annealing (or other design space exploration approach) may select a second set of designs to be simulated, wherein the quick search data structure provides for the ability to determine designs that overlap the first and second sets to avoid their re-simulation.

[0812] Accordingly, the system **17000** may include a server **17010** having at least one processor and a memory device. The system **17000** may further include an electronic device **17012**, one or more remote servers **17014**, **17016**, **17018**, and/or a database **17020** which may be in electronic communication with the server **17010** and/or each other via a network **17022**. The server **17010** may form part of and/or host one or more of the platforms **104** (FIG. **1**), **10404** (FIG. **104**) and/or **12504** (FIG. **125**), e.g., the simulation facilities **110** (FIG. **1**), **10410** (FIG. **104**) and/or **12510** (FIG. **125**); and/or the computational resources **150** (FIG. **1**), **10450** (FIG. **104**), and/or **12550** (FIG. **125**).

[0813] The server **17010** may be structured to execute a SA process forming part of a clinical trial design simulation. The server **17010** may use a quick search data structure to determine/retrieve/lookup results of simulations (if previously simulated), as opposed to performing a more traditional simulation, for one or more designs identified during an SA process (or other searching procedure). For example, the server **17010** may select an initial clinical trial design to serve as the starting point for SA analysis/exploration. The server **17010** may determine the direction in which to move from the initial clinical trial design and then identify a new design in the selected direction. The server **17010** may then check, via a quick search data structure, to see if results for the design have already been simulated, and then begin the process over again until termination of the SA path.

[0814] The electronic device **17012** may a user device, e.g., **102** (FIG. **1**), such as a desktop, laptop, smart device, etc. In embodiments, the electronic device **17012** may provide for and/or present an interactive interface, e.g., **112** (FIG. **1**) that presents a plurality of prompts to a user for configuring the clinical trial design and/or SA process. The electronic device **17012** may also receive and display the results of the clinical trial simulation, SA process, properties of the quick search data structure, and/or receive and/or provide notifications from the server to a user regarding the SA process and/or quick search data structure. The database **17020** may form part of a data facility, e.g., **138** (FIG. **1**) and store the quick search data structure in memory. The remote servers **17014**, **17016**, and/or **17018** may form part of a collection of computation resources, e.g., **150** (FIG. **1**) which can be accessed by the server **17010** to distribute processing tasks.

[0815] In embodiments, the quick search data structure may take the form of a SimCube having a structure that is a natural fit for simulated annealing algorithms, e.g., a single step in simulated annealing involves moving from a position/cell (within the SimCube) to an adjacent position/cell (within the SimCube) by changing just one design parameter or one scenario variable. The number of iterations of a simulated annealing path from a design to a locally optimal design may be the Manhattan distance between the two designs in the hypercube. For example, in embodiments, the quick search data structure may be a hypercube having a number of dimensions equal to the sum of the number of design parameters and the number of scenario variables that form a plurality of cells, each of which may contain a vector of simulation results that may include a multi-criteria vector.

[0816] Turning now to FIGS. **171**(*a*-*b*), an example of a quick search data structure **17100** in the form of a SimCube is shown, wherein the example data set corresponds to one thousand (1,000) replications for each of 40,824 scenario-design combinations, e.g., fifty-four (54) scenarios by seven-hundred and fifty-six (756) designs with three (3) criteria (power, trial costs, and trial duration). The quick search data structure **17100** may include a results data repository **17110** and an index **17112**. As shown in FIGS. **171**(*a*-*b*), the results data repository **17110** may be expressed as a flat file, e.g., a text file, where each row represents the results of simulating a particular design and/or design replication. Each row may include a key determined, in part, by a ranking of distinct values of design parameters **17114** in the index **17112**. For example, the key for row "**1724**" is "4, 3, 3, 4, 2, 4", wherein the value of '70' for "% Events Observed at Interim" is assigned a rank of 4, the value of '0.5' for "min Promising Zone Point" is assigned a rank of '3', the value of '0.99' for "max Promising Zone Point" is assigned a rank of 3, the value of '1.733333' for "max Events Multiplier" is assigned a rank of '4', the value of '1.5' for "max Subjs Multiplier" is assigned a rank of '2', and the value of '0.7' for "Adaptive Wt1" is assigned a rank of '4'. Thus, the index **17112** can be used to locate a design with a desired set of design parameters **17114** with the following relationship: SimCube Row #for a design=(sum of (rank*corresponding rank multiplier) over all dimensions)−sum (rank multipliers). For example, the row of a design having '70' for "% Events Observed at Interim", '0.5' for "min Promising Zone Point", '0.99' for "max Promising

Zone Point", '1.733333' for "max Events Multiplier", '1.777778' for "max Subjs Multiplier", and '0.5' for "Adaptive Wt1" can be calculated as sum((4*432)+(3*144)+(3*48)+(4*12)+(3*4)+(2*1)) −(432+144+48+12+4+1)=1725, with a corresponding key of '4, 3, 3, 4, 3, 2'. In embodiments, the repository **17110** can be stored in a compressed form where empty rows can be removed to save memory space. For example, in the scenario shown in FIGS. **171**(*a*-*b*), the total number of empty cells/rows in the repository **17110** may be 40,068, i.e., there repository **17110** may only contain the results for seven-hundred and fifty-six designs. Thus, where the full design of such a SimCube has dimensions of 4×3×4×4×4 with 1,728 cells, the corresponding density of the SimCube would be 43.75%. In embodiments where the repository **17110** is compressed, the rows may be sorted in order of the full row value of a design so that a binary search may be used. In embodiments, the quick search data structure **17100** may include one or more of heaps and/or hash tables (using the full table row value as a key), e.g., some embodiments may combine aspects of SimCubes with heaps and/or hash tables, which may provide for intermediate time-memory usage trade-offs.

[0817] Some embodiments of the current disclosure may also include network implementations of SimCubes, wherein each design may be a node within undirected edges joining each pair of designs that differ in rank in only one parameter for which the ranks differ by one (1). In such embodiments, the network data structure may be useful to efficiently compute neighbors to a design of interest and/or for constructing clusters of similar designs. In embodiments, samples of scenario-design combinations, rather than simulating each design for all scenarios, may be used. For example, embodiments of the quick search data structures described herein may be extended to this setting by increasing the number of parameters (and hence SimCube dimensions) to be the sum of design and scenario parameters. As will be further understood, embodiments of the quick search data structures described herein may also be used for simulations of clinical trials operations such as recruitment forecasting and drug supply.

[0818] Illustrated in FIG. **172** is a method **17200** of design exploration and search that utilizes a quick search data structure with simulated annealing (SA). A set of initial combination of design parameters is defined **17210**. Exclusion criteria are tested for **17212** and a determination is made as to whether the combination of design parameters should be excluded from the SA path **17214** and written to an exclusion log **17216**. Combinations passing the exclusion test **17214** are then searched for (looked up) in a quick search data structure **17218** and **17220**. If corresponding simulation results are found in the quick search data structure, they are written to a details log **17222**. If corresponding simulation results are not found, then the combination of design parameters is simulated **17224** with the results written to the quick search data structure **17226**. After the results have been retrieved and/or generated via simulation, they may be checked against the results of prior replications to determine if they are superior/optional as compared to the results of two or more previous replications **17228**, and if so, written to an output log **17230**. Results that are not superior, as compared to the two or more previous replications, are then evaluated for inclusion in the SA path **17232** and **17234**, the next parameter combination/design replication is retrieved and/or generated **17238**, and the process beings again until there are no more replications to evaluate. Design parameter combinations that are written to the output log may also be tested to determine if they are the best results thus far, and if so, written to a best output log **17240** and **17242**.

[0819] Referring now to FIG. **173**, in embodiments, simulated annealing may provide for the identification of similar designs by exploring region of interest, e.g., local neighborhoods, around a particular design. Accordingly, another method **17300** for design exploration and search is shown that finds/evaluates one or more designs within a distance d and/or score difference $\Delta\hat{e}$. The method **17300** may be based at least in part on one or more of the following premises: 1) that the starting point for design search is a "good" design, e.g., can be found using a SA process; 2) that SA can be used to find twin (or close to twin) designs within a small score variation $\Delta\hat{e}$, provided the result is within d Manhattan distance of the starting design; and 3) that multiple designs can be found by parallel instances. As such, the method **17300** may provide for rapid discovery of equally (or close to equally) "good" designs in close proximity to a desired design. The method **17300** may include a user providing a "good"/desirable design for use as a starting point **17310**. A use score of the initially provided design may then be calculated as Z.sub.0 **17312**. A proximal design may then be selected **17314**. An SA process may then be executed until Z.sub.0 is accomplished wherein each replication is evaluated to see if it is within a Manhattan distance d, and if yes, the simulation results are written to an output log **17316**, **17318**, and **17320**. Replications not falling within d may be discarded **17322**.

[0820] Turning to FIG. **174**, another method **17400** of design exploration and search may be based on one or more of the following premises: 1) near-optimal designs tend to have many "twins" in terms of same or similar scores; 2) once one near-optimal design is found, the score may be used as a target score for finding other designs with other starting points that are twins or are otherwise very close; and 3) such twins are typically found in a small number of replicates/engine calls. As such, the method **17400** may include defining an initial parameter combination **17410**, executing a SA process with a large number of replicates R **17412**, and noting the best score found Z.sub.0 **17414**. The method **17400** may then enter a loop where various starting design parameter combinations are tested with a SA process until Z.sub.0 is accomplished with the results written to an output log **17416**, **17418**, and **17420**.

[0821] Referring now to FIG. **175**, another method **17500** for design exploration and search may be based on one or more of the following premises: 1) the starting point may be a user-specified design already having a good score and desirable attributes (parameter combination); and 2) SA will find twin (or close to twin) designs within the desired type (e.g., Sample Size Re-estimation (SSR) or Group Sequential). The method **17500** may include a user providing a "good"/desirable design for use as a starting point **17510**. The score of the provided design may be used as Z.sub.0 **17512**. The method **17500** may then enter a loop where subsequent proximal designs are selected and evaluated with SA until Z.sub.0 is accomplished with the results written to an output log **17514**, **17516**, and **17518**.

[0822] Shown in FIG. **176** is a graphical user interface **17600** that may be provided on the electronic device **17012** (FIG. **170**) for configuring the server **17010** (FIG. **170**) or other device executing one or more of the methods for design exploration and search disclosed herein. The interface **17600** may include fields for specifying the Manhattan distance d **17610**, Δê **17612**, and/or one or more design parameters **17614**. A button **17616** (or other user input widget) may provide for execution of one or more of the methods described herein using the values specified in the interface **17600** to populate the property **17614** and performance criteria **17618** of one or more neighboring designs **17622**.

[0823] Illustrated in FIG. **177** is another method **17700** for design exploration and search. The method **17700** may include allocating memory, in a memory device, that defines a quick search data structure having a plurality of storage cells **17710** and simulating a plurality of clinical trial designs to obtain a plurality of simulation results **17712**. In embodiments, each of the plurality of simulation results may correspond to one of the plurality of clinical trial designs. The method **17700** may further include storing each of the plurality of simulation results in a corresponding one of the plurality of storage cells based on one or more relationships between two or more of the plurality of clinical trial designs **17714**. In embodiments, the one or more relationships between the two or more of the plurality of clinical trial designs is based at least in part on the value of parameters for each of the two or more of the plurality of clinical trial designs. In embodiments, the method **17700** may further include scoring the two or more of the plurality of clinical trial designs based at least in part on the value of the parameters **17716** and determining whether the two or more of the plurality of clinical trial designs are similar designs **17718**. Determining whether the two or more of the plurality of clinical trial designs are similar designs may include determining if the two or more of the plurality of clinical trial designs are within an epsilon of a desired score

17720 and/or determining if the two or more of the plurality of clinical trial designs are within an epsilon of each other **17722**. In embodiments, the quick search data structure may be a SimCube as described herein.

[0824] Referring to FIG. **178**, another method **17800** of design exploration and search includes obtaining initial simulation results for a set of clinical trial designs **17810** and identifying an initial clinical trial design based at least in part on the initial simulation results **17812**. The method **17800** further includes predicting performance for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design **17814** and identifying a first new clinical trial design for simulation based on the predicting **17816**. The method **17800** further includes determining if a quick search data structure contains first simulation results for the first new clinical trial design **17818** and if the quick search data structure does not contain the first simulation results, simulating the first new clinical trial design to obtain the first simulation results **17820**. The method **17800** further includes identifying, based at least in part on the first simulation results, a second new clinical trial design for simulation by varying parameters of the first new clinical trial design **17822**. In embodiments, the method **17800** may include storing the first simulation results in the quick search data structure **17824**, which may include determining one or more relationships between the first new clinical trial design and another clinical trial design stored in the quick search data structure **17826**. In embodiments the one or more relationships between the new clinical trial design and the other clinical trial design may be based at least in part on the value of the parameters for the first new clinical trial design and parameters of the other clinical trial design.

[0825] Shown in FIG. **179** is another method **17900** for design exploration and search. The method **17900** includes interpreting, via at least one processor, simulation results data for a set of clinical trial designs **17910**, and populating, via the at least one processor, a quick search data structure, defined within a memory device, with the simulation results data **17912**. The method **17900** may further include identifying, via the at least one processor, a region of interest within at least one of a performance criteria space of the set of clinical trial designs or the quick search data structure **17914**. Referring briefly to FIG. **180**, an example performance criteria space **18000** is shown having a plurality of designs **18010**. In embodiments, a region of interest may be a region **18012** in the performance criteria space **18000** that is close to a grouping of designs but itself devoid of a design. A region of interest may also be a region **18014** that is distal from designs and/or encircled by designs, e.g., a void. It is to be understood that regions of interest may take other forms as well, i.e., regions that appear interesting to a user and which may contain designs the user wishes to search and/or evaluate, and that similar regions of interest may be found in a quick search data structure and/or various tornado diagrams, as described herein. Accordingly, returning back to FIG. **179**, identifying a region of interest may include determining a void **17916**. The method **17900** may further include identifying, via at least one processor, a first clinical trial design based at least in part on the region of interest **17918**, and determining, via the at least one processor and based at least in part on the quick search data structure and the first clinical trial design, a second clinical trial design **17920**. Data corresponding to the second clinical trial design may then be transmitted, e.g., sent to the electronic device **17012** (FIG. **170**) for display to a user **17922**. In embodiments determining the second clinical trial design may include determining that the second clinical trial design is within a Manhattan distance within the quick search data structure of the first clinical trial design **17924** and/or determining that the second clinical trial design is within an epsilon of a desired score **17926**. In embodiments, the region of interest corresponds to two or more similar designs.

[0826] In embodiments, the relationship for storing designs in the quick search data structure may be based at least in part on machine learning. For example, a machine learning module, e.g., a neural network, may be trained, via supervised and/or unsupervised learning, to determine one or more relationships, which may optimize the quick search data structure for a particular evaluation session.

[0827] FIGS. **181**(*a-k*) show an example use case of the platform described herein. The platform may include various interfaces for inputting and analyzing data. The example use case shows how users may use the platform to specify design parameters, simulate designs, analyze the simulated data, and identify globally optimum or nearly globally optimum designs for a trial. The platform may be used to identify an efficient design that addresses requirements for criteria (such as power, sample size, trial durations, cost, etc.). In the example, the platform may be used to answer questions related to what is the optimal sample size and number of events, what is the optimal number and timing of interim analyses, what is the optimal alpha spending function, and the like.

[0828] In embodiments, data entry into the platform may involve data entry into one or more forms. In embodiments, forms may be web based or browser based applications, native applications, or other executable code that proves an interface for data entry. In some embodiment, data entry may be provided with a specification file that that may be read by the platform or via an API connection to another platform or data source.

[0829] FIG. **181**(*a*) shows one example of an initial data entry interface for specifying design and simulation parameters into the platform. In this example, data may be entered via one or more data entry fields (drop down menus, input boxes, lists and the like). Data entry may include a series of tabs or screens that may guide the user to enter the required data. The first data entry may be related to the “Plan” for the clinical trial. As shown in FIG. **181**(*a*), entries related to the “Plan” may include general aspects defining types of designs. Data entry may include specifying a Target Population, Control Arm, Treatment Arm, Endpoints and the like for the study.

[0830] FIG. **181**(*b*) shows one example of an interface for data entry for specification of design for the study. As shown in the figure, entries related to the “Design” may include specifications of designs and may include data entry for the type of statistical designs, the number of arms for the design and the like. Data entry may further include data related to the design such as hypothesis, follow up sample size, number of events, allocation ratio, the type statistical design, and the like. Data entry may include specifications related to early stopping parameters, sample size re-estimation parameters, and the like.

[0831] The next data entry may be related to the “Response” parameters. As shown in FIG. **181**(*c*), entries related to the “Response” may include data entry to define the time-to-event distributions that may be used by the platform to simulate the individual subjects' data.

[0832] The next data entry may be related to the enrollment parameters. As shown in FIG. **181**(*d*), entries related to “Enrollment” may include data entry to target populations, population distributions, geography, enrollment, and the like.

[0833] The next data entry may be related to the cost parameters. As shown in FIG. **181**(*e*), entries related to the “Costs” may include data entry to define costs per subject or the average investigator grant per patient.

[0834] Another portion of the data entry may be related to revenue parameters. As shown in FIG. **181**(*f*), entries related to the “Revenues” may include data entry to define when and how the expected revenue will be generated. Data entry may include a regulatory review period in years, annual revenue in a peak year, time to peak annual revenue, and other parameters, including as shown in the figure.

[0835] Another data entry may be related to the scoring parameters. As shown in FIG. **181**(*g*), entries related to the “Scoring” may include data entry to define weights for computing a score. Data entry may include selections and weights (in % of total score) to minimize study cost, minimize study duration, maximize power, and/or minimize sample size.

[0836] Throughout the data entry process, the input advisor may monitor user entries and identify conflicts in data values and/or suggest entries of data values. In some instances, the input advisor may predict, based on historical data and/or data entry what values or types of data are associated with some inputs. The input advisor may highlight or identify ranges of values that are consistent with historical data of data entry values. In the case where some data values are outside of expected or historical data values the entry area may be flagged or highlighted for review.

[0837] Once data is entered, the entry data from each input field are assembled and compiled to define the simulation set via the "Collections" tab as shown in FIG. **181**(*h*). Once the data is assembled it may be formatted to generate models that may be ready for simulation. In this example, **540** models are generated based on the input data. Assembly of data may include generating design and scenario permutations for simulation. Assembly of data may include removing scenarios or design combinations that are invalid or unlikely.

[0838] In some embodiments, generation of models may be a trigger to request and allocate computation resources for simulation. In the case of batch mode computation, the resources may be requested before they are needed to allow time for the allocation.

[0839] In the next step, simulations may be started by selecting the "simulate" button. In embodiments, before simulations are queued to run, the user may be informed of the cost of the simulations in units such as dollars or credits. Then the "Simulate" button may be clicked to start the simulations. The models for each simulation may be submitted to one or more engines for simulation. The engines may use one or more cloud computing resources to execute the models to determine the performance of each design model.

[0840] In embodiments, simulations may be exhaustive for all of the models. In some cases, only a partial set of the models may be simulated. In some embodiments, the partial set of models may be randomly selected or may be selected based on predictions (based on historical data) as to which designs in the models are likely to have the best performance for the specified criteria. In some embodiments, simulated annealing may be used to simulate a partial set of the models. Simulated annealing may be used to search for local maxima in performance space.

[0841] When the simulations end, the user may be prompted to view the results of the simulations via the tradeoff advisor. Clicking the "View Results" button may initiate calculation of scores and robustness scores from the simulation results and may load the simulation results into the tradeoff advisor. In embodiments, simulated data may be analyzed using one or more Pareto, convex hull, or other techniques to identify the optimum or near optimum designs. These Pareto, convex hull, and other recommended designs may be marked or highlighted in various interfaces of the tradeoff advisor.

[0842] In embodiments, the tradeoff advisor may include interfaces and tools to explore performance parameters of designs, compare designs, initiate additional simulations, and the like. The tradeoff advisor may include heatmaps as shown in FIG. **181**(*i*). The heatmaps may provide a visual view of the relative performance of the simulated designs for one or more performance parameters. The heatmap may be sorted, filtered, rearranged to help identify designs with the desired performance. The heatmap in FIG. **181**(*i*) shows designs sorted by robustness score, scenarios sorted by hazard ratio and by control group rate. Users may explore the designs by marking relative cells, viewing details of each design (such as with the tooltip data shown in FIG. **181**(*i*)).

[0843] In embodiments, the tradeoff advisor may include scatterplots as shown in FIG. **181**(*j*). The scatterplot in the upper left is power by duration; note that the 3 clustered rows correspond to the three HR's 0.67, 0.7, and 0.73 from top to bottom.

[0844] In embodiments, tradeoff advisor may include boxplots as shown in FIG. **181**(*k*) The boxplots may show the distributions of duration, power, cost, and score for simulated designs.

[0845] In embodiments, the tradeoff advisor may include additional interfaces for comparing designs (such as card interfaces, tornado diagrams, and the like described herein). Additional interfaces may be shown allowing users to drill down or see related designs that are similar (such as twins, siblings, designs that are within an epsilon-distance of a recommended or selected design, etc.).

[0846] An example method for determining globally optimum trial designs, the method including obtaining a simulation output for a set of clinical trial designs, where the simulation output includes performance parameters and performance parameter values associated with each design in the set of designs for a set of criteria; determining an optimality criteria for evaluating the clinical trial designs; searching, within the set of clinical trial designs, for globally optimum designs based on the optimality criteria; and recommending globally optimum designs.

[0847] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The set of clinical trial designs includes all design options for a set of criteria. The optimality criteria is based on historical data and includes performance parameters of a benchmark design. The optimality criteria is based on a weighted sum of performance criteria values of each of clinical trial designs. Further including changing the optimality criteria based on a number of globally optimum designs. Further including determining a second optimality criteria; and searching, within the set of clinical trial designs, for a second set of globally optimum designs based on the second optimality criteria. Further including determining a second optimality criteria; and searching, within the set of globally optimum designs, for a second set of globally optimum designs based on the second optimality criteria. Further including dynamically changing the optimality criteria in response to properties of globally optimum designs. Further including dynamically changing the optimality criteria in response to user feedback. The optimality criteria includes Pareto optimality. The optimality criteria includes convex hull optimality. The optimality criteria includes Pareto optimality and the optimality criteria includes convex hull optimality.

[0848] An example apparatus including a data processing circuit configured to obtain design data for a set of clinical trial designs; an optimality determining circuit configured to determine an optimality criteria for evaluating the clinical trial designs, and search, from the set of clinical trial designs, for globally optimum designs based on the optimality criteria; and a design analysis circuit configured to analyze the globally optimum designs and determine a modification to the optimality criteria, where the optimality determining circuit received the modification and determines a second set of globally optimum designs.

[0849] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The set of clinical trial designs includes all design options for a set of criteria. The optimality criteria is based on historical data and includes performance parameters of a benchmark design. The optimality criteria is based on a weighted sum of performance criteria values of each of clinical trial designs. The modification is based on a number of globally optimum designs. The modification is in response to user feedback. The optimality criteria includes Pareto optimality. The optimality criteria includes convex hull optimality.

[0850] An example method including obtaining a criteria for a trial design study; determining permutations for designs in response to the criteria; determining permutations for scenarios in response to the criteria; generating combinations of the permutations for designs and the permutations for scenarios; simulating the generated combinations; and determining performance of simulated designs.

[0851] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including estimating number of combinations using the criteria. Further including examining the combinations for invalid combinations. Further including examining the permutations for invalid permutations. Further including predicting the performance of the combinations; and removing a subset of the combinations prior to simulating based on the predicted performance. The predicting is based on historical data. The combinations are exhaustive for the criteria. Further including determining optimality from the performance. Further including, in response to the estimated number being greater than a threshold, suggesting modifications to the criteria. Further including, in response to the estimated number being less than a threshold, suggesting modifications to the criteria.

[0852] An example apparatus including a space definition circuit structured to interpret criteria data for a trial design; a design parameter circuit structured to determine permutations for designs in response to the criteria data; a scenario parameter circuit structured to determine permutations for scenarios in response to the criteria data; a combinations circuit structured to generate combinations of permutations for designs and permutations for scenarios; and a simulation circuit structured to evaluate a performance of each combination.

[0853] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Further including an estimator circuit configured to estimate number of combinations using the criteria. Further including a validity checker circuit configured to examine the combinations for invalid combinations. Further including a validity checker circuit configured to examine the permutations for invalid permutations. Further including a validity checker circuit configured to predict the performance of the combinations; and remove a subset of the combinations prior to simulating based on the predicted performance. The performance is predicted based on historical data. The combinations of permutations are exhaustive for the criteria. Further including an analysis circuit configured to determine optimality from the performance. The estimator circuit is further structured to, in response to the estimated number being greater than a threshold, suggesting modifications to the criteria. The estimator circuit is further structured to, in response to the estimated number being less than a threshold, suggesting modifications to the criteria.

[0854] An example method including configuring an execution flow for a clinical trial design evaluation using a configurable interface having at least one node element and at least one arc element, where the execution flow is defined, in part, via the at least one node element and the at least one arc element; executing the clinical trial design evaluation using the execution flow; reconfiguring at least one of the at least one node element or the at least one arc element in the execution flow; and executing the clinical trial design evaluation using the reconfigured execution flow.

[0855] An example method including configuring an execution flow for a clinical trial design evaluation using a configurable interface, where the execution flow is defined using at least one node element and at least one arc element; determining a first user type interacting with the execution flow; configuring a first view of the execution flow for the first user type; determining a second user type interacting with the execution flow; and configuring a second view of the execution flow for the second user type.

[0856] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including defining, via the at least one node element, an execution engine for inclusion in the execution flow. Further including defining, via the at least one node element, a design parameter of the execution flow. Further including defining, via the at least one node element, an analysis type for inclusion in the execution flow. Further including saving the execution flow. The first user type and the second user type are located in different geographic locations. Further including the first user type and the second user type viewing the execution flow simultaneously. The first view and the second view are distinct. The first view provides a different configuration level over the execution flow than a configuration level of the second view. The configuration level of the first view is higher than the configuration level of the second view.

[0857] An example apparatus including an interface configuration circuit structured to generate interface data corresponding to a configurable interface having a node element and an arc element, the node element and the arc element defining execution flow data for a trial design evaluation; a user input circuit structured to interpret user input data based at least in part on the node element and the arc element; an interface reconfiguration circuit structured to reconfigure the execution flow data based at least in part on the user input data; an evaluation circuit structured to generate evaluation data via executing the trial design evaluation based at least in part on the reconfigured

execution flow data; and an evaluation processing circuit structured to transmit the evaluation data.
[0858] An example method including configuring an execution flow for a clinical trial design evaluation using a configurable interface having at least one node element and at least one arc element, where the execution flow is defined, in part, via the at least one node element and the at least one arc element; receiving a plurality of optimality criteria from a plurality of users, where each optimality criteria is associated with a different user; executing the clinical trial design evaluation using the execution flow; determining performance of designs according to each of the plurality of optimality criteria; and reporting the performance of designs for each optimality criteria to the user associated with each optimality criteria.
[0859] An example method including configuring an execution flow for a clinical trial design evaluation using a configurable interface having at least one node element and at least one arc element, where the execution flow is defined, in part, via the at least one node element and the at least one arc element; adding a plurality of nodes, where the plurality of nodes define the scenario space, design space, performance space, and criteria space; executing the clinical trial design evaluation using the execution flow; determining performance of designs according to performance space definitions; and reporting the performance of designs.
[0860] An example method including generating an interactive interface; presenting, via the interactive interface, one or more prompts to a user structured to determine one or more trial design criteria; and evaluating historical trial design selections to identify one or more trial design parameters based at least in part on the one or more trial design criteria.
[0861] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including simulating one or more clinical trial designs based at least in part on the one or more trial design parameters. At least one of the one or more prompts concerns a study duration. The interactive interface is a graphical user interface. The interactive interface is command line based. Further including presenting, via at least one of the one or more prompts, a recommended value for at least one of the one or more trial design criteria; or the trial design parameters. Further including generating the recommended value via artificial intelligence based at least in part on the historical trial design selections. Evaluating historical trial design selections to identify the one or more trial design parameters includes evaluating the historical trial design selections via artificial intelligence.
[0862] An example apparatus including an interface generation circuit structured to generate interactive interface data including one or more user prompts structured to determine one or more trial design criteria; an interface processing circuit structured to transmit the interactive interface data; a user input circuit structured to receive the one or more trial design criteria; and a historical evaluation circuit structured to identify one or more trial design parameters based at least in part on the one or more trial design criteria via evaluating historical data corresponding to one or more previously simulated clinical trial designs.
[0863] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Further including a simulation circuit structured to simulate one or more clinical trial designs based at least in part on the trial design parameters. At least one of the one or more prompts concerns a study duration. Further including a recommendation circuit structured to generate a recommended value for at least one of the one or more trial design criteria; or the one or more trial design parameters. The recommendation circuit is further structured to generate the recommended value based at least in part on historical trial design selections. The recommended value corresponds to at least one of a cost for a clinical trial; a number of patients required for a clinical trial; a duration of a clinical trial; or a site for a clinical trial. The historical data include one or more of a type of a clinical trial design; a duration of a clinical trial; a cost of a clinical trial; or an outcome of a clinical trial.
[0864] An example non-transitory computer-readable medium storing instructions that adapt at least one processor to generate interactive interface data including one or more user prompts

structured to determine one or more trial design criteria; transmit the interactive interface data; receive the one or more trial design criteria; and identify one or more trial design parameters based at least in part on the one or more trial design criteria via evaluating historical data corresponding to one or more previously simulated clinical trial designs.

[0865] Certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be present in certain embodiments. The stored instructions further adapt the at least one processor to simulate one or more clinical trial designs based at least in part on the trial design parameters. At least one of the one or more prompts concerns a study duration. The stored instructions further adapt the at least one processor to generate a recommended value for at least one of the one or more design trial design criteria; or the one or more trial design parameters. The stored instructions further adapt the at least one processor to generate the recommended value based at least in part on historical trial design selections.

[0866] An example method including generating an interactive interface; presenting, via the interactive interface, one or more prompts to a user structured to determine one or more trial design criteria for evaluating trial designs; and determining workflow components for determining exhaustive permutations of the trial designs consistent with the design criteria.

[0867] An example method including obtaining a set of simulation outputs for a set of clinical trial designs; obtaining a set of supplemental data; determining a relationship between at least one simulation output of the set to at least one supplemental data of the set; generating modified supplemental data based at least in part on the relationship; and generating a substitute of the at least one simulation output based at least in part on the modified supplemental data.

[0868] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The supplemental data is based at least in part on a performance parameter of the set of clinical trial designs that is based at least in part on one of costs of a clinical trial; time to completion of a clinical trial; net present value of a clinical trial; actual personnel costs of a clinical trial; or actual facility costs of a clinical trial. The at least one simulation output includes relative data. The at least one simulation output includes general data. The relationship is based at least in part on at least one of metadata; labels; or unit values. The set of supplemental data is derived, in part, from one or more clinical trial sites.

[0869] An example method including obtaining a set of simulation outputs for a set of clinical trial designs; determining a subset of the set of simulation outputs identified as potentially associated with a performance criteria of one or more of the set of clinical trial designs; mapping the subset of the simulation outputs to a data source for the performance criteria; and determining a value for the performance criteria based at least in part on the data source.

[0870] An example method including obtaining a set of simulation outputs of a set of clinical trial designs; determining a subset of simulation outputs identified as having a possible association with a performance criteria of one or more of the set of clinical trial designs; and relating the subset of the simulation outputs to a data source for the performance criteria.

[0871] An example apparatus including a simulated output processing circuit structured to interpret a simulated output dataset of clinical trial designs; a supplemental processing circuit structured to interpret supplemental data; a relation determining circuit structured to determine a relationship between the simulated output dataset of clinical trial designs and the supplemental data; a supplemental data modification circuit structured to generate modified supplemental data based at least in part on the relationship; a substitute circuit structured to generate, based at least in part on the modified supplemental data, substitute data of the simulated output dataset of clinical trial designs; and a substitute data provisioning circuit structured to transmit the substitute data.

[0872] An example method including obtaining a design space; obtaining a scenario space; generating a set of simulation models by combining the design space and the scenario space; executing a simulation of the set of simulation models; and providing an interface with results of the execution.

[0873] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The set of simulation models are generated by taking cross product of parameters from the design space and parameters from the scenario space. Further including determining a relevancy score for each simulation model. The relevancy score is based on priority rating of design parameters in each model. The relevancy score is based on priority rating of scenario parameters in each model. The relevancy score is based on frequency of occurrence of parameters in historical simulations.
[0874] An example method including obtaining a set of scenarios models; obtaining a set of design models; generating a set of simulation models by combining each design model with each of the scenario models; and executing a simulation of the set of simulation models; and providing an interface with results of the execution.
[0875] An example method including obtaining a set of scenarios models; obtaining a set of design models; generating a set of simulation models by combining each design model with each of the scenario models; evaluating a relevancy score for each simulation model that is a combination of a scenario model and design model based on parameters associated with each; selecting simulation models with scores above a threshold value; and executing a simulation of the selected set of simulation models.
[0876] An example apparatus including a scenario model processing circuit structured to interpret scenario model data; a design model processing circuit structured to interpret design model data; a model generation circuit structured to generate simulation model data by combining the design model data with the scenario model data; a simulation circuit structured to generate simulation data via executing a simulation model defined by the simulation model data; and a simulation data provisioning circuit structured to transmit the simulation data.
[0877] An example method including simulating a first configuration of a trial design to determine trial data; simulating a second configuration of the trial design to determine counterfactual data; comparing the trial data and the counterfactual data to determine an estimand for an outcome of the trial; determining, for the outcome of the trial, an estimator of the trial design; and scoring the design based on differences between the estimator and the estimand.
[0878] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The simulation of the first configuration and second configuration sample subjects from a virtual population. The counterfactual data is missing data. The first configuration and the second configuration use the same subject from different virtual populations. Further including determining the virtual population from real-world population data. Further including determining the virtual population from a population model. Further including saving an identification of the subject used in the simulating. The virtual population includes demographics, medical history, and socioeconomic status of each subject. The virtual population represents a population from one or more of a city, a region, a state, a country, or the globe. The estimator specifies an estimate for a hazard ratio of the design.
[0879] An example apparatus including a simulation circuit structured to simulate a configuration of a design to determine a trial outcome; a counterfactual simulation circuit structured to simulate a second configuration of trial design to determine counterfactual trial outcome; an estimand determining circuit structured to determine an estimand for the design; as estimate determining circuit structured to determined an estimator for the design; and an evaluation circuit structured to determine similarity of the estimand and the estimator and score the design based the similarity.
[0880] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The simulation circuit and the counterfactual simulation circuit are configured to sample subject from a virtual population. The counterfactual trial outcome is missing data. The simulation circuit and the counterfactual simulation circuit are configured to sample subjects from different virtual populations. The virtual population is determined from real-world population data. The simulation circuit and the counterfactual

simulation circuit are configured to save an identification of the subject used in the simulating. The virtual population includes demographics, medical history, and socioeconomic status of each subject. The virtual population represents a population from one or more of a city, a region, a state, a country, or the globe. The estimator specifies an estimate for a hazard ratio of the design. The apparatus of claim **104**, where the estimand specifies a hazard ratio of the design.

[0881] An example method including obtaining trial design simulation results for a set of trial designs; recommending a first subset of trial designs to a user; receiving feedback from the user from a user interface; identifying characteristics of trial designs preferred by the user from the feedback; determining additional trial designs with identified characteristics; and simulating trial designs with the identified characteristics.

[0882] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including tracking user interactions with the recommended first subset. The feedback includes tracked user interactions. The user interface provides a comparison between the first subset of designs. The user interface is a card interface. The recommended designs are Pareto designs. Further including identifying preferred regions of a design space. The user interactions include at least one of: removing a design, moving a design, or saving a design. Further including saving the tracked interactions and training an artificial intelligence model to identify preferences based on interactions. The first subset of trial design includes designs that are substantially equal except for one parameter.

[0883] An example apparatus including a simulation results processing circuit structured to interpret trial design simulation results data; a recommendation circuit structured to determine a first subset of trial designs for display on an interface; a user input circuit structured to receive user input using the interface; and a criteria determination circuit structured to determine optimality criteria from the user input; where the recommendation circuit is further structured to determine a second subset of trial designs based at least in part on the optimality criteria.

[0884] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The user input circuit is further structured to track user interactions with the recommended first subset. User input includes tracked user interactions. The interface provides a comparison between the first subset of designs. The interface is a card interface. The first subset of designs are Pareto designs. Further including region preference circuit configured to identify preferred regions of the design space. The user interactions include at least one of: removing a design, moving a design, saving a design. Further including an artificial intelligence circuit configured to save the tracked interactions and train a model to identify preferences based on interactions. The first subset of trial design includes designs that are substantially equal except for one parameter.

[0885] An example method including obtaining trial design simulation results for a set of trial designs; recommending a first subset of trial designs to a user; receiving feedback from the user from a user interface; identifying optimality criteria from the feedback; and evaluating trial designs based on the optimality criteria.

[0886] An example method for determining a clinical trial study, the method including presenting, on a graphical interface, a set of cards, each card in the set of cards is representative of a different trial design from a set of trial designs; monitoring a first set of user interactions with the set of cards; determining a user preference for one or more values of one or more parameters of the set of trial study design from the first set of user interactions; presenting, on the graphical interface, a new card, where the new card is representative of a trial design from the set of trial study options consistent with the determined user preference; monitoring a second set of user interactions with the new card; and refining the determined user preference based at least in part on the second set of user interactions with the new card.

[0887] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including emphasizing values shown on each card based on the relative value compared to other displayed cards. The interactions include at least one of moving a card, saving a card, or deleting a card. The new card is added to the set of cards. The new card replaces a card from the set of cards. The set of cards is representative of Pareto designs. Each card represents a different trial type. The set of cards is representative of convex hull designs. Further including saving the user interactions and training an artificial intelligence model to identify preferences based on interactions. Determining a user preference using an artificial intelligence model trained on historical interactions.

[0888] An example apparatus including a simulation results data processing circuit structured to interpret trial design simulation results data for a set of trial designs; a recommendation circuit structured to determine a first subset of trial designs; a card suggestion circuit structured to display the first subset of trial designs with a card interface; and an interaction analysis circuit structured to interpret user interactions with the card interface; where the card suggestion circuit is further structured to display a second subset of trial designs with the card interface based on the user interactions.

[0889] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Further including a graphic enhancement circuit configured to emphasizing values shown on each card based on the relative value compared to other displayed cards. The interactions include at least one of moving a card, saving a card, or deleting a card. The second subset of trial designs includes at least one design from the first subset of trial designs. The first subset of trial designs is a set of Pareto designs. The first subset of trial designs is a set of convex hull designs. Each design in the first subset of designs is a different trial type.

[0890] An example method for determining a clinical trial study, the method including presenting, on a graphical interface, a set of cards, each card in the set of cards is representative of a different trial design from a set of trial designs; monitoring a first set of user interactions with the set of cards; determining trial design optimality criteria from the first set of user interactions; and presenting, on the graphical interface, new cards representative of design that meet the optimality criteria.

[0891] An example method including obtaining a trial design specification for a clinical trial design; obtaining one or more component specifications for one or more components of an analysis platform for analyzing the clinical trial design; determining, based at least in part on the trial design specification and the one or more component specifications, a configuration for the analysis platform; and executing an analysis of the clinical trial design via the analysis platform using the configuration.

[0892] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The one or more components include at least one of an engine; an analysis algorithm; a model; a database; computing resources; storage resources; or a visualization. The one or more components include at least one of a Pareto analysis algorithm; a convex hull algorithm; a simulated annealing algorithm; or a Monte Carlo algorithm. Determining the configuration further includes determining an order of execution for one or more analysis algorithms used by the analysis platform when executing the analysis of the clinical trial design. The one or more component specifications include at least one of a cost; a runtime; a required resource; or a version. The trial design specification includes at least one of a simulation time; a runtime; a type of analysis; or performance criteria. The trial design specification includes at least one of a preference for a number of recommended designs; a type of visual output; or a type of interactive interface. Determining the configuration for the analysis platform is further based at least in part on previous analysis data. Determining the configuration for the analysis platform includes predicting the configuration via machine learning.

[0893] An example apparatus including a specification receiving circuit structured to interpret a trial design specification data for a clinical trial design; and one or more component specification data for one components of an analysis platform for analyzing the clinical trial design; a configuration determination circuit structured to generate a platform configuration data based at least in part on the trial design specification data and the one or more component specification data; and an evaluation circuit structured to analyze the clinical trial design via the analysis platform using the configuration data.

[0894] An example method including obtaining trial design simulation results for a set of trial designs; determine a score for each trial design based on a performance criteria; evaluating Pareto optimality for each design in the set of trial designs to determine a Pareto frontier; filtering designs that are not on the Pareto frontier; and presenting the Pareto frontier designs.

[0895] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including recommending designs within epsilon-distance from the Pareto frontier. Further including identifying large separations in the Pareto frontier and performing simulated annealing based on the large separations. Further including identifying different design types on the Pareto frontier and recommending different design types. Further including identifying a second level Pareto frontier. Further including receiving feedback for recommended designs and determining epsilon values for additional recommendations. Further including clustering designs dominated by designs in the Pareto frontier. Further including clustering designs that are within a margin of error. Further including updating the Pareto designs in response to addition/subtraction of designs from the set of trial designs. Further including updating the Pareto designs in response to an update of scenario probabilities.

[0896] An example apparatus including a data processing circuit configured to obtain design data for a set of clinical trial designs; an optimality determining circuit configured to determine optimum designs using Pareto analysis from the set of clinical trial designs; and a design analysis circuit configured to analyze the Pareto designs and determine a modification to Pareto analysis; where the optimality determining circuit received the modification and determines a second set of optimum designs.

[0897] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The set of clinical trial designs includes all design options for a set of criteria. The optimality determining circuit modifies Pareto analysis to determine designs within epsilon-distance of Pareto designs. The optimality determining circuit modifies Pareto analysis to determine design dominated by the Pareto designs. The optimality determining circuit modifies Pareto analysis to determine designs clustered by the Pareto designs. The optimality determining circuit modifies Pareto analysis to determine twins of the Pareto designs. The optimality determining circuit modifies Pareto analysis to determine siblings of the Pareto designs. The optimality determining circuit modifies Pareto analysis to determine second level Pareto designs. The optimality determining circuit is configured to receive epsilon values from a user and modifies Pareto analysis to determine designs within epsilon-distance of Pareto designs. The optimality determining circuit modifies Pareto analysis to determine different design types within an epsilon-distance of Pareto designs.

[0898] An example method including obtaining trial design simulation results for a set of trial designs; determine a score for each trial design based on a performance criteria; evaluating the designs in the set of trial designs to determine a convex hull for the set of trial designs; filtering designs that are not on the convex hull; and presenting the convex hull designs.

[0899] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including recommending designs within epsilon-distance from designs on the convex hull. Further including identifying large facets in the convex hull and performing simulated annealing based on the large facets. Further including identifying different design types on the convex hull and recommending different design types. Further including identifying a second level convex hull. Further including receiving feedback for recommended designs and determining epsilon values for additional recommendations. Further including clustering designs dominated by designs in the convex hull. Further including clustering designs that are within a margin of error. Further including updating the convex hull designs in response to addition/subtraction of designs from the set of trial designs. Further including updating the convex hull designs in response to an update of scenario probabilities.

[0900] An example apparatus including a data processing circuit configured to obtain design data for a set of clinical trial designs; an optimality determining circuit configured to determine optimum designs using convex hull analysis from the set of clinical trial designs; and a design analysis circuit configured to analyze the convex hull designs and determine a modification to convex hull analysis, where the optimality determining circuit received the modification and determines a second set of optimum designs.

[0901] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The set of clinical trial designs includes all design options for a set of criteria. The optimality determining circuit modifies convex hull analysis to determine designs within epsilon-distance of convex hull designs. The optimality determining circuit modifies convex hull analysis to determine design dominated by the convex hull designs. The optimality determining circuit modifies convex hull analysis to determine designs clustered by the convex hull designs. The optimality determining circuit modifies convex hull analysis to determine twins of the convex hull designs. The optimality determining circuit modifies convex hull analysis to determine siblings of the convex hull designs. The optimality determining circuit modifies convex hull analysis to determine second level convex hull designs. The optimality determining circuit is configured to receive epsilon values from a user and modifies convex hull analysis to determine designs within epsilon-distance of convex hull designs. The optimality determining circuit modifies convex hull analysis to determine different design types withing an epsilon-distance of convex hull designs.

[0902] An example method including receiving outputs of a plurality of trial design simulations for a plurality of scenarios; evaluating the outputs to determine changes in performance over the plurality of scenarios; and providing a visual tornado diagram to visualize the changes.

[0903] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including determining a span of acceptable performance values over the scenarios. Determining a robustness value based at least in part on the changes. The robustness value is based on a probability associated with each scenario. Further including determining a risk assessment based at least in part on the robustness value. Further including categorizing scenarios based on their probability. The scenarios are categorized as optimistic, base, or pessimistic. Further including determining robustness based on the score in each category of scenarios. Further including determining scenario parameters that have the largest impact on performance parameters. Further including determining weighting criteria for the scenario parameters; and determining a robustness value of a trial design of the plurality based at least in part on the weighting criteria.

[0904] An example apparatus including an output processing circuit structured to interpret output data of a plurality of trial design simulations for a plurality of scenarios; an evaluation circuit structured to evaluate the output data to determine differences in performance over the plurality of scenarios; a graphic generation circuit structured to generate a tornado diagram that visualizes differences; and a graphic provisioning circuit structured to transmit the tornado diagram.

[0905] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Further including a robustness circuit structured to determining a span of acceptable performance values over the scenarios. Further including a robustness circuit structured to determine a robustness value based at least in part on the changes.

[0906] An example non-transitory computer-readable medium storing instructions that adapt at least one processor to receive outputs of a plurality of trial design simulations for a plurality of scenarios; evaluate the outputs to determine changes in performance over the plurality of scenarios;

and provide a visual tornado diagram to visualize the changes.

[0907] Certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be present in certain embodiments. Evaluating the outputs includes generating a visualization. The visualization is a tornado diagram. The stored instructions further adapt the at least one processor to determine a robustness value based at least in part on the changes. The stored instructions further adapt the at least one processor to determine a risk assessment based at least in part on the robustness value. The stored instructions further adapt the at least one processor to determine scenario parameters that have the largest impact on performance parameters. The stored instructions further adapt the at least one processor to determine weighting criteria for the scenario parameters; and determine a robustness value of a trial design of the plurality based at least in part on the weighting criteria.

[0908] An example method including obtaining initial trial design simulation results for a set of trial designs; identifying an initial design from the design simulation results; predicting performance for designs for variations of parameters; identifying a new design for simulation by varying parameters of the initial simulated design based on the predicting; simulating the new design and determining the performance of the new design; and identifying a second new design for simulation by varying parameters of the new design based on the simulated performance of the new design.

[0909] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The initial design is a Pareto design. The initial design is a convex hull design. The predicting is based on historical data. The predicting is based on Delaunay triangulations. Variations of different parameters are simulated in parallel. Further including determining a magnitude of variations based on historical data. Varying of parameters is directed to large gaps in the simulated designs. Varying of parameters based on a parameter priority rating. The initial trial design simulation results provide a coarse representation of design options.

[0910] An example apparatus including an analysis circuit structured to receive data for an initial design; an evaluation circuit structured to vary parameters of the initial design to generate a second design; and a simulation circuit configured for simulating the second design and determining a performance of the second design; where the evaluation circuit is further structured to vary parameters of the second design to generate a third design based at least in part on the performance of the second design.

[0911] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The initial design is a Pareto design. The initial design is a convex hull design. The evaluation circuit is structured to predict the performance of the second design based on historical data. The evaluation circuit is structured to predict the performance of the second design is based on Delaunay triangulations. Variations of different parameters are simulated in parallel. Further including determining magnitude of variations of parameters based on historical data. Variations of parameters are directed to large gaps in the simulated designs. Variations of parameters based on a parameter priority rating. The evaluation circuit is structured to evaluate a validity of the second design.

[0912] An example method including obtaining a first plurality of clinical trial designs with determined performance parameters; generating a performance surface based at least in part on the first plurality of clinical trial designs, where points on the performance surface represent interpolated performance parameters for a second plurality of clinical trial designs; and evaluating one or more clinical trial designs based at least in part on the performance surface.

[0913] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The performance surface is based at least in part on Delaunay triangulation. Evaluating includes simulated annealing. Further including generating a visualization based at least in part on the performance surface. The visualization is of weighted criteria functions over the design space. Generating the performance surface includes interpolation based at least in part on barycentric coordinates of a point. One or more of the clinical trial designs of the second plurality are not simulated. Evaluating includes determining that a clinical trial design of the second plurality is not a Pareto design. The first plurality of clinical trial designs are based at least in part a Monte Carlo simulation.

[0914] An example apparatus including a design processing circuit structured to interpret clinical trial design data corresponding to a first plurality of clinical trial designs with determined performance parameters; a surface circuit structured to generate a performance surface data object based at least in part on the clinical trial design data, where the performance surface data object includes data points representing interpolated performance criteria data for a second plurality of clinical trial designs; and a criterion surface provisioning structured to transmit the performance surface data object.

[0915] An example method including obtaining clinical trial design simulation results for a set of clinical trial designs; determining a set of Pareto designs in the set of clinical trial designs based at least in part on the clinical trial design simulation results and one or more performance parameters; determining a set of convex hull designs in the set of clinical trial designs; determining a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs; and transmitting the set of recommended designs.

[0916] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including filtering one or more of the set of clinical trial designs that are dominated by at least one of the set of convex hull designs. Further including filtering one or more of the set of clinical trial designs that are dominated by at least one of the set of Pareto designs. Determining the set of recommended designs includes determining at least one of the set of recommended designs within an epsilon-distance from at least one of the set of Pareto designs. Determining the set of recommended designs includes determining at least one of the set of recommended designs within an epsilon-distance from at least one of the set of convex hull designs. Determining a set of recommended designs includes performing simulated annealing on one or more of the set of clinical trial designs. Simulated annealing is based at least in part on facets of the set of convex hull designs. Further including identifying different design types in the set of Pareto designs. The set of Pareto designs is determined prior to the set of convex hull designs; the set of convex hull designs is derived from the set of Pareto designs such that each of the set of convex hull designs is in the set of Pareto designs; and at least one of the set of recommended designs is in the set of convex hull designs. The set of convex hull designs is determined prior to the set of Pareto designs; the set of Pareto designs is derived from the set of convex hull designs such that each of the set of Pareto designs is in the set of convex hull designs; and at least one of the set of recommended designs is in the set of convex hull designs. Further including identifying a number of clinical trial designs in the set of Pareto designs; where determining the set of convex hull designs occurs when the number is greater-than-or-equal-to a threshold; and the set of convex hull designs is derived from the set of Pareto designs. Further including identifying a number of clinical trial designs in the set of Pareto designs; and if the number is less-than-or-equal-to a threshold, identifying, for inclusion in the set of recommended designs, one or more of the set of clinical trial designs within an epsilon distance of at least one of the set of Pareto designs. Further including for each of the set of Pareto designs, determining a design type; determining a first clinical trial design of the set of Pareto designs is of a different design type from and within an epsilon-distance to a second clinical trial design of the set of Pareto designs; and including the first clinical trial design and the second clinical trial design in the set of recommended designs.

[0917] An example apparatus including a results processing circuit structured to interpret clinical trial design simulation results for a set of clinical trial designs; a Pareto evaluation circuit structured to determine a set of Pareto designs in the set of clinical trial designs based at least in part on the clinical trial design simulation results and one or more performance parameters; a convex hull evaluation circuit structured to determine a set of convex hull designs in the set of clinical trial designs; a recommendation circuit structured to determine a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs; and a recommendation provisioning circuit structured to transmit the set of recommended designs.

[0918] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Further including a filtering circuit structured to filter one or more of the set of clinical trial designs that are dominated by at least one of the set of convex hull designs. Further including a filtering circuit structured to filter one or more of the set of clinical trial designs that are dominated by at least one of the set of Pareto designs. The recommendation circuit is further structured to determine at least one of the set of recommended designs within an epsilon-distance from at least one of the set of Pareto designs.

[0919] An example non-transitory computer-readable medium storing instructions that adapt at least one processor to interpret clinical trial design simulation results for a set of clinical trial designs; determine a set of Pareto designs in the set of clinical trial designs based at least in part on the clinical trial design simulation results and one or more performance parameters; determine a set of convex hull designs in the set of clinical trial designs; determine a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs; and transmit the set of recommended designs.

[0920] Certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be present in certain embodiments. The stored instructions further adapt the at least one processor to filter one or more of the set of clinical trial designs that are dominated by at least one of the set of convex hull designs. The stored instructions further adapt the at least one processor to determine at least one of the set of recommended designs within an epsilon-distance from at least one of the set of Pareto designs.

[0921] An example method including obtaining clinical trial design simulation results for a set of clinical trial designs; determining a first set of designs using a first optimality criteria from the set of clinical trial designs; determining a second set of designs using a second optimality criteria from the set of clinical trial designs; determining a set of recommended designs based at least in part on the first and the second set of designs; and transmitting the set of recommended designs.

[0922] An example method including determining simulation runs for a trial design study; selecting a subset of the simulation runs; populating a simulation queue with the subset of the simulation runs; and executing the subset of simulation runs according to the simulation queue.

[0923] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. In response to executing the subset of simulation runs, performing simulated annealing on one or more of the executed simulation runs.

[0924] An example method including determining simulation runs of clinical trial designs for a clinical trial design study; evaluating, for each of the simulation runs, an expected performance; determining rankings for each of the simulation runs according to the expected performance; populating a simulation queue according to the rankings; and executing simulation runs from the simulation queue.

[0925] An example apparatus including a trial design processing circuit structured to interpret trial design study data; a first evaluation circuit structured to execute simulation runs of clinical trial designs defined, in part, by the trial design study data; a ranking circuit structured to, in response to executing the simulation runs, rank the simulation runs according to expected performance; a simulation populating circuit structured to populate a simulation queue according to the simulation run rankings; and a second evaluation circuit structured to execute simulation runs from the simulation queue.

[0926] An example method including determining simulation runs for a clinical trial design study; selecting a subset of the simulation runs; populating a simulation queue with the subset of the simulation runs; and executing the simulations according to the simulation queue; where the simulation queue is organized based at least in part on at least one of: time or costs.

[0927] An example method including identifying, in a marketplace, a simulation engine for simulating a clinical trial design; importing specifications of the simulation engine; and populating a user interface based on the specification.

[0928] An example method including selecting a simulation engine from a marketplace, the simulation engine for simulating a clinical trial design; determining inputs to the simulation engine; executing a simulation of the clinical trial design using the simulation engine with the inputs; and saving the inputs.

[0929] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The inputs include a random number seed. The inputs include a version of the simulation engine. The selected simulation is structured for a first type of the clinical trial design; and the marketplace includes additional simulation engines structured for additional types of clinical trial designs distinct from the first type. Further including importing previously saved inputs; and re-executing a simulation of the clinical trial design using the previously saved inputs.

[0930] An example apparatus including a user input processing circuit structured to interpret user input data; a simulation selection circuit structured to determine a simulation engine based at least in part on the user input data; an engine input selection circuit structured to determine inputs to the simulation engine based at least in part on the user input data; an evaluation circuit structured to execute a simulation using the determined simulation engine and determined inputs; and a recording circuit structured to save the determined inputs and the determined simulation engine to a memory device.

[0931] An example method including providing inputs to a plurality of clinical trial design simulation engines; receiving first outputs of the plurality of clinical trial design simulation engines in response to the inputs; providing variations of the inputs to the plurality of clinical trial design simulation engines; receiving second outputs of the plurality of clinical trial design simulation engines in response to the variations; evaluating the first and the second outputs to determine delta values; and determining, based in part on the delta values, a plurality of normalization factors for the plurality of clinical trial design simulation engines.

[0932] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. A first clinical trial design simulation engine of the plurality is structured to simulate a first clinical trial design that is of a different type than a second clinical trial design which a second clinical trial design simulation engine of the plurality is structured to simulate. A first clinical trial design simulation engine of the plurality is a different version of a second clinical trial design simulation engine of the plurality. A first clinical trial design simulation engine of the plurality was generated by a first entity and a second clinical trial design simulation engine of the plurality was generated by a second entity of the plurality distinct from the first entity. The first and the second outputs include metadata. Further including multiplying at least one of the first or the second outputs by at least one of the plurality of normalization factors. Each of the plurality of normalization factors differ in value based at least in part on differing performance criteria defined, in part, by the inputs. Further including determining, for each of the clinical trial design simulation engines, an output variability; and displaying the variabilities to a user. Further including determining a valid range of output values based on the delta values; and determining that at least one of the plurality of clinical trial design simulation engines outputs invalid values.

[0933] An example method including providing inputs to a plurality of clinical trial design simulation engines; receiving outputs of the plurality of clinical trial design simulation engines in response to the inputs; comparing outputs to expected outputs; and determining, based on the comparing, a plurality of normalization factors for the plurality of clinical trial design simulation engines.

[0934] An example apparatus including an output processing circuit structured to interpret output data from a plurality of clinical trial design simulation engines; a comparison circuit structured to compare the interpreted output data to expected output data; a normalization circuit structured to determine a plurality of normalization factors for the plurality of clinical trial design simulation engines; and a normalization provisioning circuit structured to transmit the plurality of normalization factors.

[0935] An example method including obtaining a specification that defines one or more associations between two or more clinical trials; determining, based at least in part on the specification, clinical trial designs for each of the two or more clinical trials; generating a permutation set of combinations of the clinical trial designs; determining combined performance criteria for each of the permutation set; and recommending one or more of the permutation set based at least in part on the combined performance criteria.

[0936] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Each of the combinations associates a first clinical trial design of the clinical trial designs with at least a second clinical trial design of the clinical trial designs, the first clinical trial design corresponding to a first clinical trial of the two or more clinical trials and the second clinical trial design corresponding to a second clinical trial of the two or more clinical trials, the second clinical trial distinct from the first clinical trial. The combined performance criteria for each of the permutation set is based at least in part on the one or more associations. At least one of the associations is based at least in part on one or more of the clinical trials having a sequential order of execution. At least one of the associations is based at least in part on one or more of the clinical trials having a concurrent order of execution. At least one of the associations is based at least in part on an execution order of a first portion of a first of the two or more clinical trials and a second of portion of a second of the two or more clinical trials. At least one of the associations is based at least in part on a first clinical trial of the two or more clinical trials corresponding to a different phase than a second clinical trial of the two or more clinical trials. A least one of the associations is based at least in part on at least two of the two or more clinical trials corresponding to a same test subject. The same test subject is at least one of a drug; a treatment; a medical device; or a procedure. Further including filtering the permutation set based at least in part on a Pareto analysis to generate a combination Pareto set; where the recommended one or more of the permutation set are in the combination Pareto set. Further including filtering the combination Pareto set based at least in part on a convex hull analysis; where the recommended one or more of the permutation set are on a convex hull of the combination Pareto set. Further including filtering the permutation set based at least in part on a convex hull analysis; where the recommended one or more of the permutation set are on a convex hull of the permutation set.

[0937] An example apparatus including a specification receiving circuit structured to obtain specification data that defines one or more associations between two or more clinical trials; a variation determining circuit structured to determine, based at least in part on the specification, clinical trial designs for each of the two or more clinical trials; a permutation circuit structured to generate a permutation set of combinations of the clinical trial designs; an evaluation circuit structured to determine combined performance criteria for each of the permutation set; and a recommendation circuit structured to recommend one or more of the permutation set based at least in part on the combined performance criteria.

[0938] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. Each of the combinations associates a first clinical trial design of the clinical trial designs with at least a second clinical trial design of the clinical trial designs, the first clinical trial design corresponding to a first clinical trial of the two or more clinical trials and the second clinical trial design corresponding to a second clinical trial of the two or more clinical trials, the second clinical trial distinct from the first clinical trial. The evaluation circuit is further structured to determine combined performance criteria based at least in part on the one or more associations. At least one of the associations is based at least in part on one or more of the clinical trials having a sequential order of execution. At least one of the associations is based at least in part on one or more of the clinical trials having a concurrent order of execution. Further including a first filtering circuit structured to filter the permutation set based at least in part on a Pareto analysis to generate a combination Pareto set; where the recommendation circuit is further structured to select the recommended one or more of the permutation set from the combination Pareto set. Further including a second filtering circuit structured to filter the combination Pareto set based at least in part on a convex hull analysis; where the recommendation circuit is further structured to select the recommended one or more of the permutation set from a convex hull of the combination Pareto set.

[0939] An example non-transitory computer-readable medium storing instructions that adapt at least one processor to obtain specification data that defines one or more associations between two or more clinical trials; determine, based at least in part on the specification, clinical trial designs for each of the two or more clinical trials; generate a permutation set of combinations of the clinical trial designs; determine combined performance criteria for each of the permutation set; and recommend one or more of the permutation set based at least in part on the combined performance criteria.

[0940] Certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be present in certain embodiments. Each of the combinations associates a first clinical trial design of the clinical trial designs with at least a second clinical trial design of the clinical trial designs, the first clinical trial design corresponding to a first clinical trial of the two or more clinical trials and the second clinical trial design corresponding to a second clinical trial of the two or more clinical trials, the second clinical trial distinct from the first clinical trial.

[0941] An example method including obtaining a clinical trial design; determining a space of scenario probability variations for the clinical trial design; and evaluating the space of scenario probability variations to determine a robustness of the clinical trial design.

[0942] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including weighting one or more design criteria for the clinical trial design; where determining the space of scenario probability variations is based at least in part on the one or more weighted design criteria. Weights of the one or more weighted design criteria are fixed. Further including reducing a dimensionality of the space of scenario probability variations by evaluating relations between two or more scenarios within the space. The robustness corresponds to a size of a range of scenario probability variations within the space for which the clinical trial design is optimal. Evaluating the space of scenario probabilities includes conducting a Pareto analysis. Evaluating the space of scenario probabilities includes conducting a convex hull analysis.

[0943] An example method including determining a globally optimum clinical trial design by executing a platform for optimizing clinical trial designs in a forward mode of operation; determining a robustness value of the globally optimum clinical trial design by executing the platform in an inverse mode of operation; and providing the globally optimum clinical trial design and the robustness value.

[0944] An example apparatus including a specification processing circuit structured to interpret clinical trial design data corresponding to a clinical trial design; a space determining circuit structured to determine, based at least in part on the clinical trial design data, a space of scenario probability variations for the clinical trial design; an evaluation circuit structured to determine, based at least in part on the space of scenario probability variations, a robustness value of the clinical trial design; and a robustness provisioning circuit structured to transmit the robustness value.

[0945] An example method for updating a clinical trial, the method including obtaining, during conduction of the clinical trial, a simulation output for a set of clinical trial designs for the clinical trial, where the simulation output includes performance parameters associated with each design in the set of clinical trial designs for a set of criteria; determining, from the set of criteria, an optimality criteria for evaluating the set of clinical trial designs; determining, within the set of clinical trial designs, a globally optimum design based at least in part on the optimality criteria and the performance parameters; and recommending the globally optimum design.

[0946] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including adjusting, during conduction of the clinical trial, the clinical trial based at least in part on the globally optimum design. Adjusting the clinical trial conforms the clinical trial to the globally optimum design. The set of clinical trial designs includes all design options for the set of criteria. The optimality criteria is based on historical data and includes performance parameters of a benchmark design. The optimality criteria is based on a weighted sum of performance criteria values of each of clinical trial designs.

[0947] An example method for updating a clinical trial, the method including obtaining a first simulation output for a first set of clinical trial designs for the clinical trial, where the first simulation output includes first performance parameters associated with each design in the first set of clinical trial designs for a first set of criteria; determining, from the first set of criteria, a first optimality criteria for evaluating the first set of clinical trial designs; determining, within the first set of clinical trial designs, a first globally optimum design based at least in part on the first optimality criteria and the first performance parameters; conducting the clinical trial based at least in part on the first globally optimum design; obtaining, during conduction of the clinical trial, a second simulation output for a second set of clinical trial designs for the clinical trial, where the second simulation output includes second performance parameters associated with each design in the second set of clinical trial designs for a second set of criteria; determining, from the second set of criteria, a second optimality criteria for evaluating the second set of clinical trial designs; determining, within the second set of clinical trial designs, a second globally optimum design based at least in part on the second optimality criteria and the second performance parameters; and adjusting the clinical trial based at least in part on the second globally optimum design.

[0948] An example method including determining a plurality of possible sites for recruiting patients from for a clinical trial; determining, for each of one or more subgroupings of the plurality of possible sites, a predicted patient recruitment value; and determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes a desired site selection criteria.

[0949] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Determining the predicted patient recruitment value for each of the subgroupings of the plurality of possible sites includes simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. The difference between the types of engines is based at least in part on a version number. Further including determining one or more site selection parameters, where simulating each of the one or more subgroupings is based at least in part on the one or more site selection parameters. The one or more site selection parameters are based at least in part on at least one of a country; a state/province; a county; a city; a zip code; or a patient enrollment matriculation number. The method further includes determining the desired site selection criteria, where simulating each of the one or more subgroupings is based at least in part on the determined site selection criteria. The determined site selection criteria is based at least in part on at least one of a number of required patients; a start date of the clinical trial; an end date of the clinical trial; or a total cost of the clinical trial. Determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria includes use of one or more of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. Determining which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria is based at least in part on a machine learning engine.

[0950] An example apparatus including a site selection data processing circuit structured to interpret possible site selection data identifying a plurality of possible sites for recruiting patients from for a clinical trial; a patient recruitment determination circuit structured to determine a predicted patient recruitment value for each of one or more subgroupings of the plurality of possible sites; a site searching circuit structured to determine which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes a desired site selection criteria; and a site selection provisioning circuit structured to transmit the subgrouping of the plurality of possible sites that has the predicted patient recruitment value that globally optimizes the desired site selection criteria.

[0951] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The patient recruitment determination circuit is further structured to determine the predicted patient recruitment value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. Further including a user input circuit structured to interpret user input data; and a criteria determining circuit structured to determine the desired site selection criteria based at least in part on the user input data. The site searching circuit includes at least one of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine.

[0952] An example system including a database storing site selection data identifying a plurality of possible sites for recruiting patients from for a clinical trial; a server structured to: access the site selection data stored in the database; determine a patient recruitment value for each of one or more subgroupings of the plurality of possible sites; and determine which subgrouping of the plurality of possible sites has a patient recruitment value that globally optimizes a desired site selection criteria; and an electronic display structured to depict the determined subgrouping.

[0953] Certain further aspects of the example system are described following, any one or more of which may be present in certain embodiments. The server is further structured to determine the patient recruitment value for each of one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. The server is further structured to determine the desired site selection criteria, where simulating each of the one or more subgroupings is based at least in part on the determined site selection criteria. The determined site selection criteria is based at least in part on at least one of a number of required patients; a start date of the clinical trial; an end date of the clinical trial; or a total cost of the clinical trial.

[0954] An example method including displaying a graphical user interface structured to configure a system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria; receiving, via the graphical user interface, one or more user inputs that define one or more selection-parameters used by the system; and storing the defined selection-parameters in a memory device.

[0955] An example apparatus including a display generation circuit structured to generate a graphical user interface for configuring a system for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria; a display transmission circuit structured to transmit the graphical user interface to an electronic device for display; a user interaction circuit structured to: interpret user inputs received by the graphical user interface; and in response to, and based at least in part on, interpreting the user inputs, define selection parameters used by the system; and a selection-parameter provisioning circuit structured to store the defined selection-parameters in a memory device.

[0956] An example method including configuring, via a graphical user interface, a recruitment site selection system via entering one or more user inputs into the graphical user interface that define one or more selection-parameters; determining, via the recruitment site selection system, which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired criteria; and transmitting data identifying the determined subgrouping.

[0957] An example method including accessing past trial site selection data stored in a database; predicting, based at least in part on the past trial site selection data, an initial site selection for recruiting patients for a clinical trial, the initial site selection corresponding to a global optimization of a desired site selection criteria; evaluating the initial site selection with respect to being the global optimization; and displaying the initial site selection in a graphical user interface.

[0958] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The desired site selection criteria is at least one of a number of required patients; a start date of the clinical trial; an end date of the clinical trial; or a total cost of the clinical trial. The desired site selection criteria is based at least in part on a patient recruitment related number. Further including adjusting the initial site selection via the graphical user interface. The past trial site selection data is derived from one or more previously conducted clinical trials. The past trial site selection data is derived from one or more previously simulated clinical trials. Further including interpreting one or more user inputs, where the prediction of the initial site selection is based at least in part on the one or more user inputs. Further including simulating the initial site selection to determine performance criteria. Further including conducting a sensitivity analysis of the initial site selection. Evaluating the initial site selection with respect to being the global optimization is based at least in part on at least one of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. Predicting the initial site selection is based at least in part on artificial intelligence.

[0959] An example apparatus including a past trial data processing circuit structured to interpret past trial site selection data; a patient recruitment prediction circuit structured to generate, based at least in part on the past trial site selection data, initial site selection data for recruiting patients for a clinical trial, the initial site selection data corresponding to a global optimization of a desired site selection criteria; a patient recruitment evaluation circuit structured to evaluate the initial site selection with respect to the global optimization; and a prediction provisioning circuit structured to transmit the initial site selection data.

[0960] An example method including receiving an initial site selection for recruiting patients for a clinical trial; and conducting a clinical trial based as least in part on the initial site selection, the initial site selection corresponding to a global optimization of a desired criteria; where the initial site selection was predicted from past trial site selection data.

[0961] An example method including generating a graphical user interface structured to provide for interactive exploration of one or more spaces corresponding to one or more selection parameters for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes a desired site selection criteria; adjusting at least one of the selection parameters via the graphical user interface; and updating the graphical user interface in response to adjusting the at least one selection parameter.

[0962] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The desired selection criteria is based at least in part on a patient recruitment related number. The one or more spaces include at least one of site selection criteria space; site selection space; site selection scenario space; or site selection performance space. The graphical user interface depicts the one or more spaces as a computer-generated graphic. The computer-generated graphic is based at least in part on at least one of a heatmap; or a tornado graph. Generating the graphical user interface occurs prior to simulating any one of the possible sites. Generating the graphical user interface occurs after simulation of one or more of the possible sites.

[0963] An example apparatus including a patient recruitment space processing circuit structured interpret space data corresponding to one or more spaces related to subgroupings of possible sites for use in conducting a clinical trial; a graphics circuit structured to generate interactive interface data in response to the space data, the interactive interface data corresponding to a computerized interface for globally optimizing a desired site selection criteria; a user input circuit structured to receive user input data responsive to presentation of the interactive interface data; a patient recruitment space exploration circuit structured to modify the interactive interface data in response to the user input data; and an interactive provisioning circuit structured to transmit the modified interactive interface data.

[0964] An example method for updating a site selection, the method including obtaining, during conduction of a clinical trial, a simulation output for a set of site selections for the clinical trial, where the simulation output includes site selection performance parameters associated with each site selection in the set of site selections for a set of site selection criteria; determining, from the set of site selection criteria, a site selection optimality criteria for evaluating the set of site selections; determining, within the set of site selections, a globally optimum site selection based at least in part on the site selection optimality criteria and the site selection performance parameters; and recommending the globally optimum site selection.

[0965] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including adjusting, during conduction of the clinical trial, the site selection based at least in part on the globally optimum site selection. Adjusting the site selection conforms the site selection to the globally optimum site selection. The set of site selections includes all site selection options for the set of site selection criteria. The site selection optimality criteria is based on historical data and includes site selection performance parameters of a benchmark site selection. The site selection optimality criteria is based on a weighted sum of site selection performance criteria values of each of site selections.

[0966] An example method for updating a site selection the method including obtaining a first simulation output for a first set of site selections for a clinical trial, where the first simulation output includes first site selection performance parameters associated with each site selection in the first set of site selections for a first set of site selection criteria; determining, from the first set of site selection criteria, a first site selection optimality criteria for evaluating the first set of site selections; determining, within the first set of site selections, a first globally optimum site selection based at least in part on the first site selection optimality criteria and the first site selection performance parameters; conducting the clinical trial based at least in part on the first globally optimum site selection; obtaining, during conduction of the clinical trial, a second simulation output for a second set of site selection for the clinical trial, where the second simulation output includes second site selection performance parameters associated with each site selection in the second set of site selections for a second set of site selection criteria; determining, from the second set of site selection criteria, a second site selection optimality criteria for evaluating the second set of site selections; determining, within the second set of site selections, a second globally optimum site selection at least in part on the second site selection optimality criteria and the second site selection performance parameters; and adjusting the site selection based at least in part on the second globally site selection.

[0967] An example method including determining a plurality of possible sites for recruiting patients from for a clinical trial; determining, for each of one or more subgroupings of the plurality of possible sites, a predicted available resources value; and determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria.

[0968] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Determining the predicted available resources value for each of the subgroupings of the plurality of possible sites includes simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. The difference between the types of engines is based at least in part on a version number. Further including determining one or more site resource parameters, where simulating each of the one or more subgroupings is based at least in part on the one or more site resource parameters. The one or more site resource parameters are based at least in part on at least one of a supply of a drug; administrative personnel; or equipment. Further including determining the desired site resource criteria, where simulating each of the one or more subgroupings is based at least in part on the determined site resource criteria. The determined site resource criteria is based at least in part on at least one of a supply of a drug; administrative personnel; or equipment. Determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria includes use of one or more of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. Determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria is based at least in part on a machine learning engine.

[0969] An example apparatus including a site selection data processing circuit structured to interpret possible site selection data identifying a plurality of possible sites for recruiting patients from for a clinical trial; an available resources determination circuit structured to determine a predicted available resources value for each of one or more subgroupings of the plurality of possible sites; a site searching circuit structured to determine which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria; and a site selection provisioning circuit structured to transmit the subgrouping of the plurality of possible sites that has the predicted available resources value that globally optimizes the desired site resource criteria.

[0970] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The available resources determination circuit is further structured to determine the predicted available resources value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. Further including a user input circuit structured to interpret user input data; and a criteria determining circuit structured to determine the desired site resource criteria based at least in part on the user input data. The site searching circuit includes at least one of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine.

[0971] An example system including a database storing site resource data identifying a plurality of possible sites for recruiting patients from for a clinical trial; a server structured to access the site resource data stored in the database; determine an available resources value for each of one or more subgroupings of the plurality of possible sites; and determine which subgrouping of the plurality of possible sites has an available resources value that globally optimizes a desired site resource criteria; and an electronic display structured to depict the determined subgrouping.

[0972] Certain further aspects of the example system are described following, any one or more of which may be present in certain embodiments. The server is further structured to determine the available resources value for each of one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. Simulating each of the one or more subgroupings is based at least in part on use of different types of engines. The server is further structured to determine the desired site resource criteria, where simulating each of the one or more subgroupings is based at least in part on the determined site resource criteria. The determined site resource criteria is based at least in part on at least one of a number of required patients; a start date of the clinical trial; an end date of the clinical trial; or a total cost of the clinical trial.

[0973] An example method including displaying a graphical user interface structured to configure a system for determining which subgrouping, of a plurality of possible sites for a clinical trial, globally optimizes available clinical trial resources; receiving, via the graphical user interface, one or more user inputs that define one or more resource selection parameters used by the system; and storing the defined resource selection parameters in a memory device.

[0974] An example apparatus including a display generation circuit structured to generate a graphical user interface for configuring a system for determining which subgrouping, of a plurality of possible sites for a clinical trial, globally optimizes available clinical trial resources; a display transmission circuit structured to transmit the graphical user interface to an electronic device for display; a user interaction circuit structured to: interpret user inputs received by the graphical user interface; and in response to, and based at least in part on, interpreting the user inputs, define resource selection parameters used by the system; and a selection-parameter provisioning circuit structured to store the defined selection-parameters in a memory device.

[0975] An example method including configuring, via a graphical user interface, a recruitment site selection system via entering one or more user inputs into the graphical user interface that define one or more selection-parameters; determining, via the recruitment site selection system, which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes available clinical trial resources; and transmitting data identifying the determined subgrouping.

[0976] An example method including accessing past trial site selection data stored in a database; predicting, based at least in part on the past trial site selection data, an initial site selection for globally optimizing access to clinical trial resources; evaluating the initial site selection with respect to being the global optimization; and displaying the initial site selection in a graphical user interface.

[0977] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The clinical trial resources are based at least in part on at least one of a supply of a drug; administrative personnel; or equipment. Further including adjusting the initial site selection via the graphical user interface. The past trial site selection data is derived from one or more previously conducted clinical trials. The past trial site selection data is derived from one or more previously simulated clinical trials. Further including interpreting one or more user inputs, where the prediction of the initial site selection is based at least in part on the one or more user inputs. Further including simulating the initial site selection to determine performance criteria. Further including conducting a sensitivity analysis of the initial site selection. Evaluating the initial site selection with respect to being the global optimization is based at least in part on at least one of a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. Predicting the initial site selection is based at least in part on artificial intelligence.

[0978] An example apparatus including a past trial data processing circuit structured to interpret past trial site selection data; a resource prediction circuit structured to generate, based at least in part on the past trial site selection data, initial site selection data for globally optimizing access to clinical trial resources; a resource evaluation circuit structured to evaluate the initial site selection with respect to the global optimization; and a prediction provisioning circuit structured to transmit the initial site selection data.

[0979] An example method including receiving an initial site selection for a clinical trial resources; and conducting a clinical trial based as least in part on the initial site selection, the initial site selection corresponding to a global optimization of access to clinical trial resources; where the initial site selection was predicted from past trial site selection data.

[0980] An example method including generating a graphical user interface structured to provide for interactive exploration of one or more spaces corresponding to one or more selection parameters for determining which subgrouping, of a plurality of possible sites for recruiting patients from for a clinical trial, globally optimizes available clinical trial resources; adjusting at least one of the selection parameters via the graphical user interface; and updating the graphical user interface in response to adjusting the at least one selection parameter.

[0981] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The clinical trial resources are based at least in part on at least one of a supply of a drug; administrative personnel; or equipment. The one or more spaces include at least one of resource criteria space; site resource space; resource scenario space; or site resource performance space. The graphical user interface depicts the one or more spaces as a computer-generated graphic. The computer-generated graphic is based at least in part on at least one of a heatmap; or a tornado graph. Generating the graphical user interface occurs prior to simulating any one of the possible sites. Generating the graphical user interface occurs after simulation of one or more of the possible sites.

[0982] An example apparatus including a resource space processing circuit structured interpret space data corresponding to one or more spaces related to subgroupings of possible sites for use in conducting a clinical trial; a graphics circuit structured to generate interactive interface data in response to the space data, the interactive interface data corresponding to a computerized interface for globally optimizing available clinical trial resources; a user input circuit structured to receive user input data responsive to presentation of the interactive interface data; a resource space exploration circuit structured to modify the interactive interface data in response to the user input data; and an interactive provisioning circuit structured to transmit the modified interactive interface data.

[0983] An example method for updating a site selections, the method including obtaining, during conduction of a clinical trial, a simulation output for a set of site selections for the clinical trial, where the simulation output includes site selection performance parameters associated with each site selection in the set of site selections for a resource availability; determining, a site selection optimality criteria for evaluating the set of site selections; determining, within the set of site selections, a globally optimum site selection based at least in part on the site selection optimality criteria and the resource availability; and recommending the globally optimum site selection.

[0984] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including adjusting, during conduction of the clinical trial, the site selection based at least in part on the globally optimum site selection. Adjusting the site selection conforms the site selection to the globally optimum site selection. The set of site selections includes all site selection options for the resource availability. The site selection optimality criteria is based on historical data and includes the resource availability of a benchmark site selection. The site selection optimality criteria is based on a weighted sum of site selection performance criteria values of each of site selections.

[0985] An example method for updating a site selection the method including obtaining a first simulation output for a first set of site selections for a clinical trial, where the first simulation output includes first site selection performance parameters associated with each site selection in the first set of site selections for a first set of site selection criteria; determining, from the first set of site selection criteria, a first resource availability; determining, within the first set of site selections, a first globally optimum site selection based at least in part on the resource availability; conducting the clinical trial based at least in part on the first globally optimum site selection; obtaining, during conduction of the clinical trial, a second simulation output for a second set of site selection for the clinical trial, where the second simulation output includes a second resource availability; determining, within the second set of site selections, a second globally optimum site selection at least in part on the second resource availability; an adjusting the site selection based at least in part on the second globally site selection.

[0986] An example method includes interpreting, via at least one processor, replication results data for a replication of a clinical trial design, the replication forming part of a replication process of a clinical trial design simulation; determining, via the at least one processor, a performance criteria value based at least in part on the replication results data; determining, via the at least one processor and based at least in part on the performance criteria value, an adjustment value; and in response to determining the adjustment value, adjusting, via the at least one processor, the replication process.

[0987] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The performance criteria value includes a standard error. The replication processor includes ceasing the replication process when the standard error is below a threshold. The performance criteria value includes an upper confidence interval of the clinical trial design. Adjusting the replication processor include ceasing the replication process when a difference from a lower confidence interval of another clinical trial design is higher than the upper confidence interval. The lower confidence interval and the upper confidence interval are each 99%. The replication process includes batches for execution in parallel processing. Further including retrieving at least some of the replication results data from a quick search data structure. The quick search data structure is a SimCube. The clinical trial simulation is based at least in part on simulated annealing. Adjusting the replication processor includes increasing a number of replications in the replication process. Adjusting the replication processor includes decreasing a number of replications in the replication process.
[0988] An example apparatus including a replication circuit structured to execute a replication process including a plurality of replications of a clinical trial design, where each replication of the plurality generates corresponding replication results data; a results interpretation circuit structured to interpret the replication results data of at least one of the plurality of replications; a performance circuit structured to determine a performance criteria value based at least in part on the replication results data; an adjustment determining circuit structured to determine, based at least in part on the performance criteria value, an adjustment value to the replication process; and an adjustment circuit structured to adjust the replication process based at least in part on the adjustment value.
[0989] Certain further aspects of the example apparatus are described following, any one or more of which may be present in certain embodiments. The performance criteria value includes a standard error. The adjustment determining circuit is structured to configure the adjustment value to cease the replication process when the standard error is below a threshold. The performance criteria value includes an upper confidence interval of the clinical trial design. The adjustment determining circuit is structured to configure the adjustment value to cease the replication process when a difference from a lower confidence interval of another clinical trial design is higher than the upper confidence interval. The replication circuit is further structured to batch the plurality of replications into a plurality of batches for parallel execution on two or more processors. Further including a results retrieval circuit structured to retrieve at least some of the replication results data from a quick search data structure.
[0990] An example system including a server structured to execute a replication process forming part of a clinical trial design simulation, the replication process including a plurality of replications of a clinical trial design; determine a performance criteria value for at least one of the plurality of replications; and adjust, based at least in part on the performance criteria value, the replication process; and an electronic device structured to: display an interactive interface that presents a plurality of prompts to a user for configuring the clinical trial design simulation.
[0991] An example method including allocating memory, in a memory device, that defines a quick search data structure having a plurality of storage cells; simulating a plurality of clinical trial designs to obtain a plurality of simulation results, each of the plurality of simulation results corresponding to one of the plurality of clinical trial designs; and storing each of the plurality of simulation results in a corresponding one of the plurality of storage cells based on one or more relationships between two or more of the plurality of clinical trial designs.
[0992] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The one or more relationships between the two or more of the plurality of clinical trial designs is based at least in part on the value of parameters for each of the two or more of the plurality of clinical trial designs. Further including scoring the two or more of the plurality of clinical trial designs based at least in part on the value of the parameters; and determining whether the two or more of the plurality of clinical trial designs are similar

designs. Determining whether the two or more of the plurality of clinical trial designs are similar designs include determining if the two or more of the plurality of clinical trial designs are within an epsilon of a desired score. Determining whether the two or more of the plurality of clinical trial designs are similar designs include determining if the two or more of the plurality of clinical trial designs are within an epsilon of each other. The quick search data structure is a SimCube. The SimCube has dimensions based at least in part on a number of design parameters and a number of scenario variables. Each of the dimensions is equal to a sum of the number of design parameters and the number of scenario variables.

[0993] An example method including obtaining initial simulation results for a set of clinical trial designs; identifying an initial clinical trial design based at least in part on the initial simulation results; predicting performance for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting; determining if a quick search data structure contains first simulation results for the first new clinical trial design; if the quick search data structure does not contain the first simulation results, then simulating the first new clinical trial design to obtain the first simulation results; and based at least in part on the first simulation results, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[0994] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including storing the first simulation results in the quick search data structure. Storing the first simulation results in the quick search data structure include determining one or more relationships between the first new clinical trial design and another clinical trial design stored in the quick search data structure. The one or more relationships between the new clinical trial design and the another clinical trial design is based at least in part on the value of the parameters for the first new clinical trial design and parameters of the another clinical trial design. The quick search data structure is a SimCube. The SimCube has dimensions based at least in part on a number of the parameters of the first new clinical trial design and a number of scenario variables. Each of the dimensions is equal to a sum of the number of design parameters and the number of scenario variables.

[0995] An example method including interpreting, via at least one processor, simulation results data for a set of clinical trial designs; populating, via the at least one processor, a quick search data structure, defined within a memory device, with the simulation results data; identifying, via the at least one processor, a region of interest within at least one of a performance criteria space of the set of clinical trial designs or the quick search data structure; identifying, via at least one processor, a first clinical trial design based at least in part on the region of interest; determining, via the at least one processor and based at least in part on the quick search data structure and the first clinical trial design, a second clinical trial design; and transmitting, via the at least one processor, data corresponding to the second clinical trial design.

[0996] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Identifying the region include determining a void within at least one of the quick search data structure or the design criteria space. Determining the second clinical trial design include determining that the second clinical trial design is within a Manhattan distance within the quick search data structure of the first clinical trial design. Determining the second clinical trial design include determining that the second clinical trial design is within an epsilon of a desired score. The region of interest corresponds to two or more similar designs. The quick search data structure is a SimCube.

[0997] An example method including interpreting initial simulation results data for a set of clinical trial designs; identifying an initial clinical trial design based at least in part on the initial simulation results data; predicting performance data for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting; predicting, via machine learning, first simulation results data for the first new clinical trial design; and based at least in part on the first simulation results data, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[0998] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. The machine learning is based at least in part on a neural network. The neural network is trained via reinforcement learning. The machine learning is based at least in part on a regression model. The regression model is based at least in part on a regression tree. The first simulation results data are based on an interpolation of one or more clinical trial designs. The one or more clinical designs are neighbors to the first new clinical trial design. Further including interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by the set of clinical trial designs; where identifying the first new clinical trial design for simulation is further based at least in part on the convex hull tunnel data. Identifying the first new clinical trial design for simulation is further based at least in part on a penalty function related to the convex hull tunnel. The penalty function discourages selection of designs that are farther away from a center line of the convex hull tunnel.

[0999] An example method including interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by a set of clinical trial designs; identifying an initial clinical trial design based at least in part on the convex hull tunnel data; predicting performance for clinical trial designs based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting and on the convex hull tunnel data; determining first simulation results for the first new clinical trial design; and based at least in part on the first simulation results, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1000] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Identifying the first new clinical trial design for simulation is further based at least in part on a penalty function related to the convex hull tunnel. The penalty function discourages selection of designs that are farther away from a center line of the convex hull tunnel. The penalty function scores clinical trial designs. Determining first simulation results for the first new clinical trial design includes predicting the first simulation results via machine learning. The machine learning is based at least in part on a neural network. The neural network is trained via reinforcement learning. The machine learning is based at least in part on a regression model.

[1001] An example method including interpreting initial simulation results data for a set of clinical trial designs; identifying, based at least in part on the initial simulation results data, a clinical trial design for simulation; predicting, via machine learning and based at least in part on the initial simulation results data, simulation results data for the clinical trial design; and transmitting the simulation results data.

[1002] Certain further aspects of the example method are described following, any one or more of which may be present in certain embodiments. Further including interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by the set of clinical trial designs; where identifying the clinical trial design for simulation is further based at least in part on the convex hull tunnel data.

[1003] An example apparatus including a results interpretation circuit structured to interpret initial simulation results data for a set of clinical trial designs; a first identification circuit structured to identify an initial clinical trial design based at least in part on the initial simulation results data; a performance prediction circuit structured to predict performance data for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design; a second identification circuit structured to identify a first new clinical trial design for simulation based on the predicting; a results prediction circuit structured to predict, via machine learning, first simulation results data for the first new clinical trial design; and a third identification circuit structured to identify, based at least in part on the first simulation results data, a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1004] An example apparatus including a convex hull interpretation circuit structured to interpret convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by a set of clinical trial designs; a first identification circuit structured to identify an initial clinical trial design based at least in part on the convex hull tunnel data; a performance prediction circuit structured to predict performance data for clinical trial designs based at least in part on varying parameters for the initial clinical trial design; a second identification circuit structured to identify a first new clinical trial design for simulation based on the performance data and on the convex hull tunnel data; a results determining circuit structured to determine first simulation results data for the first new clinical trial design; and a third identification circuit structured to identify, based at least in part on the first simulation results data, a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1005] An example method for determining trial designs includes obtaining simulation data for a set of trial designs. The simulation data includes performance parameters and performance parameter values associated with each design in the set of designs for a set of criteria. The example method further includes determining an optimality criteria for evaluating the trial designs, and searching, within the set of trial designs, for globally optimum designs based on the optimality criteria. The example method further includes recommending globally optimum designs.

[1006] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the set of trial designs includes all combinations of design options for a set of criteria. In certain aspects, the optimality criteria is based on historical data and includes performance parameters of a benchmark design. In certain aspects, the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs. In embodiments, the example method may further include changing the optimality criteria based on a number of globally optimum designs. In embodiments, the example method may further include determining a second optimality criteria, and searching, within the set of trial designs, for a second set of globally optimum designs based on the second optimality criteria. In certain embodiments, the example method may further include determining a second optimality criteria; and searching, within the set of globally optimum designs, for a second set of globally optimum designs based on the second optimality criteria. In certain embodiments, the example method may further include dynamically changing the optimality criteria in response to properties of globally optimum designs. In certain embodiments, the example method may further include dynamically changing the optimality criteria in response to user feedback. In certain aspects, the optimality criteria includes Pareto optimality. In certain aspects, the optimality criteria includes convex hull optimality. In certain aspects, the optimality criteria includes Pareto optimality and the optimality criteria includes convex hull optimality. In certain embodiments, the example method may further include evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Obtaining the simulation data is based at least in part on a quick search data structure and the one or more trial design parameters. In certain embodiments, the example method further includes generating a substitute for at least some of the simulation data based at least in part on a relationship between the simulation data and supplemental data; and generating a performance surface based at least in part on the set of trial designs. The example method further includes evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the simulation data.

[1007] An example apparatus includes a data processing circuit, an optimality determining circuit, and a design analysis circuit. The data processing circuit is configured to obtain design data for a set of trial designs. The optimality determining circuit is configured to determine an optimality criteria for evaluating the trial designs, and search, from the set of trial designs, for globally optimum designs based on the optimality criteria. The design analysis circuit is configured to analyze the globally optimum designs and determine a modification to the optimality criteria. The optimality determining circuit is structured to receive the modification and determine a second set of globally optimum designs.

[1008] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the set of trial designs includes all combinations of design options for a set of criteria. In certain aspects, the optimality criteria is based on historical data and includes performance parameters of a benchmark design. In certain aspects, the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs. In certain aspects, the modification is based on a number of globally optimum designs. In certain aspects, the modification is in response to user feedback.

[1009] An example non-transitory computer-readable medium stores instructions that adapt at least one processor to obtain a simulation data for a set of trial designs, wherein the simulation data includes performance parameters and performance parameter values associated with each design in the set of designs for a set of criteria. The stored instructions further adapt the at least one processor to determine an optimality criteria for evaluating the trial designs, search, within the set of trial designs, for globally optimum designs based on the optimality criteria, and recommend globally optimum designs.

[1010] An example method for determining trial designs includes receiving, via at least one processor, one or more trial design criteria and one or more scenarios corresponding to a set of trial designs, and generating, via the at least one processor, simulation data based at least in part on replicating each of the set of trial designs with the one or more trial design criteria and the one or more scenarios. The simulation data includes performance parameters and performance parameter values associated with each design in the set of designs for a set of criteria. The example method further includes determining, via the at least one processor, an optimality criteria for evaluating the trial designs, searching, within the set of trial designs, via the at least one processor, for globally optimum designs based on the optimality criteria; and transmitting, via the at least one processor, globally optimum designs.

[1011] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the set of trial designs includes all combinations of design options for a set of criteria. In certain aspects, the optimality criteria is based on historical data and includes performance parameters of a benchmark design. In certain aspects, the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs. In certain embodiments, the example method further includes changing the optimality criteria based on a number of globally optimum designs. In certain embodiments, the example method further includes determining a second optimality criteria, and searching, within the set of trial designs, for a second set of globally optimum designs based on the second optimality criteria. In certain embodiments, the example method further includes determining a second optimality criteria, and searching, within the set of globally optimum designs, for a second set of globally optimum designs based on the second optimality criteria. In certain embodiments, the example method further includes dynamically changing the optimality criteria in response to properties of globally optimum designs. In certain embodiments, the example method further includes dynamically changing the optimality criteria in response to user feedback. In certain aspects, the optimality criteria includes Pareto optimality. In certain aspects, the optimality criteria includes convex hull optimality. In certain aspects, the optimality criteria includes Pareto optimality and the optimality criteria includes convex hull optimality. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Generating the simulation data is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the simulation data based at least in part on a relationship between the simulation data and supplemental data, generating a performance surface based at least in part on the set of trial designs, evaluating one or more trial designs based at least in part on the performance surface, and calculating a score based on normalized score component values corresponding to the simulation data.

[1012] An example apparatus includes a data processing circuit, a simulation circuit structured, an optimality determining circuit, and a design analysis circuit. The data processing circuit is structured to interpret design data for a set of trial designs. The design data includes one or more trial design criteria and defining one or more scenarios. The simulation circuit is structured to generated simulation data based at least in part on replicating each of the set of trial designs with the one or more trial design criteria and the one or more scenarios. The simulation data includes performance parameters and performance parameter values associated with each design in the set of designs for a set of criteria. The optimality determining circuit is structured to determine an optimality criteria for evaluating the set of trial designs, and search, from the set of trial designs, for globally optimum designs based on the optimality criteria. The design analysis circuit is structured to analyze the globally optimum designs and determine a modification to the optimality criteria. The optimality determining circuit is further structured to receive the modification and determine a second set of globally optimum designs.

[1013] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the set of trial designs includes all combinations of design options for a set of criteria. the optimality criteria is based on historical data and includes performance parameters of a benchmark design. The optimality criteria is based on a weighted sum of performance criteria values of each of trial designs. In certain embodiments, the modification is based on a number of globally optimum designs. In certain embodiments, the modification is in response to user feedback.

[1014] An example apparatus includes at least one memory and at least one processor that, upon executing instructions stored in the at least one memory, is structured to function as a data processing circuit, an optimality determining circuit, and a design analysis circuit. The data processing circuit is configured to obtain design data for a set of trial designs. The optimality determining circuit is configured to determine one or more optimality criteria for evaluating the trial designs, and search, from the set of trial designs, for globally optimum designs based on the one or more optimality criteria. The design analysis circuit is configured to analyze the globally optimum designs, and determine a modification to the one or more optimality criteria. The optimality determining circuit receives the modification and determines a second set of globally optimum designs based on the modified one or more optimality criteria.

[1015] An example apparatus includes at least one memory and at least one processor structured to, upon executing instructions stored in the at least one memory: obtain design data for a set of trial designs; determine one or more optimality criteria for evaluating the trial designs; search, from the set of trial designs, for globally optimum designs based on the one or more optimality criteria, to determine a first set of globally optimum designs; analyze the first set of globally optimum designs and determine a modification to the one or more optimality criteria; and search, from the set of trial designs, for globally optimum designs based on the modified one or more optimality criteria, to determine a second set of globally optimum designs.

[1016] An example method includes obtaining trial design simulation results for a set of trial designs; determining a score for each trial design based on a performance criteria; evaluating Pareto optimality for each design in the set of trial designs to determine a Pareto frontier; filtering designs that are not on the Pareto frontier; and communicating the Pareto frontier designs.

[1017] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method includes recommending designs within epsilon-distance from the Pareto frontier. In certain embodiments, the example method includes identifying separations in the Pareto frontier and performing simulated annealing based on the separations. In certain aspects, the example method includes identifying different design types on the Pareto frontier and recommending different design types. In certain aspects, the example method further includes identifying a second level Pareto frontier. In certain aspects, the example method further includes receiving feedback for recommended designs and determining epsilon values for additional recommendations. In certain aspects, the example method further includes clustering designs dominated by designs in the Pareto frontier. In certain aspects, the example method further includes clustering designs that are within a margin of error. In certain aspects, the example method further includes updating the Pareto designs in response to at least one of addition or subtraction of designs from the set of trial designs. In certain aspects, the example method further includes updating the Pareto designs in response to an update of scenario probabilities. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Obtaining the trial design simulation results is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data, generating a performance surface based at least in part on the set of trial designs; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the design simulation results.

[1018] An example apparatus includes a data processing circuit, an optimality determining circuit, and a design analysis circuit. The data processing circuit is configured to obtain design data for a set of trial designs. The optimality determining circuit is configured to determine optimum designs using Pareto analysis from the set of trial designs. The design analysis circuit is configured to analyze the Pareto designs and determine a modification to the Pareto analysis. The optimality determining circuit receives the modification and determines a second set of optimum designs.

[1019] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the set of trial designs includes all design options for a set of criteria. In certain aspects, the optimality determining circuit modifies the Pareto analysis to determine designs within epsilon-distance of Pareto designs. In certain embodiments, the optimality determining circuit modifies the Pareto analysis to determine designs dominated by the Pareto designs. In certain embodiments, the optimality determining circuit modifies the Pareto analysis to determine designs clustered by the Pareto designs. In certain embodiments, the optimality determining circuit modifies the Pareto analysis to determine twins of the Pareto designs. In certain embodiments, the optimality determining circuit modifies the Pareto analysis to determine siblings of the Pareto designs. In certain embodiments, the optimality determining circuit modifies the Pareto analysis to determine second level Pareto designs.

[1020] An example system includes an electronic device having an electronic display, and a server in electronic communication with the electronic device and having at least one processor. The at least one processor is structured to: obtain trial design simulation results for a set of trial designs; determine a score for each trial design based on a performance criteria; evaluate Pareto optimality for each design in the set of trial designs to determine a Pareto frontier; filter designs that are not on the Pareto frontier; and transmit the Pareto frontier designs to the electronic device. The electronic device displays the Pareto frontier on the electronic display.

[1021] An example method includes obtaining trial design simulation results for a set of trial designs; determining a score for each trial design based on a performance criteria; evaluating the designs in the set of trial designs to determine a convex hull for the set of trial designs; filtering designs based on the convex hull; and communicating the convex hull designs.

[1022] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes recommending designs within epsilon-distance from designs on the convex hull. In certain embodiments, the example method further includes identifying facets in the convex hull and performing simulated annealing based on the facets. In certain embodiments, the example method further includes identifying different design types on the convex hull and recommending different design types. In certain embodiments, the example method further includes identifying a second level convex hull. In certain embodiments, the example method further includes receiving feedback for recommended designs and determining epsilon values for additional recommendations. In certain embodiments, the example method further includes clustering designs dominated by designs in the convex hull. In certain embodiments, the example method further includes clustering designs that are within a margin of error. In certain embodiments, the example method further includes updating the convex hull designs in response to at least one of addition or subtraction of designs from the set of trial designs. In certain embodiments, the example method further includes updating the convex hull designs in response to an update of scenario probabilities. In certain aspects, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Obtaining the trial design simulation results is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data; generating a performance surface based at least in part on the set of trial designs; and evaluating one or more trial designs based at least in part on the performance surface. Calculating the score is further based on normalized score component values corresponding to the trial design simulation results.

[1023] An example apparatus includes a data processing circuit, an optimality determining circuit, a design analysis circuit, and a design analysis circuit. The data processing circuit is configured to obtain design data for a set of trial designs. The optimality determining circuit is configured to determine optimum designs using convex hull analysis from the set of trial designs. The design analysis circuit is configured to analyze the convex hull designs and determine a modification to the convex hull analysis. The optimality determining circuit is further structured to receive the modification and determine a second set of optimum designs.

[1024] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the set of trial designs includes all design options for a set of criteria. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine designs within epsilon-distance of convex hull designs. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine designs dominated by the convex hull designs. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine designs clustered by the convex hull designs. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine twins of the convex hull designs. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine siblings of the convex hull designs. In certain aspects, the optimality determining circuit modifies the convex hull analysis to determine second level convex hull designs.

[1025] An example system includes an electronic device including an electronic display, and a server in electronic communication with the electronic device and including at least one processor. The at least one processor is structured to: obtain trial design simulation results for a set of trial designs; determine a score for each trial design based on a performance criteria; evaluate the designs in the set of trial designs to determine a convex hull for the set of trial designs; filter designs based on the convex hull; and transmit the filtered designs to the electronic device. The electronic device is structured to display the filtered designs on the electronic display.

[1026] An example method includes receiving, via at least one processor, output data of a plurality of trial design simulations for a plurality of scenarios; evaluating, via the at least one processor, the output data to determine changes in performance over the plurality of scenarios; generating, via the at least one processor, visual tornado diagram data structured to generate a visual tornado diagram on an electronic display of an electronic device, and transmitting, via the at least one processor, the visual tornado diagram data to the electronic device.

[1027] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes determining, via the at least one processor, a span of acceptable performance values over the scenarios. In certain embodiments, the example method further includes determining, via the at least one processor, a robustness value based at least in part on the changes. In certain aspects, the robustness value is based on a probability associated with each scenario. In certain embodiments, the example method further includes determining, via the at least one processor, a risk assessment value based at least in part on the robustness value. In certain embodiments, the example method further includes categorizing, via the at least one processor, scenarios based on their probability. In certain aspects, the scenarios are categorized as at least one of optimistic, base, or pessimistic. In certain embodiments, the example method further includes determining, via the at least one processor, a robustness value based on a score value in each of the scenario categories. In certain embodiments, the example method further includes determining, via the at least one processor, scenario parameters that have the largest impact on performance parameters. In certain embodiments, the example method further includes determining, via the at least one processor, weighting criteria data for the scenario parameters; and determining, via the at least one processor, a robustness value of a trial design of the plurality based at least in part on the weighting criteria. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Receiving the output data of the plurality of trial design simulations is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the output data based at least in part on a relationship between the plurality of trial design simulations and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to the trial design simulations; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the plurality of trial design simulations.

[1028] An example apparatus includes an output processing circuit, an evaluation circuit, a graphic generation circuit, and a graphic provisioning circuit. The output processing circuit is structured to interpret output data of a plurality of trial design simulations for a plurality of scenarios. The evaluation circuit is structured to evaluate the output data to determine differences in performance over the plurality of scenarios. The graphic generation circuit is structured to generate a tornado diagram that visualizes differences. The graphic provisioning circuit is structured to transmit the tornado diagram.

[1029] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example apparatus further includes a robustness circuit structured to determine a span of acceptable performance values over the scenarios. In certain embodiments, the example apparatus further includes a robustness circuit structured to determine a robustness value based at least in part on

changes in performance.
[1030] An example non-transitory computer-readable medium stores instructions that adapt at least one processor to: receive outputs of a plurality of trial design simulations for a plurality of scenarios; evaluate the outputs to determine changes in performance over the plurality of scenarios; and provide a visual tornado diagram to visualize the changes.
[1031] One or more certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, evaluating the outputs includes generating a visualization. In certain aspects, the visualization is a tornado diagram. In certain aspects, the stored instructions further adapt the at least one processor to: determine a robustness value based at least in part on the changes. In certain aspects, the stored instructions further adapt the at least one processor to determine a risk assessment based at least in part on the robustness value. In certain aspects, the stored instructions further adapt the at least one processor to determine scenario parameters that have the largest impact on performance parameters.
[1032] An example method includes obtaining, via at least one processor of a trial design platform, initial trial design simulation results data for a set of trial designs and generated, in part, via the trial design platform; identifying, via the at least one processor, an initial design from the design simulation results data; predicting, via the at least one processor, performance data of designs for variations of parameters corresponding to the set of trial designs; identifying, via the at least one processor, a new design for simulation by varying parameters of the initial simulated design based on the predicting; simulating, via the at least one processor, the new design and determining, via the at least one processor, performance data of the new design; and identifying, via the at least one processor, a second new design for simulation by varying parameters of the new design based on the simulated performance of the new design.
[1033] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the initial design is a Pareto design. In certain aspects, the initial design is a convex hull design. In certain aspects, the predicting is based on historical data. In certain aspects, the predicting is based on Delaunay triangulations. In certain aspects, variations of different parameters are simulated in parallel. In certain embodiments, the example method further includes determining, via the at least one processor, a magnitude of variations based on historical data. In certain aspects, varying of the parameters is directed to gaps in the simulated designs. In certain aspects, varying of the parameters is based on a parameter priority rating. In certain aspects, the initial trial design simulation results data provides a coarse representation of design options. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Obtaining the initial trial design simulations results data is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the initial trial design simulations results data based at least in part on a relationship between the initial trial design simulations results data and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to the initial trial design simulations results data; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the initial trial design simulations results data.
[1034] An example apparatus includes an analysis circuit, an evaluation circuit, and a simulation circuit. The analysis circuit is structured to receive data for an initial design. The evaluation circuit is structured to vary parameters of the initial design to generate a second design. The simulation circuit is configured for simulating the second design and determining a performance of the second design. The evaluation circuit is further structured to vary parameters of the second design to

generate a third design based at least in part on the performance of the second design.

[1035] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the initial design is a Pareto design. In certain aspects, the initial design is a convex hull design. In certain aspects, the evaluation circuit is structured to predict the performance of the second design based on historical data. In certain aspects, the evaluation circuit is structured to predict the performance of the second design based on Delaunay triangulations. In certain aspects, variations of different parameters are simulated in parallel. In certain embodiments, the example apparatus further includes determining one or more magnitudes of variations of parameters based on historical data. In certain embodiments, variations of parameters are directed to gaps in the simulated designs.

[1036] An example system includes an electronic device having an electronic display, and a server in electronic communication with the electronic device and having at least one processor and a memory device. The memory device stores an application that adapts the at least one processor to: obtain initial trial design simulation results data for a set of trial designs; identify an initial design from the design simulation results data; predict performance for designs for variations of parameters; identify a new design for simulation by varying parameters of the initial simulated design based on the predicting; simulate the new design and determine the performance of the new design; identify a second new design for simulation by varying parameters of the new design based on the simulated performance of the new design; and transmit, to the electronic device, data structured for display on the electronic display and corresponding to the second new design.

[1037] An example method includes displaying an interface structured to evaluate design data by a group of users; identifying user parameters for each user in the group; configuring the interface for each user in the group based at least in part on the user parameters; receiving, via the interface, user input data from one or more users in the group; and scoring designs based on the user input and user parameters.

[1038] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, one or more users in the group are located in different locations. In certain aspects, the different locations differ by at least one of: a building; a city; a zip code; at least one of a state or province; a country; or a continent. In certain embodiments, the example method further includes receiving additional user input from the one or more users in the group view the interface; and re-scoring the designs in real-time based at least in part on the additional user input. In certain aspects, the designs include at least one of: sibling designs; or twin designs. In certain aspects scoring the designs includes weighting one or more scores based on the user parameters. In certain aspects the user parameters include at least one of: a subject matter ranking, an organizational position ranking, or a job description. In certain embodiments, the example method further includes configuring distinct instances of the interface to distinct users of the group based at least in part on the user parameters. In certain aspects, at least two of the distinct instances are different for at least two distinct users of the group. In certain aspects, the at least two of the distinct instances differ by one or more hidden elements. In certain embodiments, the example method further includes presenting, via the interface, the designs to each of the users in the group; and voting, via the interface, by each of the users in the group on the designs. In certain embodiments, the example method further includes evaluating historical design selections to identify one or more design parameters based at least in part on one or more design criteria determined from at least one of the group of users via the interface; obtaining initial design simulations results data based at least in part on a quick search data structure and the one or more design parameters; generating a substitute for at least some of the initial design simulations results data based at least in part on a relationship between the initial design simulations results data and supplemental data; generating a performance surface based at least in part on a set of designs corresponding to the initial design simulations results data; and evaluating one or more designs based at least in part on the performance surface. Scoring the designs includes calculating a score based on normalized score component values corresponding to the initial design simulations results data.

[1039] An example apparatus includes a collaborative interface circuit, a user interaction circuit, and a selection-parameter provisioning circuit. The collaborative interface circuit is structured to generate interface for evaluation of design by a group of users. The user interaction circuit is structured to interpret user inputs received by the interface; and in response to, and based at least in part on, interpreting the user inputs, define selection parameters. The selection-parameter provisioning circuit is structured to evaluate selection parameters and identify designs based on the selection parameters.

[1040] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the collaborative interface circuit is further structured to update the interface in real-time based at least in part on the received user inputs. In certain aspects, the collaborative interface circuit is further structured to configure distinct instances of the interface to distinct users of the group based at least in part on user parameters corresponding to the distinct users. In certain aspects, at least two of the distinct instances are different for at least two distinct users of the group. In certain aspects, the at least two of the distinct instances differ by one or more hidden elements.

[1041] An example method includes displaying, via at least one processor, an interface structured to evaluate designs by a group of users; receiving, via the at least one processor and the interface, from one or more users of the group, evaluation input related to designs; identifying, via the at least one processor, alternative designs based on the evaluation input; identifying, via the at least one processor, parameters of the designs and alternative designs that correspond to one or more tradeoffs between the designs; receiving, at the at least one processor, evaluation input related to the parameters; generating, via the at least one processor, a hierarchy of parameters based on the evaluation input; scoring, via the at least one processor, designs based on the hierarchy of parameters; and presenting, via the at least one processor, on the interface, designs based on the scores.

[1042] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes receiving, at the at least one processor, via the interface, votes from each of the users in the group on the designs. In certain embodiments, the example method further includes adjusting distinct instances of the interface corresponding to distinct user of the group. The adjusting is based at least in part on hiding one or more elements of the interface.

[1043] An example method includes: providing inputs to a plurality of trial design simulation engines; receiving first outputs of the plurality of trial design simulation engines in response to the inputs; providing variations of the inputs to the plurality of trial design simulation engines; receiving second outputs of the plurality of trial design simulation engines in response to the variations; evaluating the first and the second outputs to determine delta values; and determining, based in part on the delta values, a plurality of normalization factors for the plurality of trial design simulation engines.

[1044] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, a first trial design simulation engine of the plurality is structured to simulate a first trial design that is of a different type than a second trial design which a second trial design simulation engine of the plurality is structured to simulate. In certain aspects, a first trial design simulation engine of the plurality is a different version of a second trial design simulation engine of the plurality. In certain aspects, a first trial design simulation engine of the plurality was generated by a first entity and a second trial design simulation engine of the plurality was generated by a second entity of the plurality distinct from the first entity. In certain aspects, the first and the second outputs include metadata. In certain embodiments, the example method further includes multiplying at least one of the first or the second outputs by at least one of the plurality of normalization factors. In certain aspects, each of the plurality of normalization factors differ in value based at least in part on differing performance criteria defined, in part, by the inputs. In certain embodiments, the example method further includes determining, for each of the trial design simulation engines, an output variability; and displaying the variabilities to a user. In certain embodiments, the example method further includes determining a valid range of output values based on the delta values; and determining that at least one of the plurality of trial design simulation engines outputs invalid values. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Receiving the first outputs is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the first outputs based at least in part on a relationship between the first outputs and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to first outputs; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the first outputs.

[1045] An example method includes providing inputs to a plurality of trial design simulation engines; receiving outputs of the plurality of trial design simulation engines in response to the inputs; comparing outputs to expected outputs; and determining, based on the comparing, a plurality of normalization factors for the plurality of trial design simulation engines.

[1046] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, a first trial design simulation engine of the plurality is structured to simulate a first trial design that is of a different type than a second trial design which a second trial design simulation engine of the plurality is structured to simulate. In certain aspects, a first trial design simulation engine of the plurality is a different version of a second trial design simulation engine of the plurality. In certain aspects, a first trial design simulation engine of the plurality was generated by a first entity and a second trial design simulation engine of the plurality was generated by a second entity of the plurality distinct from the first entity. In certain aspects, each of the plurality of normalization factors differ in value based at least in part on differing performance criteria defined, in part, by the inputs.

[1047] An example apparatus includes an output processing circuit, a comparison circuit, a normalization circuit, and a normalization provisioning circuit. The output processing circuit is structured to interpret output data from a plurality of trial design simulation engines. The comparison circuit is structured to compare the interpreted output data to expected output data. The normalization circuit is structured to determine a plurality of normalization factors for the plurality of trial design simulation engines. The normalization provisioning circuit structured to transmit the plurality of normalization factors.

[1048] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, a first trial design simulation engine of the plurality is structured to simulate a first trial design that is of a different type than a second trial design which a second trial design simulation engine of the plurality is structured to simulate. In certain aspects, a first trial design simulation engine of the plurality is a different version of a second trial design simulation engine of the plurality. In certain aspects, a first trial design simulation engine of the plurality was generated by a first entity and a second trial design simulation engine of the plurality was generated by a second entity of the plurality distinct from the first entity. In certain aspects, each of the plurality of normalization factors differ in value based at least in part on differing performance criteria.

[1049] An example method includes obtaining a criteria for a trial design study; determining permutations for designs in response to the criteria; determining permutations for scenarios in response to the criteria; generating combinations of the permutations for the designs and the permutations for the scenarios; simulating designs corresponding to the generated combinations; and determining performance of the simulated designs.

[1050] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes estimating a number of the combinations using the criteria. In certain embodiments, the example method further includes in response to the estimated number being greater than a threshold, suggesting modifications to the criteria. In certain embodiments, the example method further includes in response to the estimated number being less than a threshold, suggesting modifications to the criteria. In certain embodiments, the example method further includes examining the combinations for invalid combinations. In certain embodiments, the example method further includes examining the permutations for invalid permutations. In certain embodiments, the example method further includes predicting the performance of the combinations; and removing a subset of the combinations, prior to simulating the designs, based on the predicted performance. In certain aspects, the predicting is based on historical data. In certain aspects, the combinations are exhaustive for the criteria. In certain embodiments, the example method further includes determining optimality from the performance of the simulated designs.

[1051] An example apparatus includes a space definition circuit, a design parameter circuit, a scenario parameter circuit, a combinations circuit, and a simulation circuit. The space definition circuit is structured to interpret criteria data for a trial design. The design parameter circuit is structured to determine permutations for designs in response to the criteria data. The scenario parameter circuit is structured to determine permutations for scenarios in response to the criteria data. The combinations circuit is structured to generate combinations of permutations for designs and permutations for scenarios. The simulation circuit is structured to evaluate a performance of each combination.

[1052] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example apparatus further includes an estimator circuit configured to estimate number of combinations using the criteria. In certain embodiments, the example apparatus further includes a validity checker circuit configured to examine the combinations for invalid combinations. In certain embodiments, the example apparatus further includes a validity checker circuit configured to examine the permutations for invalid permutations. In certain embodiments, the example apparatus further includes a validity checker circuit configured to: predict the performance of the combinations; and remove a subset of the combinations prior to simulating based on the predicted performance. In certain aspects, the performance is predicted based on historical data. In certain aspects, the combinations of permutations are exhaustive for the criteria. In certain embodiments, the example apparatus further includes an analysis circuit configured to determine optimality from the performance.

[1053] An example method includes configuring an execution flow for a trial design evaluation using a configurable interface having at least one node element and at least one arc element. The execution flow is defined, in part, via the at least one node element and the at least one arc element. The example method further includes: executing the trial design evaluation using the execution flow; reconfiguring at least one of the at least one node element or the at least one arc element in the execution flow; and executing the trial design evaluation using the reconfigured execution flow.

[1054] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Executing the trial design evaluation is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some results from the execution of the trial design evaluation based at least in part on a relationship between the results and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to the results; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the results from the execution of the trial design evaluation.

[1055] An example method includes obtaining trial design simulation results for a set of trial designs; determining a set of Pareto designs in the set of trial designs based at least in part on the trial design simulation results and one or more performance parameters; determining a set of convex hull designs in the set of trial designs; determining a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs; and transmitting the set of recommended designs.

[1056] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes filtering one or more of the set of trial designs that are dominated by at least one of the set of convex hull designs. In certain embodiments, the example method further includes filtering one or more of the set of trial designs that are dominated by at least one of the set of Pareto designs. In certain aspects, determining the set of recommended designs includes determining at least one of the set of recommended designs within an epsilon-distance from at least one of the set of Pareto designs. In certain aspects, determining the set of recommended designs includes determining at least one of the set of recommended designs within an epsilon-distance from at least one of the set of convex hull designs. In certain aspects, determining a set of recommended designs includes performing simulated annealing on one or more of the set of trial designs. In certain aspects, simulated annealing is based at least in part on facets of the set of convex hull designs. In certain embodiments, the example method further includes identifying different design types in the set of Pareto designs. In certain aspects, the set of Pareto designs is determined prior to the set of convex hull designs; the set of convex hull designs is derived from the set of Pareto designs such that each of the set of convex hull designs is in the set of Pareto designs; and at least one of the set of recommended designs is in the set of convex hull designs. In certain aspects, the set of convex hull designs is determined prior to the set of Pareto designs; the set of Pareto designs is derived from the set of convex hull designs such that each of the set of Pareto designs is in the set of convex hull designs; and at least one of the set of recommended designs is in the set of convex hull designs. In certain embodiments, the example method further includes identifying a number of trial designs in the set of Pareto designs. Determining the set of convex hull designs occurs when the number is greater-than-or-equal-to a threshold, and the set of convex hull designs is derived from the set of Pareto designs. In certain embodiments, the example method further includes identifying a number of trial designs in the set of Pareto designs; and, if the number is less-than-or-equal-to a threshold, identifying, for inclusion in the set of recommended designs, one or more of the set of trial designs within an epsilon distance of at least one of the set of Pareto designs. In certain embodiments, the example method further includes for each of the set of Pareto designs, determining a design type; determining a first trial design of the set of Pareto designs is of a different design type from and within an epsilon-distance to a second trial design of the set of Pareto designs; and including the first trial design and the second trial design in the set of recommended designs. In certain embodiments, the example method further includes: evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface. Obtaining trial design simulation results is based at least in part on a quick search data structure and the one or more trial design parameters. The example method further includes generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to the trial design simulation results; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the trial design simulation results.

[1057] An example apparatus includes a results processing circuit, a Pareto evaluation circuit, a convex hull evaluation circuit, a recommendation circuit, and a recommendation provisioning circuit. The results processing circuit is structured to interpret trial design simulation results for a set of trial designs. The Pareto evaluation circuit is structured to determine a set of Pareto designs in the set of trial designs based at least in part on the trial design simulation results and one or more performance parameters. The convex hull evaluation circuit is structured to determine a set of convex hull designs in the set of trial designs. The recommendation circuit is structured to determine a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs. The recommendation provisioning circuit is structured to transmit the set of recommended designs.

[1058] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example apparatus further includes a filtering circuit structured to filter one or more of the set of trial designs that are dominated by at least one of the set of convex hull designs. In certain embodiments, the example apparatus further includes a filtering circuit structured to filter one or more of the set of trial designs that are dominated by at least one of the set of Pareto designs. In certain aspects the recommendation circuit is further structured to determine at least one of the set of recommended designs within an epsilon-distance from at least one of the set of Pareto designs.

[1059] An example non-transitory computer-readable medium stores instructions that adapt at least one processor to: interpret trial design simulation results for a set of trial designs; determine a set of Pareto designs in the set of trial designs based at least in part on the trial design simulation results and one or more performance parameters; determine a set of convex hull designs in the set of trial designs; determine a set of recommended designs based at least in part on the set of Pareto designs and the set of convex hull designs; and transmit the set of recommended designs.

[1060] One or more certain further aspects of the example non-transitory computer-readable medium are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the stored instructions further adapt the at least one processor to filter one or more of the set of trial designs that are dominated by at least one of the set of convex hull designs.

[1061] An example method includes: obtaining, via at least one processor of a trial design platform server, trial design simulation results data for a set of trial designs; determining, via a recommendation engine of the trial design platform executing on the at least one processor, a set of recommended designs in the set of trial designs based at least in part on the trial design simulation results data and one or more performance parameters; and transmitting, via the at least one processor, the set of recommended designs.

[1062] An example method includes determining, via at least one processor, a plurality of possible sites for recruiting patients from for a trial; determining, via the at least one processor and for each of one or more subgroupings of the plurality of possible sites, a predicted patient recruitment value; determining, via the at least one processor, a candidate subgrouping of the plurality of possible sites having a predicted patient recruitment value that globally optimizes a desired site selection criteria; and transmitting, via the at least one processor, data corresponding to the candidate subgrouping.

[1063] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, determining the predicted patient recruitment value for each of the subgroupings of the plurality of possible sites includes simulating, via the at least one processor, each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain aspects, the difference between the types of engines is based at least in part on a version number. In certain embodiments, the example method further includes determining one or more site selection parameters, wherein simulating each of the one or more subgroupings is based at least in part on the one or more site selection parameters. In certain aspects, the one or more site selection parameters are based at least in part on at least one of: a country; a state/province; a county; a city; a zip code; or a patient enrollment matriculation number. In certain embodiments, the example method further includes determining, via the at least one processor, the desired site selection criteria, wherein simulating each of the one or more subgroupings is based at least in part on the determined site selection criteria. In certain aspects, the determined site selection criteria is based at least in part on at least one of: a number of required patients; a start date of the trial; an end date of the trial; or a total cost of the trial. In certain aspects, determining the candidate subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria comprises use of one or more of: a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. In certain aspects, determining the candidate subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes the desired site selection criteria is based at least in part on a machine learning engine. In certain embodiments, the example method further includes evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface, obtaining trial design simulation results based at least in part on a quick search data structure and the one or more trial design parameters; generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to trial design simulation results; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the trial design simulation results.

[1064] An example apparatus includes a site selection data processing circuit, a patient recruitment determination circuit, a site searching circuit, and a site selection provisioning circuit. The site selection data processing circuit is structured to interpret possible site selection data identifying a plurality of possible sites for recruiting patients from for a trial. The patient recruitment determination circuit is structured to determine a predicted patient recruitment value for each of one or more subgroupings of the plurality of possible sites. The site searching circuit is structured to determine which subgrouping of the plurality of possible sites has a predicted patient recruitment value that globally optimizes a desired site selection criteria. The site selection provisioning circuit is structured to transmit the subgrouping of the plurality of possible sites that has the predicted patient recruitment value that globally optimizes the desired site selection criteria.

[1065] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the patient recruitment determination circuit is further structured to determine the predicted patient recruitment value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain embodiments, the example apparatus further includes a user input circuit structured to interpret user input data; and a criteria determining circuit structured to determine the desired site selection criteria based at least in part on the user input data. In certain aspects, the site searching circuit comprises at least one of: a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine.

[1066] An example system includes a database, a server, and an electronic display. The database stores site selection data identifying a plurality of possible sites for recruiting patients from for a trial. The server is structured to: access the site selection data stored in the database; determine a patient recruitment value for each of one or more subgroupings of the plurality of possible sites; and determine which subgrouping of the plurality of possible sites has a patient recruitment value that globally optimizes a desired site selection criteria. The electronic display is structured to depict the determined subgrouping.

[1067] One or more certain further aspects of the example system are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the server is further structured to: determine the patient recruitment value for each of one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain aspects, the server is further structured to: determine the desired site selection criteria, wherein simulating each of the one or more subgroupings is based at least in part on the determined site selection criteria.

[1068] An example method includes determining, via at least one processor, a plurality of possible sites for recruiting patients from for a trial; determining, via the at least one processor and for each of one or more subgroupings of the plurality of possible sites, a predicted available resources value; and determining, via the at least one processor, which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria.

[1069] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, determining the predicted available resources value for each of the subgroupings of the plurality of possible sites includes simulating, via the at least one processor, each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain aspects, the difference between the types of engines is based at least in part on a version number. In certain embodiments, the example method includes determining, via the at least one processor, one or more site resource parameters, wherein simulating each of the one or more subgroupings is based at least in part on the one or more site resource parameters. In certain aspects, the one or more site resource parameters are based at least in part on at least one of: a supply of a drug; administrative personnel; or equipment. In certain embodiments, the example method further includes determining, via the at least one processor, the desired site resource criteria, wherein simulating each of the one or more subgroupings is based at least in part on the determined site resource criteria. In certain embodiments, the determined site resource criteria is based at least in part on at least one of: a supply of a drug; administrative personnel; or equipment. In certain embodiments, determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria includes use of one or more of: a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine. In certain embodiments, determining which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes the desired site resource criteria is based at least in part on a machine learning engine. In certain embodiments, the example method further includes: evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface, obtaining trial design simulation results based at least in part on a quick search data structure and the one or more trial design parameters; generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to trial design simulation results; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the trial design simulation results.

[1070] An example apparatus includes a site selection data processing circuit, an available resources determination circuit, a site searching circuit, and a site selection provisioning circuit.

The site selection data processing circuit is structured to interpret possible site selection data identifying a plurality of possible sites for recruiting patients from for a trial. The available resources determination circuit is structured to determine a predicted available resources value for each of one or more subgroupings of the plurality of possible sites. The site searching circuit is structured to determine which subgrouping of the plurality of possible sites has a predicted available resources value that globally optimizes a desired site resource criteria. The site selection provisioning circuit is structured to transmit the subgrouping of the plurality of possible sites that has the predicted available resources value that globally optimizes the desired site resource criteria.
[1071] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the available resources determination circuit is further structured to determine the predicted available resources value for each of the one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain embodiments, the example apparatus further includes a user input circuit structured to interpret user input data; and a criteria determining circuit structured to determine the desired site resource criteria based at least in part on the user input data. In certain embodiments, the site searching circuit includes at least one of: a convex hull engine; a Pareto engine; a Monte Carlo engine; or a simulated annealing engine.
[1072] An example system includes a database storing site resource data identifying a plurality of possible sites for recruiting patients from for a trial; a server structured, and an electronic display. The server is structured to: access the site resource data stored in the database; determine an available resources value for each of one or more subgroupings of the plurality of possible sites; and determine which subgrouping of the plurality of possible sites has an available resources value that globally optimizes a desired site resource criteria. The electronic display is structured to depict the determined subgrouping.
[1073] One or more certain further aspects of the example system are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the server is further structured to: determine the available resources value for each of one or more subgroupings of the plurality of possible sites by simulating each of the subgroupings. In certain aspects, simulating each of the one or more subgroupings is based at least in part on use of different types of engines. In certain aspects, the server is further structured to: determine the desired site resource criteria, wherein simulating each of the one or more subgroupings is based at least in part on the determined site resource criteria.
[1074] An example method includes: presenting on a graphical interface, via at least one processor, a set of cards wherein each card in the set is representative of a different trial design from a set of trial designs; monitoring, via the at least one processor, a first set of user interactions with the set of cards; determining, via the at least one processor, a user preference for one or more values of one or more parameters of the set of trial designs from the first set of user interactions; presenting on the graphical interface, via the at least one processor, a new card that is representative of a trial design consistent with the determined user preference; monitoring, via the at least one processor, a second set of user interactions with the new card; and refining, via the at least one processor, the determined user preference based at least in part on the second set of user interactions with the new card.
[1075] One or more certain further aspects of the example method are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example method further includes emphasizing, via the at least one processor, values shown on each card based on a relative value compared to other displayed cards. In certain aspects, the interactions include at least one of moving a card, saving a card, or deleting a card. In certain aspects, the new card is added to the set of cards. In certain aspects, the new card replaces a card from the set of cards. In certain aspects, the set of cards is representative of Pareto designs. In certain aspects, each

card represents a different trial type. In certain aspects, the set of cards is representative of convex hull designs. In certain embodiments, the example method further includes: saving, via the at least one processor, at least some of the first and the second sets of user interactions; and training, via the at least one processor, an artificial intelligence model to identify preferences based on interactions. In certain embodiments, the example method further includes determining the user preference for the one or more values of the one or more parameters of the set of trial designs via an artificial intelligence model trained on historical interactions. In certain embodiments, the example method further includes: evaluating historical trial design selections to identify the one or more parameters of the set of trial designs based at least in part on the first set of user interactions; obtaining trial design simulation results based at least in part on a quick search data structure and the one or more parameters; generating a substitute for at least some of the trial design simulation results based at least in part on a relationship between the trial design simulation results and supplemental data; generating a performance surface based at least in part on a set of trial designs corresponding to the trial design simulation results; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the trial design simulation results.

[1076] An example apparatus includes a simulation results data processing circuit, a recommendation circuit, a card suggestion circuit, and an interaction analysis circuit. The simulation results data processing circuit is structured to interpret trial design simulation results data for a set of trial designs. The recommendation circuit is structured to determine a first subset of trial designs. The card suggestion circuit is structured to display the first subset of trial designs with a card interface. The interaction analysis circuit is structured to interpret user interactions with the card interface. The card suggestion circuit is further structured to display a second subset of trial designs with the card interface based on the user interactions.

[1077] One or more certain further aspects of the example apparatus are described following, any one or more of which may be incorporated in certain embodiments. In certain embodiments, the example apparatus further includes a graphic enhancement circuit structured to emphasize values shown on each card based on a relative value compared to other displayed cards. In certain aspects, the user interactions include at least one of moving a card, saving a card, or deleting a card. In certain aspects, the second subset of trial designs includes at least one design from the first subset of trial designs. In certain aspects, the first subset of trial designs is a set of Pareto designs. In certain aspects, the first subset of trial designs is a set of convex hull designs. In certain aspects, each design in the first subset of designs is a different trial type.

[1078] An example system includes an electronic device having an electronic display, and a server in electronic communication with the electronic device and including at least one processor. The at least one processor is structured to: present, on the electronic display, a graphical interface having a set of cards, wherein each card in the set is representative of a different trial design from a set of trial designs; monitor, a first set of user interactions with the set of cards; determine, a user preference for one or more values of one or more parameters of the set of trial designs from the first set of user interactions; present, in the graphical interface, a new card that is representative of a trial design consistent with the determined user preference; monitor a second set of user interactions with the new card; and refine the determined user preference based at least in part on the second set of user interactions with the new card.

[1079] One or more certain further aspects of the example system are described following, any one or more of which may be incorporated in certain embodiments. In certain aspects, the at least one processor refines that determined user preference by storing at least some of the first or the second set of user interactions and determines at least one additional user preference based at least in part on the stored user interactions.

[1080] Another example method includes: monitoring progress of a design study specification; comparing monitored progress to historical progress data; predicting time to execution of design study simulations; and in response to the time to execution being less than a threshold, requesting computational resources for simulations.

[1081] Another example method includes: monitoring progress of a design study specification; determining, based on the specification, resource requirements for computation; determining a batch time allocation based on the requirement for computation; and allocating resources based on the determined batch time.

[1082] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. Predicting is based on amount of data entered. Predicting is based on location in the interface. Predicting is based on user calendar schedules. Further including predicting an amount of computational resources based on historical data.

[1083] Another example method includes: identifying components of a score from simulation data; determining a normalization function for each component; and calculating a score based on a function of the components.

[1084] Another example method includes: identifying a first set of components from first simulation data; determining a first normalization function for each component of the first set of components; associating the first normalization function with each component of the first set of components; identifying a second set of components from second simulation data; determining a second normalization function for each component of the second set of components; associating the second normalization function with each component of the second set of components; determining a new normalization function based on the first normalization function and the second normalization function; and applying the new normalization function to the first set of components and the second set of components.

[1085] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. The normalization function is based on the minimum and maximum value of the component. The normalization function is based on substitution of values. The score is a proxy for Net Present Value. The components of the first set of components are the same as the components of the second set of components. Further including ranking designs based on the score. Further including determining a second score based on a different function of the components. Further including ranking designs based on a combination of the first score and the second score. Further including ranking designs based on a priority of the first score and the second score

[1086] Another example method includes: displaying a graphical user interface structured to evaluate designs by a group of users; identifying expertise parameters for each user in the group of users; configuring the graphical user interface for each user based at least in part on the expertise parameters; receiving user input from users via the graphical user interface; and scoring designs based on the user input and expertise parameters.

[1087] Another example apparatus includes: a display generation circuit structured to generate a graphical user interface for evaluation of design by a group of users; a user interaction circuit structured to: interpret user inputs received by the graphical user interface, and in response to, and based at least in part on, interpreting the user inputs, defining selection parameters; and a selection-parameter provisioning circuit structured to evaluate selection parameters and identify designs based on the parameters.

[1088] Another example method includes displaying a graphical user interface structured to evaluate designs by a group of users; receiving, from one or more users of the group of users, evaluation input related to designs; identifying alternative designs based on the evaluation input; identifying parameters of the designs and alternative designs that are indicative of tradeoffs between the designs; receiving evaluation input related to the parameters; generating a hierarchy of parameters based on the evaluation input; scoring designs based on the hierarchy of parameters; and presenting designs with the highest scores.

[1089] One or more certain further aspects of the example methods and apparatus are described following, any one or more of which may be incorporated in certain embodiments. Users are in different physical locations. The interface is updated in real time. The identified designs include sibling or twin designs. Scoring of designs includes a weighted score based on the expertise parameters. Further including presenting designs and voting on the designs. Instances of the interface are different for each user. The interface instance for at least one user hides elements of the interface.
[1090] Another example method includes: interpreting replication results for a replication of a clinical trial design, the replication forming part of a replication process of a clinical trial design simulation; determining a performance criteria based at least in part on the replication results; determining, based at least in part on the performance criteria, an adjustment to the replication process; and, in response to determining the adjustment, adjusting the replication process.
[1091] Another example system includes a server structured to: execute a replication process forming part of a clinical trial design simulation, the replication process including a plurality of replications of a clinical trial design; determine a performance criteria for at least one of the plurality of replications; and adjust, based at least in part on the performance criteria, the replication process; and an electronic device structured to: display an interactive interface that presents a plurality of prompts to a user for configuring the clinical trial design simulation.
[1092] Another example apparatus includes: a replication circuit structured to execute a replication process including a plurality of replications of a clinical trial design, wherein each replication of the plurality generates corresponding replication results; a results interpretation circuit structured to interpret the replication results of at least one of the plurality of replications; a performance circuit structured to determine a performance criteria based at least in part on the replication results; an adjustment determining circuit structured to determine, based at least in part on the performance criteria, an adjustment value to the replication process; and an adjustment circuit structured to adjust the replication process based at least in part on the adjustment value.
[1093] One or more certain further aspects of the example system, method and apparatus are described following, any one or more of which may be incorporated in certain embodiments. The performance criteria includes a standard error and the adjustment is ceasing the replication process when the standard error is below a threshold. The performance criteria includes an upper confidence interval of the clinical trial design and the adjustment is ceasing the replication process when a difference from a lower confidence interval of another clinical trial design is higher than the upper confidence interval. The lower confidence level and the upper confidence interval are each 99%. The replication process includes batches for execution in parallel processing. The replication results are from a SimCube. The clinical trial simulation is based at least in part on simulated annealing.
[1094] Another example method includes determining a first subset of designs from a set of designs that are on a convex hull of the set of designs; removing the first subset of designs from the set of designs to generate a second set of designs; determining a second subset of designs from the second set of designs that are on a convex hull of the second set of designs; and recommending the first subset of designs and the second subset of designs.
[1095] Another example method includes: determining designs on a first convex hull; peeling the first hull; determining designs on a second convex hull; generating a hierarchical data structure of the designs on the first convex hull and the second convex hull; and recommending designs based on the hierarchical data structure.
[1096] Another example method includes: determining a first subset of designs from a set of designs that are on a convex hull of the set of designs for a first scenario; simulating the first subset of designs for a second scenario; removing the first subset of designs from the set of designs to generate a second set of designs; determining a second subset of designs from the second set of designs that are on a convex hull of the second set of designs for the first scenario; simulating the

second subset of designs for the second scenario; and determining a convex hull for the first subset and the second subset of designs for the second scenario.

[1097] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. Removing the first subset of designs includes further removing designs within an epsilon-distance of the first subset of designs. Further including determining a third subset of designs. Further including iterating the simulations and determining a convex hull for the second scenario until no change to the convex hull for the second scenario is observed. Further including analyzing the hierarchy of designs to identify designs within a distance of a design.

[1098] Another example method includes: interpreting initial simulation results for a set of clinical trial designs; identifying, based at least in part on the initial simulation results, a clinical trial design for simulation; predicting, via machine learning and based at least in part on the initial simulation results, simulation results for the clinical trial design; and transmitting the simulation results.

[1099] Another example method includes: interpreting initial simulation results for a set of clinical trial designs; identifying an initial clinical trial design based at least in part on the initial simulation results; predicting performance for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting; predicting, via machine learning, first simulation results for the first new clinical trial design; and based at least in part on the first simulation results, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1100] Another example method includes: interpreting initial simulation results for a set of clinical trial designs; interpreting convex hull tunnel data corresponding to a convex hull tunnel defined, in part, by the set of clinal trial designs; identifying an initial clinical trial design based at least in part on the convex hull tunnel data; predicting performance for clinical trial designs based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting and on the convex hull tunnel data; determining first simulation results for the first new clinical trial design; and based at least in part on the first simulation results, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1101] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. The machine learning is based at least in part on a neural network. The machine learning is based at least in part on a regression model. The regression model is a regression tree. The first simulation results are based on an interpolation of one or more clinical trial designs. The one or more clinical designs are neighbors to the first new clinical trial design. Further including combining use of convex hull tunnel with artificial intelligence and vice-versa. A selection of a design for simulation is based on a penalty function related to the convex hull tunnel. The penalty function scores clinical trial designs. The penalty function discourages selection of designs that are farther away from a center line of the convex hull tunnel. The neural network is trained via reinforcement learning.

[1102] Another example method includes: allocating memory, in a memory device, that defines a quick search data structure having a plurality of storage cells; simulating a plurality of clinical trial designs to obtain a plurality of simulation results, each of the plurality of simulation results corresponding to one of the plurality of clinical trial designs; and storing each of the plurality of simulation results in a corresponding one of the plurality of storage cells based on one or more relationships between two or more of the plurality of clinical trial designs.

[1103] Another example method includes: obtaining initial simulation results for a set of clinical trial designs; identifying an initial clinical trial design based at least in part on the initial simulation results; predicting performance for clinical trial designs related to the initial clinical trial design based at least in part on varying parameters for the initial clinical trial design; identifying a first new clinical trial design for simulation based on the predicting; determining if a quick search data structure contains first simulation results for the first new clinical trial design; if the quick search data structure does not contain the first simulation results, then simulating the first new clinical trial design to obtain the first simulation results; and based at least in part on the first simulation results, identifying a second new clinical trial design for simulation by varying parameters of the first new clinical trial design.

[1104] Another example method includes: interpreting, via at least one processor, simulation results of a set of clinical trial designs; populating, via the at least one processor, a quick search data structure, defined within a memory device, with the simulation results of clinical trial designs; identifying, via the at least one processor, a region of interest within the quick search data structure; identifying, via at least one processor, a clinical trial design based at least in part on the region of interest; comparing, via at least one processor, the identified clinical trial design to another clinical trial design of the set of clinical trial designs; and transmitting, via the at least one processor and based at least in part on the comparing, data corresponding to the identified clinical trial design.

[1105] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. The one or more relationships between the two or more of the plurality of clinical trial designs is based at least in part on the value of parameters for each of the two or more of the plurality of clinical trial designs. The quick search data structure is a SimCube. The SimCube has dimensions based at least in part on a number of design parameters and a number of scenarios variables. The dimensions of the SimCube are based at least in part on the sum of the number of design parameters and the number of scenario variables. The region of interest is a gap. The region of interest corresponds to one or more similar designs. In certain embodiments, a similar design is a design having a score within epsilon of a desired score. The region of interest is based at least in part on a Manhattan distance.

[1106] Another example method includes: monitoring progress of a design study specification; comparing monitored progress to historical progress data; predicting time to execution of design study simulations; and in response to the time to execution being less than a threshold, requesting computational resources for simulations.

[1107] Another example method includes: monitoring progress of a design study specification; determining, based on the specification, resource requirements for computation; determining a batch time allocation based on the requirement for computation; and allocating resources based on the determined batch time.

[1108] One or more certain further aspects of the example methods are described following, any one or more of which may be incorporated in certain embodiments. Predicting is based on amount of data entered. Predicting is based on location in the interface. Predicting is based on user calendar schedules. Further including predicting an amount of computational resources based on historical data.

[1109] The methods and systems described herein may be deployed in part or in whole through a machine having a computer, computing device, processor, circuit, and/or server that executes computer readable instructions, program codes, instructions, and/or includes hardware configured to functionally execute one or more operations of the methods and systems herein. The terms computer, computing device, processor, circuit, and/or server, ("computing device") as utilized herein, should be understood broadly.

[1110] An example computing device includes a computer of any type, capable to access instructions stored in communication thereto such as upon a non-transient computer readable medium, whereupon the computer performs operations of the computing device upon executing the instructions. In certain embodiments, such instructions themselves comprise a computing device. Additionally or alternatively, a computing device may be a separate hardware device, one or more computing resources distributed across hardware devices, and/or may include such aspects as logical circuits, embedded circuits, sensors, actuators, input and/or output devices, network and/or communication resources, memory resources of any type, processing resources of any type, and/or hardware devices configured to be responsive to determined conditions to functionally execute one or more operations of systems and methods herein.

[1111] Network and/or communication resources include, without limitation, local area network, wide area network, wireless, internet, or any other known communication resources and protocols. Example and non-limiting hardware and/or computing devices include, without limitation, a general purpose computer, a server, an embedded computer, a mobile device, a virtual machine, and/or an emulated computing device. A computing device may be a distributed resource included as an aspect of several devices, included as an interoperable set of resources to perform described functions of the computing device, such that the distributed resources function together to perform the operations of the computing device. In certain embodiments, each computing device may be on separate hardware, and/or one or more hardware devices may include aspects of more than one computing device, for example as separately executable instructions stored on the device, and/or as logically partitioned aspects of a set of executable instructions, with some aspects comprising a part of one of a first computing device, and some aspects comprising a part of another of the computing devices.

[1112] A computing device may be part of a server, client, network infrastructure, mobile computing platform, stationary computing platform, or other computing platform. A processor may be any kind of computational or processing device capable of executing program instructions, codes, binary instructions and the like. The processor may be or include a signal processor, digital processor, embedded processor, microprocessor or any variant such as a co-processor (math co-processor, graphic co-processor, communication co-processor and the like) and the like that may directly or indirectly facilitate execution of program code or program instructions stored thereon. In addition, the processor may enable execution of multiple programs, threads, and codes. The threads may be executed simultaneously to enhance the performance of the processor and to facilitate simultaneous operations of the application. By way of implementation, methods, program codes, program instructions and the like described herein may be implemented in one or more threads. The thread may spawn other threads that may have assigned priorities associated with them; the processor may execute these threads based on priority or any other order based on instructions provided in the program code. The processor may include memory that stores methods, codes, instructions and programs as described herein and elsewhere. The processor may access a storage medium through an interface that may store methods, codes, and instructions as described herein and elsewhere. The storage medium associated with the processor for storing methods, programs, codes, program instructions or other type of instructions capable of being executed by the computing or processing device may include but may not be limited to one or more of a CD-ROM, DVD, memory, hard disk, flash drive, RAM, ROM, cache and the like.

[1113] A processor may include one or more cores that may enhance speed and performance of a multiprocessor. In embodiments, the process may be a dual core processor, quad core processors, other chip-level multiprocessor and the like that combine two or more independent cores (called a die).

[1114] The methods and systems described herein may be deployed in part or in whole through a machine that executes computer readable instructions on a server, client, firewall, gateway, hub, router, or other such computer and/or networking hardware. The computer readable instructions may be associated with a server that may include a file server, print server, domain server, internet server, intranet server and other variants such as secondary server, host server, distributed server and the like. The server may include one or more of memories, processors, computer readable transitory and/or non-transitory media, storage media, ports (physical and virtual), communication devices, and interfaces capable of accessing other servers, clients, machines, and devices through a wired or a wireless medium, and the like. The methods, programs, or codes as described herein and elsewhere may be executed by the server. In addition, other devices required for execution of methods as described in this application may be considered as a part of the infrastructure associated with the server.

[1115] The server may provide an interface to other devices including, without limitation, clients, other servers, printers, database servers, print servers, file servers, communication servers, distributed servers, and the like. Additionally, this coupling and/or connection may facilitate remote execution of instructions across the network. The networking of some or all of these devices may facilitate parallel processing of program code, instructions, and/or programs at one or more locations without deviating from the scope of the disclosure. In addition, all the devices attached to the server through an interface may include at least one storage medium capable of storing methods, program code, instructions, and/or programs. A central repository may provide program instructions to be executed on different devices. In this implementation, the remote repository may act as a storage medium for methods, program code, instructions, and/or programs.

[1116] The methods, program code, instructions, and/or programs may be associated with a client that may include a file client, print client, domain client, internet client, intranet client and other variants such as secondary client, host client, distributed client and the like. The client may include one or more of memories, processors, computer readable transitory and/or non-transitory media, storage media, ports (physical and virtual), communication devices, and interfaces capable of accessing other clients, servers, machines, and devices through a wired or a wireless medium, and the like. The methods, program code, instructions, and/or programs as described herein and elsewhere may be executed by the client. In addition, other devices required for execution of methods as described in this application may be considered as a part of the infrastructure associated with the client.

[1117] The client may provide an interface to other devices including, without limitation, servers, other clients, printers, database servers, print servers, file servers, communication servers, distributed servers, and the like. Additionally, this coupling and/or connection may facilitate remote execution of methods, program code, instructions, and/or programs across the network. The networking of some or all of these devices may facilitate parallel processing of methods, program code, instructions, and/or programs at one or more locations without deviating from the scope of the disclosure. In addition, all the devices attached to the client through an interface may include at least one storage medium capable of storing methods, program code, instructions, and/or programs. A central repository may provide program instructions to be executed on different devices. In this implementation, the remote repository may act as a storage medium for methods, program code, instructions, and/or programs.

[1118] The methods and systems described herein may be deployed in part or in whole through network infrastructures. The network infrastructure may include elements such as computing devices, servers, routers, hubs, firewalls, clients, personal computers, communication devices, routing devices and other active and passive devices, modules, and/or components as known in the art. The computing and/or non-computing device(s) associated with the network infrastructure may include, apart from other components, a storage medium such as flash memory, buffer, stack, RAM, ROM and the like. The methods, program code, instructions, and/or programs described herein and elsewhere may be executed by one or more of the network infrastructural elements.

[1119] The methods, program code, instructions, and/or programs described herein and elsewhere may be implemented on a cellular network having multiple cells. The cellular network may either be frequency division multiple access (FDMA) network or code division multiple access (CDMA) network. The cellular network may include mobile devices, cell sites, base stations, repeaters, antennas, towers, and the like.

[1120] The methods, program code, instructions, and/or programs described herein and elsewhere may be implemented on or through mobile devices. The mobile devices may include navigation devices, cell phones, mobile phones, mobile personal digital assistants, laptops, palmtops, netbooks, pagers, electronic books readers, music players and the like. These devices may include, apart from other components, a storage medium such as a flash memory, buffer, RAM, ROM and one or more computing devices. The computing devices associated with mobile devices may be enabled to execute methods, program code, instructions, and/or programs stored thereon. Alternatively, the mobile devices may be configured to execute instructions in collaboration with other devices. The mobile devices may communicate with base stations interfaced with servers and configured to execute methods, program code, instructions, and/or programs. The mobile devices may communicate on a peer to peer network, mesh network, or other communications network. The methods, program code, instructions, and/or programs may be stored on the storage medium associated with the server and executed by a computing device embedded within the server. The base station may include a computing device and a storage medium. The storage device may store methods, program code, instructions, and/or programs executed by the computing devices associated with the base station.

[1121] The methods, program code, instructions, and/or programs may be stored and/or accessed on machine readable transitory and/or non-transitory media that may include: computer components, devices, and recording media that retain digital data used for computing for some interval of time; semiconductor storage known as random access memory (RAM); mass storage typically for more permanent storage, such as optical discs, forms of magnetic storage like hard disks, tapes, drums, cards and other types; processor registers, cache memory, volatile memory, non-volatile memory; optical storage such as CD, DVD; removable media such as flash memory (e.g. USB sticks or keys), floppy disks, magnetic tape, paper tape, punch cards, standalone RAM disks, Zip drives, removable mass storage, off-line, and the like; other computer memory such as dynamic memory, static memory, read/write storage, mutable storage, read only, random access, sequential access, location addressable, file addressable, content addressable, network attached storage, storage area network, bar codes, magnetic ink, and the like.

[1122] Certain operations described herein include interpreting, receiving, and/or determining one or more values, parameters, inputs, data, or other information ("receiving data"). Operations to receive data include, without limitation: receiving data via a user input; receiving data over a network of any type; reading a data value from a memory location in communication with the receiving device; utilizing a default value as a received data value; estimating, calculating, or deriving a data value based on other information available to the receiving device; and/or updating any of these in response to a later received data value. In certain embodiments, a data value may be received by a first operation, and later updated by a second operation, as part of the receiving a data value. For example, when communications are down, intermittent, or interrupted, a first receiving operation may be performed, and when communications are restored an updated receiving operation may be performed.

[1123] Certain logical groupings of operations herein, for example methods or procedures of the current disclosure, are provided to illustrate aspects of the present disclosure. Operations described herein are schematically described and/or depicted, and operations may be combined, divided, re-ordered, added, or removed in a manner consistent with the disclosure herein. It is understood that the context of an operational description may require an ordering for one or more operations, and/or an order for one or more operations may be explicitly disclosed, but the order of operations should be understood broadly, where any equivalent grouping of operations to provide an equivalent outcome of operations is specifically contemplated herein. For example, if a value is used in one operational step, the determining of the value may be required before that operational step in certain contexts (e.g. where the time delay of data for an operation to achieve a certain effect is important), but may not be required before that operation step in other contexts (e.g. where usage of the value from a previous execution cycle of the operations would be sufficient for those purposes). Accordingly, in certain embodiments an order of operations and grouping of operations as described is explicitly contemplated herein, and in certain embodiments re-ordering, subdivision, and/or different grouping of operations is explicitly contemplated herein.

[1124] The methods and systems described herein may transform physical and/or or intangible items from one state to another. The methods and systems described herein may also transform data representing physical and/or intangible items from one state to another.

[1125] The methods and/or processes described above, and steps thereof, may be realized in hardware, program code, instructions, and/or programs or any combination of hardware and methods, program code, instructions, and/or programs suitable for a particular application. The hardware may include a dedicated computing device or specific computing device, a particular aspect or component of a specific computing device, and/or an arrangement of hardware components and/or logical circuits to perform one or more of the operations of a method and/or system. The processes may be realized in one or more microprocessors, microcontrollers, embedded microcontrollers, programmable digital signal processors or other programmable device, along with internal and/or external memory. The processes may also, or instead, be embodied in an application specific integrated circuit, a programmable gate array, programmable array logic, or any other device or combination of devices that may be configured to process electronic signals. It will further be appreciated that one or more of the processes may be realized as a computer executable code capable of being executed on a machine readable medium.

[1126] The computer executable code may be created using a structured programming language such as C, an object oriented programming language such as C++, or any other high-level or low-level programming language (including assembly languages, hardware description languages, and database programming languages and technologies) that may be stored, compiled or interpreted to run on one of the above devices, as well as heterogeneous combinations of processors, processor architectures, or combinations of different hardware and computer readable instructions, or any other machine capable of executing program instructions.

[1127] Thus, in one aspect, each method described above and combinations thereof may be embodied in computer executable code that, when executing on one or more computing devices, performs the steps thereof. In another aspect, the methods may be embodied in systems that perform the steps thereof, and may be distributed across devices in a number of ways, or all of the functionality may be integrated into a dedicated, standalone device or other hardware. In another aspect, the means for performing the steps associated with the processes described above may include any of the hardware and/or computer readable instructions described above. All such permutations and combinations are intended to fall within the scope of the present disclosure.

[1128] While the disclosure has been disclosed in connection with certain embodiments shown and described in detail, various modifications and improvements thereon will become readily apparent to those skilled in the art. Accordingly, the spirit and scope of the present disclosure is not to be limited by the foregoing examples, but is to be understood in the broadest sense allowable by law.

Claims

1. A method for determining trial designs, the method comprising: obtaining, via at least one processor, simulation data for a set of trial designs that includes combinations of design options for a set of criteria, wherein the simulation data includes performance parameters and performance parameter values associated with each design in the set of trial designs for the set of criteria; determining, via the at least one processor, an optimality criteria for evaluating the trial designs, wherein the optimality criteria includes at least one of Pareto optimality or convex hull optimality for clinical trial design performance values; determining, via the at least one processor and based at least in part on the simulation data, at least one of a cooling cycle, a parameter change, or a direction; searching, via the at least one processor and within the set of trial designs, for a set of globally optimum designs based on the optimality criteria using simulated annealing, wherein the simulated annealing is based at least in part on at least one of the cooling cycle, the parameter

change, or the direction; and recommending, via the at least one processor, the set of globally optimum designs to a user via a user interface.
2. The method of claim 1, wherein the optimality criteria is based on historical data and includes performance parameters of a benchmark design.
3. The method of claim 1, wherein the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs.
4. The method of claim 1, further comprising: changing the optimality criteria based on a number of globally optimum designs.
5. The method of claim 1, further comprising: determining a second optimality criteria; and searching, within the set of trial designs, for a second set of globally optimum designs based on the second optimality criteria.
6. The method of claim 1, further comprising: determining a second optimality criteria; and searching, within the set of globally optimum designs, for a second set of globally optimum designs based on the second optimality criteria.
7. The method of claim 1, further comprising: dynamically changing the optimality criteria in response to properties of globally optimum designs.
8. The method of claim 1, further comprising: dynamically changing the optimality criteria in response to user feedback.
9. The method of claim 1, further comprising: evaluating historical trial design selections to identify one or more trial design parameters based at least in part on one or more trial design criteria determined from a user via an interactive interface, wherein obtaining the simulation data is based at least in part on a quick search data structure and the one or more trial design parameters; generating a substitute for at least some of the simulation data based at least in part on a relationship between the simulation data and supplemental data; generating a performance surface based at least in part on the set of trial designs; evaluating one or more trial designs based at least in part on the performance surface; and calculating a score based on normalized score component values corresponding to the simulation data.
10. An apparatus comprising: a data processing circuit configured to obtain design data for a set of trial designs that includes combinations of design options for a set of criteria; an optimality determining circuit configured to: determine an optimality criteria for evaluating the set of trial designs, wherein the optimality criteria includes at least one of Pareto optimality or convex hull optimality for clinical trial design performance values; determine, based at least in part on the design data, at least one of a parameter change or a direction; and search, from the set of trial designs, for globally optimum designs based on the optimality criteria using the at least one of the parameter change or the direction; and a design analysis circuit configured to: analyze the globally optimum designs; determine a modification to the optimality criteria; and present the modification to a user via a user interface; wherein the optimality determining circuit is structured to receive the modification and determine a second set of globally optimum designs.
11. The apparatus of claim 10, wherein the optimality criteria is based on historical data and includes performance parameters of a benchmark design.
12. The apparatus of claim 10, wherein the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs.
13. The apparatus of claim 10, wherein the modification is based on a number of globally optimum designs.
14. The apparatus of claim 10, wherein the modification is in response to user feedback.
15. A non-transitory computer-readable medium storing instructions that adapt at least one processor to: obtain simulation data for a set of trial designs; determine an optimality criteria for evaluating the set of trial designs, wherein the optimality criteria includes at least one of Pareto optimality or convex hull optimality for clinical trial design performance values; determine, based at least in part on the simulation data, at least one of a parameter change or a direction; search,

within the set of trial designs, for globally optimum designs based on the optimality criteria and the at least one of the parameter change or the direction; and recommend the globally optimum designs to a user via a user interface.

16. The non-transitory computer-readable medium of claim 15, wherein the stored instructions further adapt the at least one processor to: analyze the globally optimum designs; determine a modification to the optimality criteria; and recommend the modification to the user via the user interface.

17. The non-transitory computer-readable medium of claim 16, wherein the optimality criteria is based on historical data and includes performance parameters of a benchmark design.

18. The non-transitory computer-readable medium of claim 16, wherein the optimality criteria is based on a weighted sum of performance criteria values of each of the set of trial designs.

19. The non-transitory computer-readable medium of claim 16, wherein the modification is based on a number of globally optimum designs.

20. The non-transitory computer-readable medium of claim 16, wherein the modification is in response to user feedback.