PoC Calibration Notebook - New Methodology

Introduction

This notebook implements the new PoC calibration methodology based on the email specification. The calibration uses null/flat scenarios to control Type I error rates.

Key Features

- **Null/Flat Scenario Construction**: Uses total probability formula for marginal efficacy calculation
- **C_poc Calibration**: Finds optimal threshold to achieve ~10% Type I error rate

Setup

```
library(knitr)
library(ggplot2)
library(dplyr)
```

```
Attaching package: 'dplyr'

The following objects are masked from 'package:stats':

    filter, lag

The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union
```

```r
# Set working directory to project root
if (basename(getwd()) == "notebooks") {
  setwd("..")
}

# Source required functions
source("src/utils/helpers.R")
source("src/utils/plotting_extensions.R")
source("src/core/simulate_data.R")
source("src/core/model_utils.R")
source("src/decision/dose_decision.R")
source("src/core/main.R")
```

```
Iso 0.0-21
```

```
    An "infelicity" in the function ufit() (whereby
    it was all too easy to conflate the location of
    the mode with its index in the entries of the
    "x" argument) has been corrected.  To this end,
    ufit() now has arguments "lmode" (the location
    of the mode), and "imode" (its index).  At most
    one of these arguments should be specified.  See
    the help for ufit().
```

```r
source("src/optimization/poc_calibration_new.R")
```

Configuration

Important: Parameter Naming Convention

Two different types of parameters with clear naming:

1. **`null_p_*`** = True probability values in the NULL scenario (used to generate data)
   - `null_p_I` = True immune response rate (e.g., 0.25)
   - `null_p_E` = True efficacy rate (e.g., 0.30)
   - `null_p_T` = True toxicity rate (e.g., 0.05)
2. **`phi_*`** = Admissibility thresholds (used for decision making)
   - `phi_I` = Immune response threshold for admissibility (e.g., 0.20)

- `phi_E` = Efficacy threshold for admissibility (e.g., 0.25)
- `phi_T` = Toxicity threshold for admissibility (e.g., 0.30)

Example: We set `null_p_I = 0.20` (true value) = `phi_I = 0.20` (threshold) for a true null scenario.

Parameter Type	Immune	Efficacy	Toxicity	Purpose
Null Scenario	null_p_I = 0.20	null_p_E = 0.25	null_p_T = 0.05	Generate data
Thresholds	phi_I = 0.20	phi_E = 0.25	phi_T = 0.30	Make decisions
Relationship	null_p_I = phi_I	null_p_E = phi_E	null_p_T < phi_T	Null scenario

```
# Calibration parameters per email specification
# Null scenario: true values equal thresholds for a true null scenario
calibration_params <- list(
  null_p_I = 0.20,      # NULL SCENARIO: True immune response rate (equals threshold phi_I=0
  null_p_E = 0.25,      # NULL SCENARIO: True efficacy rate (equals threshold phi_E=0.25)
  null_p_T = 0.05,      # NULL SCENARIO: True toxicity rate (flat, safe level)
  tox_upper = 0.30,     # Toxicity upper bound for scenario construction
  n_simulations = 1000  # Number of simulations for calibration
)

# Trial configuration for calibration
# These phi_* values are THRESHOLDS for admissibility checks (not true data values!)
trial_config <- list(
  dose_levels = c(1, 2, 3, 4, 5),
  n_stages = 5,          # 5 total stages (1 equal + 4 adaptive)
  cohort_size = 15,
  phi_T = 0.30,          # THRESHOLD: Toxicity upper limit for admissibility
  c_T = 0.2,             # PROBABILITY: P(Tox < phi_T) must exceed this
  phi_E = 0.25,          # THRESHOLD: Efficacy lower limit for admissibility
  c_E = 0.5,             # PROBABILITY: P(Eff > phi_E) must exceed this
  phi_I = 0.20,          # THRESHOLD: Immune response lower limit for admissibility
  c_I = 0.35,             # PROBABILITY: P(Imm > phi_I) must exceed this
  delta_poc = 0.8,
  enable_early_termination = TRUE,
  log_early_termination = FALSE,
  verbose_logging = FALSE  # Disable verbose logs in notebook
)

# Utility table
```

```r
utility_table <- array(0, dim = c(2, 2, 2), dimnames = list(
  E = c(0, 1),
  T = c(0, 1),
  I = c(0, 1)
))

utility_table[1, 1, 1] <- 0   # E=0, T=0, I=0
utility_table[2, 1, 1] <- 80  # E=1, T=0, I=0
utility_table[1, 2, 1] <- 0   # E=0, T=1, I=0
utility_table[2, 2, 1] <- 30  # E=1, T=1, I=0

utility_table[1, 1, 2] <- 10  # E=0, T=0, I=1
utility_table[2, 1, 2] <- 100 # E=1, T=0, I=1
utility_table[1, 2, 2] <- 0   # E=0, T=1, I=1
utility_table[2, 2, 2] <- 40  # E=1, T=1, I=1

trial_config$utility_table <- utility_table

cat("Configuration loaded successfully!\n")
```

```
Configuration loaded successfully!
```

```r
cat("\nNull Scenario True Values (for data generation):\n")
```

```

Null Scenario True Values (for data generation):
```

```r
cat("  null_p_I (immune) =", calibration_params$null_p_I, "\n")
```

```
  null_p_I (immune) = 0.2
```

```r
cat("  null_p_E (efficacy) =", calibration_params$null_p_E, "\n")
```

```
  null_p_E (efficacy) = 0.25
```

```r
cat("  null_p_T (toxicity) =", calibration_params$null_p_T, "\n")
```

```
  null_p_T (toxicity) = 0.05
```

```
cat("\nAdmissibility Thresholds (for decision making):\n")
```

```
Admissibility Thresholds (for decision making):
```

```
cat("  phi_I (immune threshold) =", trial_config$phi_I, "\n")
```

```
  phi_I (immune threshold) = 0.2
```

```
cat("  phi_E (efficacy threshold) =", trial_config$phi_E, "\n")
```

```
  phi_E (efficacy threshold) = 0.25
```

```
cat("  phi_T (toxicity threshold) =", trial_config$phi_T, "\n")
```

```
  phi_T (toxicity threshold) = 0.3
```

```
cat("\nOther parameters:\n")
```

```
Other parameters:
```

```
cat("  Simulations =", calibration_params$n_simulations, "\n")
```

```
  Simulations = 1000
```

Null/Flat Scenario Construction

This section demonstrates the construction of the null/flat scenario using the total probability formula.

```r
# Create null/flat scenario
# Note: Using null_p_* (true values for data generation), NOT phi_* (thresholds)
null_scenario <- create_null_flat_scenario(
  n_doses = 5,
  phi_I = calibration_params$null_p_I,   # True immune response rate in null scenario
  phi_E = calibration_params$null_p_E,   # True efficacy rate in null scenario
  tox_upper = calibration_params$tox_upper,
  tox_flat = calibration_params$null_p_T  # True toxicity rate in null scenario
)

cat("Null/Flat Scenario Parameters:\n")
```

```
Null/Flat Scenario Parameters:
```

```r
cat("Description:", null_scenario$description, "\n")
```

```
Description: Null/Flat:  _I=0.2,  _E=0.25, tox=0.05
```

```r
cat("\nImmune Response Probabilities (P_I):\n")
```

```

Immune Response Probabilities (P_I):
```

```r
print(round(null_scenario$p_YI, 3))
```

```
[1] 0.2 0.2 0.2 0.2 0.2
```

```r
cat("\nToxicity Probabilities (P_T|I):\n")
```

```

Toxicity Probabilities (P_T|I):
```

```r
print(round(null_scenario$p_YT_given_I, 3))
```

```
     [,1] [,2]
[1,] 0.05 0.05
[2,] 0.05 0.05
[3,] 0.05 0.05
[4,] 0.05 0.05
[5,] 0.05 0.05
```

```r
cat("\nEfficacy Probabilities (P_E|I):\n")
```

```
Efficacy Probabilities (P_E|I):
```

```r
print(round(null_scenario$p_YE_given_I, 3))
```

```
     [,1] [,2]
[1,] 0.25 0.25
[2,] 0.25 0.25
[3,] 0.25 0.25
[4,] 0.25 0.25
[5,] 0.25 0.25
```

```r
# Verify marginal efficacy calculation
cat("\nMarginal Efficacy Verification:\n")
```

```
Marginal Efficacy Verification:
```

```r
for (dose in 1:5) {
  marginal_eff <- null_scenario$p_YE_given_I[dose, 1] * (1 - null_scenario$p_YI[dose]) +
                  null_scenario$p_YE_given_I[dose, 2] * null_scenario$p_YI[dose]
  cat("Dose", dose, "marginal efficacy:", round(marginal_eff, 3), "\n")
}
```

```
Dose 1 marginal efficacy: 0.25
Dose 2 marginal efficacy: 0.25
Dose 3 marginal efficacy: 0.25
Dose 4 marginal efficacy: 0.25
Dose 5 marginal efficacy: 0.25
```

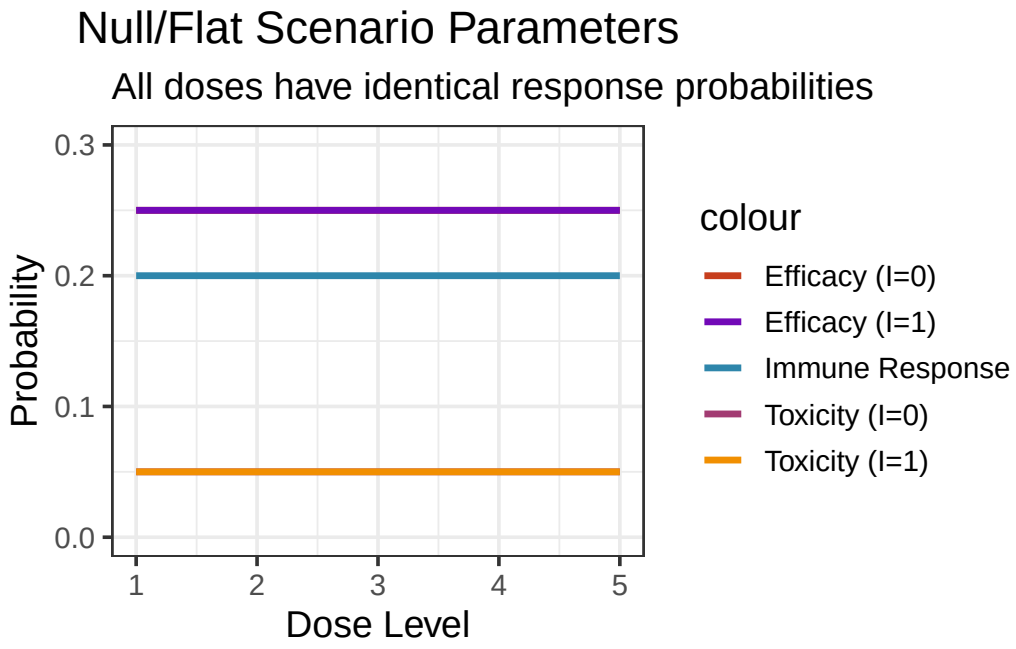
```r
# Create visualization of null scenario
null_plot_data <- data.frame(
  Dose = 1:5,
  Immune_Response = null_scenario$p_YI,
  Toxicity_I0 = null_scenario$p_YT_given_I[, 1],
  Toxicity_I1 = null_scenario$p_YT_given_I[, 2],
  Efficacy_I0 = null_scenario$p_YE_given_I[, 1],
```

```
  Efficacy_I1 = null_scenario$p_YE_given_I[, 2]
)

# Plot null scenario parameters
p_null <- ggplot(null_plot_data, aes(x = Dose)) +
  geom_line(aes(y = Immune_Response, color = "Immune Response"), size = 1.2) +
  geom_line(aes(y = Toxicity_I0, color = "Toxicity (I=0)"), size = 1.2) +
  geom_line(aes(y = Toxicity_I1, color = "Toxicity (I=1)"), size = 1.2) +
  geom_line(aes(y = Efficacy_I0, color = "Efficacy (I=0)"), size = 1.2) +
  geom_line(aes(y = Efficacy_I1, color = "Efficacy (I=1)"), size = 1.2) +
  labs(title = "Null/Flat Scenario Parameters",
       subtitle = "All doses have identical response probabilities",
       x = "Dose Level", y = "Probability") +
  theme_bw(base_size = 14) +
  theme(plot.title = element_text(hjust = 0.5)) +
  scale_color_manual(values = c("Immune Response" = "#2E86AB",
                                "Toxicity (I=0)" = "#A23B72",
                                "Toxicity (I=1)" = "#F18F01",
                                "Efficacy (I=0)" = "#C73E1D",
                                "Efficacy (I=1)" = "#7209B7")) +
  ylim(0, 0.3)
```

```
Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
i Please use `linewidth` instead.
```

```
print(p_null)
```



C_poc Calibration Process

This section runs the calibration process to find the optimal C_poc threshold.

Note on Output Verbosity: - Debug output is minimal by default to avoid console overflow in RStudio - Only shows first 3 simulations for the first c_poc candidate - Set `debug_early_termination = TRUE` in the function call below for more detailed examples

```
# Run C_poc calibration
cat("Starting C_poc calibration...\n")
```

```
Starting C_poc calibration...
```

```
cat("This may take several minutes...\n")
```

```
This may take several minutes...
```

```
start_time <- Sys.time()

calibration_results <- calibrate_c_poc(
  null_scenario = null_scenario,
```

```r
  c_poc_candidates = c(0.5, 0.6, 0.7, 0.8, 0.85, 0.9, 0.95),
  n_simulations = calibration_params$n_simulations,
  base_config = trial_config,
  debug_early_termination = FALSE,  # Set to TRUE for detailed early termination examples
  max_debug_cases_per_candidate = 2  # Number of debug examples per c_poc (if debug enabled)
)
```

```
Starting C_poc calibration...
Testing 7 C_poc values
Simulations per value: 1000

=== Configuration Parameters Used ===
Trial Design Parameters:
  dose_levels: 1, 2, 3, 4, 5
  n_stages: 5
  cohort_size: 15

Toxicity Parameters:
  phi_T: 0.3
  c_T: 0.2

Efficacy Parameters:
  phi_E: 0.25
  c_E: 0.5

Immune Response Parameters:
  phi_I: 0.2
  c_I: 0.35

PoC Parameters:
  delta_poc: 0.8
  enable_early_termination: TRUE
  log_early_termination: FALSE

=== Null Scenario Parameters ===
  p_YI: 0.2, 0.2, 0.2, 0.2, 0.2
  p_YT_given_I (rows=dose, cols=I=[0,1]):
    Dose 1 : 0.05, 0.05
    Dose 2 : 0.05, 0.05
    Dose 3 : 0.05, 0.05
    Dose 4 : 0.05, 0.05
    Dose 5 : 0.05, 0.05
```

```
  p_YE_given_I (rows=dose, cols=I=[0,1]):
    Dose 1 : 0.25, 0.25
    Dose 2 : 0.25, 0.25
    Dose 3 : 0.25, 0.25
    Dose 4 : 0.25, 0.25
    Dose 5 : 0.25, 0.25
  rho0: 1.5
  rho1: 2

=== Testing C_poc = 0.5 ===

[DEBUG] c_poc = 0.5 , sim = 1
  Early terminated: FALSE
  Final OD: 5
  PoC validated: TRUE
  PoC probability: 0.695
  A_final: 3 4 5
  P_final non-empty: TRUE

[DEBUG] c_poc = 0.5 , sim = 2
  Early terminated: FALSE
  Final OD: 5
  PoC validated: TRUE
  PoC probability: 1
  A_final: 5
  P_final non-empty: TRUE

[DEBUG] c_poc = 0.5 , sim = 3
  Early terminated: FALSE
  Final OD: 5
  PoC validated: TRUE
  PoC probability: 0.765
  A_final: 4 5
  P_final non-empty: TRUE
  PoC detection rate: 0.548 (SE: 0.0157 , 95% CI: [ 0.517 , 0.579 ])
  Early termination rate: 0.273
  Completion rate: 0.727
  PoC rate among completed trials: 0.754
=== Testing C_poc = 0.6 ===
  PoC detection rate: 0.497 (SE: 0.0158 , 95% CI: [ 0.466 , 0.528 ])
  Early termination rate: 0.288
  Completion rate: 0.712
  PoC rate among completed trials: 0.698
```

```
=== Testing C_poc = 0.7 ===
  PoC detection rate: 0.44 (SE: 0.0157 , 95% CI: [ 0.409 , 0.471 ])
  Early termination rate: 0.245
  Completion rate: 0.755
  PoC rate among completed trials: 0.583
=== Testing C_poc = 0.8 ===
  PoC detection rate: 0.365 (SE: 0.0152 , 95% CI: [ 0.335 , 0.395 ])
  Early termination rate: 0.267
  Completion rate: 0.733
  PoC rate among completed trials: 0.498
=== Testing C_poc = 0.85 ===
  PoC detection rate: 0.367 (SE: 0.0152 , 95% CI: [ 0.337 , 0.397 ])
  Early termination rate: 0.255
  Completion rate: 0.745
  PoC rate among completed trials: 0.493
=== Testing C_poc = 0.9 ===
  PoC detection rate: 0.305 (SE: 0.0146 , 95% CI: [ 0.276 , 0.334 ])
  Early termination rate: 0.202
  Completion rate: 0.798
  PoC rate among completed trials: 0.382
=== Testing C_poc = 0.95 ===
  PoC detection rate: 0.274 (SE: 0.0141 , 95% CI: [ 0.246 , 0.302 ])
  Early termination rate: 0.239
  Completion rate: 0.761
  PoC rate among completed trials: 0.36

=== CALIBRATION RESULTS SUMMARY ===
Target Type I error (PoC detection rate):   10 %
  TYPE I ERROR CONTROL NOT ACHIEVED
Selected C_poc: 0.95 (largest tested, but still exceeds target)
  WARNING: All tested C_poc values exceed target Type I error!
  Consider testing higher C_poc values (e.g., 0.96, 0.97, 0.98)
Achieved PoC detection rate: 0.274 (SE: 0.0141 )
Achieved completion rate: 0.761

=== TYPE I ERROR CONTROL TABLE ===
C_poc      | PoC Rate (95% CI)    | Control Achieved?         | Status
-------------------------------------------------------------------------------
0.50       | 0.548   [0.517, 0.579] |   No                    |
0.60       | 0.497   [0.466, 0.528] |   No                    |
0.70       | 0.440   [0.409, 0.471] |   No                    |
0.80       | 0.365   [0.335, 0.395] |   No                    |
0.85       | 0.367   [0.337, 0.397] |   No                    |
```

```
0.90       | 0.305   [0.276, 0.334] |   No                    |
0.95       | 0.274   [0.246, 0.302] |   No                    | ← SELECTED*
-------------------------------------------------------------------------------
* Selected despite exceeding target (no C_poc achieved control)

=== SANITY CHECKS ===
1. PoC rate <= completion rate for all c_poc values?
   c_poc = 0.5 :   PASS (PoC: 0.548 , Completion: 0.727 )
   c_poc = 0.6 :   PASS (PoC: 0.497 , Completion: 0.712 )
   c_poc = 0.7 :   PASS (PoC: 0.44 , Completion: 0.755 )
   c_poc = 0.8 :   PASS (PoC: 0.365 , Completion: 0.733 )
   c_poc = 0.85 :   PASS (PoC: 0.367 , Completion: 0.745 )
   c_poc = 0.9 :   PASS (PoC: 0.305 , Completion: 0.798 )
   c_poc = 0.95 :   PASS (PoC: 0.274 , Completion: 0.761 )

2. Monotonicity check (higher c_poc should generally decrease PoC rate):
   c_poc: 0.5 → 0.6 :   Non-increasing (Δ = -0.051 )
   c_poc: 0.6 → 0.7 :   Non-increasing (Δ = -0.057 )
   c_poc: 0.7 → 0.8 :   Non-increasing (Δ = -0.075 )
   c_poc: 0.8 → 0.85 :   Increased (Δ = 0.002 )
   c_poc: 0.85 → 0.9 :   Non-increasing (Δ = -0.062 )
   c_poc: 0.9 → 0.95 :   Non-increasing (Δ = -0.031 )

=== END SANITY CHECKS ===
```

```r
end_time <- Sys.time()
calibration_duration <- difftime(end_time, start_time, units = "mins")
cat("\nC_poc Calibration Complete!\n")
```

```
C_poc Calibration Complete!
```

```r
cat("Duration:", round(calibration_duration, 2), "minutes\n")
```

```
Duration: 34.05 minutes
```

```r
cat("\nCalibration Results:\n")
```

```
Calibration Results:
```

```r
cat("Optimal C_poc:", calibration_results$optimal_c_poc, "\n")
```

```
Optimal C_poc: 0.95
```

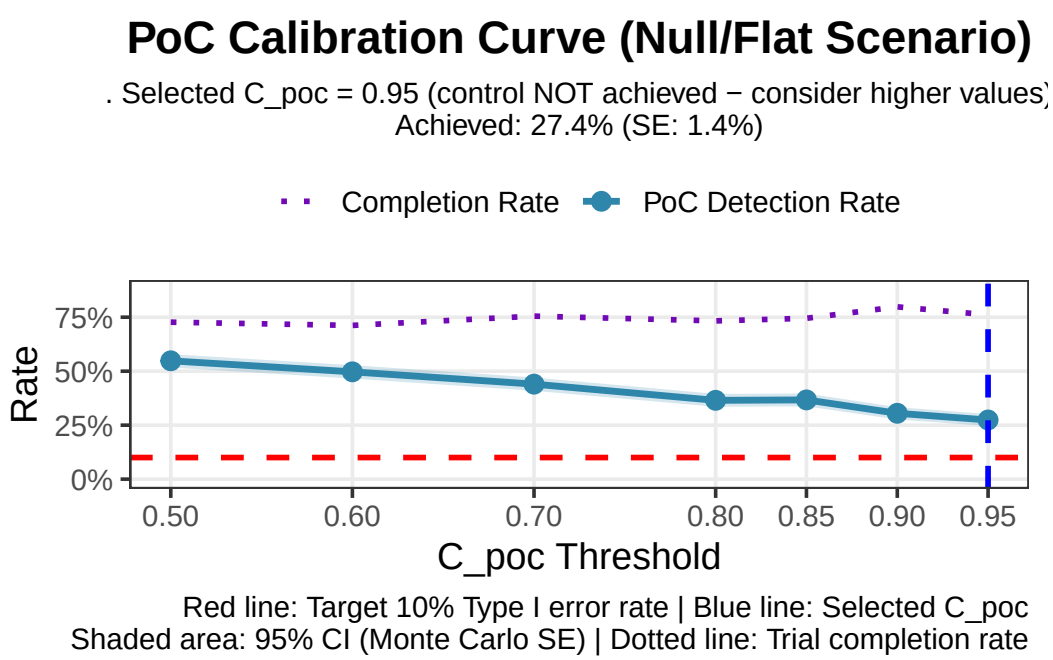
```r
cat("Target PoC detection rate: 10%\n")
```

```
Target PoC detection rate: 10%
```

```r
cat("Achieved PoC detection rate:", round(calibration_results$achieved_rate, 3), "\n")
```

```
Achieved PoC detection rate: 0.274
```

```r
# Display calibration curve
calibration_plot <- plot_calibration_curve(calibration_results)
print(calibration_plot)
```




```r
# Create detailed results table
calibration_table <- data.frame(
  C_poc = sapply(calibration_results$calibration_results, function(x) x$c_poc),
```

```
  PoC_Detection_Rate = sapply(calibration_results$calibration_results, function(x) x$poc_dete
  Early_Termination_Rate = sapply(calibration_results$calibration_results, function(x) x$earl
)

calibration_table$Optimal <- calibration_table$C_poc == calibration_results$optimal_c_poc

cat("\nCalibration Results Table:\n")
```

```
Calibration Results Table:
```

```
print(calibration_table)
```

```
  C_poc PoC_Detection_Rate Early_Termination_Rate Optimal
1  0.50              0.548                 0.273   FALSE
2  0.60              0.497                 0.288   FALSE
3  0.70              0.440                 0.245   FALSE
4  0.80              0.365                 0.267   FALSE
5  0.85              0.367                 0.255   FALSE
6  0.90              0.305                 0.202   FALSE
7  0.95              0.274                 0.239    TRUE
```

```
# Generate detailed report file
cat("\n--- Generating Detailed Report ---\n")
```

```
--- Generating Detailed Report ---
```

```
# Use relative path from notebooks/ directory (where notebook runs)
report_path <- "results/notebook_calibration/calibration_detailed_report.txt"
generate_calibration_report(
  calibration_results = calibration_results,
  null_scenario = null_scenario,
  base_config = trial_config,
  file_path = report_path
)
```

```
Detailed calibration report saved to: results/notebook_calibration/calibration_detailed_repor
```

```r
cat("Report generated successfully!\n")
```

```
Report generated successfully!
```

```r
cat("View the full report at:", report_path, "\n")
```

```
View the full report at: results/notebook_calibration/calibration_detailed_report.txt
```

View Report Summary

After generating the report, you can view key sections here or open the full text file.

```r
# Read and display key sections of the report
if (file.exists(report_path)) {
  report_lines <- readLines(report_path)

  # Display first 1000 lines (header + configuration + summary)
  cat("=== REPORT PREVIEW (First 1000 lines) ===\n\n")
  cat(paste(head(report_lines, 1000), collapse = "\n"))
  cat("\n\n... (see full report file for complete details) ...\n")
} else {
  cat("Report file not found. Please run the calibration chunk first.\n")
}
```

```
=== REPORT PREVIEW (First 1000 lines) ===

================================================================================
                    POC CALIBRATION DETAILED REPORT
================================================================================
Generated: 2026-02-04 02:56:11

================================================================================
1. CONFIGURATION SUMMARY
================================================================================

Trial Design:
  - Number of doses: 5
  - Number of stages: 5
  - Cohort size: 15
```

```
  - Total sample size (if completed): 75

Admissibility Thresholds:
  - Toxicity ( _T): 0.3   (Probability threshold c_T: 0.2 )
  - Efficacy ( _E): 0.25   (Probability threshold c_E: 0.5 )
  - Immune Response ( _I): 0.2   (Probability threshold c_I: 0.35 )

PoC Parameters:
  - delta_poc: 0.8
  - Early termination enabled: TRUE

Null Scenario Parameters:
  - True immune response (p_YI): 0.2, 0.2, 0.2, 0.2, 0.2
  - True toxicity (p_YT | I=0): 0.05, 0.05, 0.05, 0.05, 0.05
  - True toxicity (p_YT | I=1): 0.05, 0.05, 0.05, 0.05, 0.05
  - True efficacy (p_YE | I=0): 0.25, 0.25, 0.25, 0.25, 0.25
  - True efficacy (p_YE | I=1): 0.25, 0.25, 0.25, 0.25, 0.25

================================================================================
2. CALIBRATION RESULTS SUMMARY
================================================================================

Target Type I Error Rate: 10%
Optimal C_poc: 0.95
Achieved PoC Detection Rate: 27.4%

Detailed Results by C_poc:
--------------------------------------------------------------------------------
C_poc    | PoC Detection Rate     | Completion Rate      | PoC | Completed      | Status
--------------------------------------------------------------------------------
0.50     | 54.8% ± 1.6%          | 72.7%                | 75.4%                |
0.60     | 49.7% ± 1.6%          | 71.2%                | 69.8%                |
0.70     | 44.0% ± 1.6%          | 75.5%                | 58.3%                |
0.80     | 36.5% ± 1.5%          | 73.3%                | 49.8%                |
0.85     | 36.7% ± 1.5%          | 74.5%                | 49.3%                |
0.90     | 30.5% ± 1.5%          | 79.8%                | 38.2%                |
0.95     | 27.4% ± 1.4%          | 76.1%                | 36.0%                | OPTIMAL
--------------------------------------------------------------------------------
Note: PoC Detection Rate = Pr(PoC detected) across ALL trials (including early terminated)
      PoC | Completed = Pr(PoC detected | trial completed without early termination)
      Standard errors are Monte Carlo SE = sqrt(p*(1-p)/N)

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3. EARLY TERMINATION DETAILED ANALYSIS
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--- C_poc = 0.5 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 273 (27.3%)
  - Completed trials: 727 (72.7%)

  Early Termination by Stage:
    Stage 1: 1 trials (0.4% of early terminations)
    Stage 2: 38 trials (13.9% of early terminations)
    Stage 3: 83 trials (30.4% of early terminations)
    Stage 4: 72 trials (26.4% of early terminations)
    Stage 5: 79 trials (28.9% of early terminations)

  Sample Size at Early Termination:
    Mean: 55.4 patients (SD: 15.7)
    Range: 15 - 75 patients

  Common Patterns in Early Termination:

    Example 1 (Simulation 4, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.075, 0.097, 0.101, 0.115, 0.217
        Efficacy:   0.190, 0.231, 0.234, 0.259, 0.314
        Immune:     0.171, 0.186, 0.189, 0.189, 0.190
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.17, P(Imm>0.20)=0.25
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.34, P(Imm>0.20)=0.32
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.36, P(Imm>0.20)=0.34
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.55, P(Imm>0.20)=0.34
        Dose 5  : P(Tox<0.30)=0.85, P(Eff>0.25)=0.81, P(Imm>0.20)=0.34

    Example 2 (Simulation 5, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.079, 0.094, 0.099, 0.111, 0.218
        Efficacy:   0.147, 0.212, 0.218, 0.261, 0.341
        Immune:     0.180, 0.184, 0.186, 0.186, 0.186
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.08, P(Imm>0.20)=0.31
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.23, P(Imm>0.20)=0.33
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        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.26, P(Imm>0.20)=0.34
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.56, P(Imm>0.20)=0.34
        Dose 5  : P(Tox<0.30)=0.87, P(Eff>0.25)=0.93, P(Imm>0.20)=0.34

    Example 3 (Simulation 6, Stage 4):
      Posterior Estimates (Mean):
        Toxicity:   0.105, 0.126, 0.132, 0.162, 0.243
        Efficacy:   0.155, 0.222, 0.242, 0.280, 0.346
        Immune:     0.126, 0.177, 0.181, 0.181, 0.189
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.15, P(Imm>0.20)=0.13
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.33, P(Imm>0.20)=0.27
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.44, P(Imm>0.20)=0.29
        Dose 4  : P(Tox<0.30)=0.99, P(Eff>0.25)=0.70, P(Imm>0.20)=0.29
        Dose 5  : P(Tox<0.30)=0.79, P(Eff>0.25)=0.92, P(Imm>0.20)=0.35

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 548 trials (75.4% of completed trials)

--- C_poc = 0.6 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 288 (28.8%)
  - Completed trials: 712 (71.2%)

  Early Termination by Stage:
    Stage 1: 2 trials (0.7% of early terminations)
    Stage 2: 40 trials (13.9% of early terminations)
    Stage 3: 77 trials (26.7% of early terminations)
    Stage 4: 99 trials (34.4% of early terminations)
    Stage 5: 70 trials (24.3% of early terminations)

  Sample Size at Early Termination:
    Mean: 55.2 patients (SD: 15.2)
    Range: 15 - 75 patients

  Common Patterns in Early Termination:

    Example 1 (Simulation 3, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.087, 0.112, 0.113, 0.116, 0.122
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      Efficacy:   0.147, 0.170, 0.184, 0.198, 0.261
      Immune:     0.154, 0.174, 0.176, 0.186, 0.186
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.03, P(Imm>0.20)=0.19
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.06, P(Imm>0.20)=0.27
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.09, P(Imm>0.20)=0.28
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.16, P(Imm>0.20)=0.35
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.55, P(Imm>0.20)=0.35

  Example 2 (Simulation 4, Stage 1):
    Posterior Estimates (Mean):
      Toxicity:   0.225, 0.361, 0.378, 0.400, 0.434
      Efficacy:   0.179, 0.236, 0.279, 0.352, 0.496
      Immune:     0.281, 0.312, 0.328, 0.547, 0.652
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=0.75, P(Eff>0.25)=0.21, P(Imm>0.20)=0.75
      Dose 2  : P(Tox<0.30)=0.26, P(Eff>0.25)=0.42, P(Imm>0.20)=0.84
      Dose 3  : P(Tox<0.30)=0.18, P(Eff>0.25)=0.61, P(Imm>0.20)=0.86
      Dose 4  : P(Tox<0.30)=0.12, P(Eff>0.25)=0.85, P(Imm>0.20)=1.00
      Dose 5  : P(Tox<0.30)=0.08, P(Eff>0.25)=0.99, P(Imm>0.20)=1.00

  Example 3 (Simulation 5, Stage 3):
    Posterior Estimates (Mean):
      Toxicity:   0.088, 0.106, 0.112, 0.123, 0.225
      Efficacy:   0.142, 0.188, 0.217, 0.263, 0.293
      Immune:     0.103, 0.127, 0.139, 0.150, 0.154
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.07, P(Imm>0.20)=0.06
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.18, P(Imm>0.20)=0.09
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.30, P(Imm>0.20)=0.12
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.57, P(Imm>0.20)=0.15
      Dose 5  : P(Tox<0.30)=0.81, P(Eff>0.25)=0.71, P(Imm>0.20)=0.18

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 497 trials (69.8% of completed trials)

--- C_poc = 0.7 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 245 (24.5%)
  - Completed trials: 755 (75.5%)
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Early Termination by Stage:
  Stage 1: 2 trials (0.8% of early terminations)
  Stage 2: 37 trials (15.1% of early terminations)
  Stage 3: 78 trials (31.8% of early terminations)
  Stage 4: 64 trials (26.1% of early terminations)
  Stage 5: 64 trials (26.1% of early terminations)

Sample Size at Early Termination:
  Mean: 54.2 patients (SD: 15.8)
  Range: 15 - 75 patients

Common Patterns in Early Termination:

  Example 1 (Simulation 1, Stage 5):
    Posterior Estimates (Mean):
      Toxicity:   0.072, 0.080, 0.100, 0.111, 0.119
      Efficacy:   0.170, 0.213, 0.218, 0.223, 0.257
      Immune:     0.249, 0.253, 0.253, 0.266, 0.292
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.08, P(Imm>0.20)=0.83
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.17, P(Imm>0.20)=0.85
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.20, P(Imm>0.20)=0.85
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.24, P(Imm>0.20)=0.89
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.50, P(Imm>0.20)=0.95

  Example 2 (Simulation 4, Stage 5):
    Posterior Estimates (Mean):
      Toxicity:   0.097, 0.110, 0.112, 0.116, 0.121
      Efficacy:   0.140, 0.166, 0.181, 0.216, 0.451
      Immune:     0.174, 0.182, 0.184, 0.184, 0.184
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.07, P(Imm>0.20)=0.28
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.10, P(Imm>0.20)=0.31
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.15, P(Imm>0.20)=0.32
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.30, P(Imm>0.20)=0.32
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=1.00, P(Imm>0.20)=0.32

  Example 3 (Simulation 5, Stage 4):
    Posterior Estimates (Mean):
      Toxicity:   0.080, 0.090, 0.112, 0.182, 0.258
      Efficacy:   0.222, 0.379, 0.397, 0.401, 0.500
      Immune:     0.172, 0.173, 0.173, 0.173, 0.177
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      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.42, P(Imm>0.20)=0.25
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.98, P(Imm>0.20)=0.25
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=1.00, P(Imm>0.20)=0.25
        Dose 4  : P(Tox<0.30)=0.97, P(Eff>0.25)=1.00, P(Imm>0.20)=0.26
        Dose 5  : P(Tox<0.30)=0.73, P(Eff>0.25)=1.00, P(Imm>0.20)=0.28

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 440 trials (58.3% of completed trials)

--- C_poc = 0.8 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 267 (26.7%)
  - Completed trials: 733 (73.3%)

  Early Termination by Stage:
    Stage 1: 2 trials (0.7% of early terminations)
    Stage 2: 36 trials (13.5% of early terminations)
    Stage 3: 77 trials (28.8% of early terminations)
    Stage 4: 84 trials (31.5% of early terminations)
    Stage 5: 68 trials (25.5% of early terminations)

  Sample Size at Early Termination:
    Mean: 55.1 patients (SD: 15.4)
    Range: 15 - 75 patients

  Common Patterns in Early Termination:

    Example 1 (Simulation 9, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.086, 0.101, 0.115, 0.123, 0.184
        Efficacy:   0.229, 0.255, 0.266, 0.276, 0.320
        Immune:     0.102, 0.124, 0.169, 0.182, 0.183
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.40, P(Imm>0.20)=0.07
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.52, P(Imm>0.20)=0.11
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.60, P(Imm>0.20)=0.24
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.69, P(Imm>0.20)=0.32
        Dose 5  : P(Tox<0.30)=0.97, P(Eff>0.25)=0.89, P(Imm>0.20)=0.32
```

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    Example 2 (Simulation 11, Stage 3):
      Posterior Estimates (Mean):
        Toxicity:   0.100, 0.121, 0.142, 0.156, 0.179
        Efficacy:   0.164, 0.179, 0.214, 0.279, 0.300
        Immune:     0.104, 0.126, 0.175, 0.179, 0.186
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.10, P(Imm>0.20)=0.08
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.14, P(Imm>0.20)=0.12
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.27, P(Imm>0.20)=0.28
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.66, P(Imm>0.20)=0.31
        Dose 5  : P(Tox<0.30)=0.97, P(Eff>0.25)=0.76, P(Imm>0.20)=0.35

    Example 3 (Simulation 20, Stage 3):
      Posterior Estimates (Mean):
        Toxicity:   0.110, 0.133, 0.156, 0.200, 0.224
        Efficacy:   0.327, 0.343, 0.347, 0.355, 0.372
        Immune:     0.094, 0.111, 0.130, 0.170, 0.175
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.90, P(Imm>0.20)=0.04
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.96, P(Imm>0.20)=0.06
        Dose 3  : P(Tox<0.30)=0.99, P(Eff>0.25)=0.97, P(Imm>0.20)=0.10
        Dose 4  : P(Tox<0.30)=0.95, P(Eff>0.25)=0.98, P(Imm>0.20)=0.25
        Dose 5  : P(Tox<0.30)=0.88, P(Eff>0.25)=0.99, P(Imm>0.20)=0.28

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 365 trials (49.8% of completed trials)

--- C_poc = 0.85 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 255 (25.5%)
  - Completed trials: 745 (74.5%)

  Early Termination by Stage:
    Stage 1: 2 trials (0.8% of early terminations)
    Stage 2: 32 trials (12.5% of early terminations)
    Stage 3: 79 trials (31.0% of early terminations)
    Stage 4: 79 trials (31.0% of early terminations)
    Stage 5: 63 trials (24.7% of early terminations)

  Sample Size at Early Termination:
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  Mean: 54.9 patients (SD: 15.1)
  Range: 15 - 75 patients

Common Patterns in Early Termination:

  Example 1 (Simulation 2, Stage 5):
    Posterior Estimates (Mean):
      Toxicity:   0.071, 0.079, 0.083, 0.096, 0.109
      Efficacy:   0.136, 0.178, 0.208, 0.231, 0.253
      Immune:     0.099, 0.119, 0.131, 0.241, 0.268
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.04, P(Imm>0.20)=0.07
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.10, P(Imm>0.20)=0.11
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.17, P(Imm>0.20)=0.15
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.32, P(Imm>0.20)=0.76
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.49, P(Imm>0.20)=0.87

  Example 2 (Simulation 3, Stage 4):
    Posterior Estimates (Mean):
      Toxicity:   0.081, 0.094, 0.105, 0.116, 0.126
      Efficacy:   0.181, 0.192, 0.194, 0.213, 0.240
      Immune:     0.109, 0.142, 0.153, 0.246, 0.326
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.06, P(Imm>0.20)=0.11
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.09, P(Imm>0.20)=0.19
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.10, P(Imm>0.20)=0.24
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.18, P(Imm>0.20)=0.71
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.37, P(Imm>0.20)=0.97

  Example 3 (Simulation 15, Stage 5):
    Posterior Estimates (Mean):
      Toxicity:   0.065, 0.091, 0.092, 0.094, 0.107
      Efficacy:   0.181, 0.216, 0.220, 0.246, 0.254
      Immune:     0.135, 0.317, 0.329, 0.332, 0.341
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.09, P(Imm>0.20)=0.27
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.20, P(Imm>0.20)=0.96
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.23, P(Imm>0.20)=0.99
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.45, P(Imm>0.20)=0.99
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.50, P(Imm>0.20)=0.99

Completed Trials Analysis:
  Mean sample size: 75.0 patients (SD: 0.0)
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    PoC validated: 367 trials (49.3% of completed trials)

--- C_poc = 0.9 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 202 (20.2%)
  - Completed trials: 798 (79.8%)

  Early Termination by Stage:
    Stage 1: 1 trials (0.5% of early terminations)
    Stage 2: 31 trials (15.3% of early terminations)
    Stage 3: 60 trials (29.7% of early terminations)
    Stage 4: 60 trials (29.7% of early terminations)
    Stage 5: 50 trials (24.8% of early terminations)

  Sample Size at Early Termination:
    Mean: 54.4 patients (SD: 15.5)
    Range: 15 - 75 patients

  Common Patterns in Early Termination:

    Example 1 (Simulation 4, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.067, 0.083, 0.087, 0.099, 0.117
        Efficacy:   0.134, 0.181, 0.199, 0.221, 0.236
        Immune:     0.144, 0.235, 0.244, 0.244, 0.292
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.02, P(Imm>0.20)=0.32
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.07, P(Imm>0.20)=0.75
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.11, P(Imm>0.20)=0.81
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.25, P(Imm>0.20)=0.81
        Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.36, P(Imm>0.20)=0.95

    Example 2 (Simulation 5, Stage 4):
      Posterior Estimates (Mean):
        Toxicity:   0.096, 0.101, 0.108, 0.110, 0.130
        Efficacy:   0.170, 0.189, 0.203, 0.210, 0.231
        Immune:     0.191, 0.196, 0.196, 0.196, 0.312
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.05, P(Imm>0.20)=0.40
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.09, P(Imm>0.20)=0.43
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.14, P(Imm>0.20)=0.43
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        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.18, P(Imm>0.20)=0.43
        Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.32, P(Imm>0.20)=0.93

    Example 3 (Simulation 6, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.090, 0.102, 0.110, 0.113, 0.127
        Efficacy:   0.153, 0.187, 0.194, 0.200, 0.224
        Immune:     0.243, 0.245, 0.248, 0.249, 0.256
      Admissibility Probabilities:
        Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.03, P(Imm>0.20)=0.83
        Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.06, P(Imm>0.20)=0.85
        Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.08, P(Imm>0.20)=0.86
        Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.10, P(Imm>0.20)=0.87
        Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.26, P(Imm>0.20)=0.89

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 305 trials (38.2% of completed trials)

--- C_poc = 0.95 ---

Overall Statistics:
  - Total simulations: 1000
  - Early terminations: 239 (23.9%)
  - Completed trials: 761 (76.1%)

  Early Termination by Stage:
    Stage 1: 1 trials (0.4% of early terminations)
    Stage 2: 32 trials (13.4% of early terminations)
    Stage 3: 62 trials (25.9% of early terminations)
    Stage 4: 75 trials (31.4% of early terminations)
    Stage 5: 69 trials (28.9% of early terminations)

  Sample Size at Early Termination:
    Mean: 56.2 patients (SD: 15.5)
    Range: 15 - 75 patients

  Common Patterns in Early Termination:

    Example 1 (Simulation 7, Stage 5):
      Posterior Estimates (Mean):
        Toxicity:   0.066, 0.079, 0.090, 0.096, 0.114
        Efficacy:   0.228, 0.230, 0.233, 0.235, 0.244
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      Immune:     0.132, 0.142, 0.180, 0.194, 0.206
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.29, P(Imm>0.20)=0.11
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.30, P(Imm>0.20)=0.14
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.33, P(Imm>0.20)=0.34
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.34, P(Imm>0.20)=0.43
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.42, P(Imm>0.20)=0.51

  Example 2 (Simulation 8, Stage 4):
    Posterior Estimates (Mean):
      Toxicity:   0.075, 0.090, 0.099, 0.104, 0.121
      Efficacy:   0.200, 0.204, 0.209, 0.212, 0.223
      Immune:     0.118, 0.149, 0.173, 0.192, 0.205
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.12, P(Imm>0.20)=0.12
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.13, P(Imm>0.20)=0.21
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.15, P(Imm>0.20)=0.29
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.17, P(Imm>0.20)=0.40
      Dose 5  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.25, P(Imm>0.20)=0.49

  Example 3 (Simulation 17, Stage 5):
    Posterior Estimates (Mean):
      Toxicity:   0.073, 0.088, 0.095, 0.108, 0.274
      Efficacy:   0.242, 0.333, 0.339, 0.400, 0.477
      Immune:     0.168, 0.174, 0.175, 0.177, 0.179
    Admissibility Probabilities:
      Dose 1  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.49, P(Imm>0.20)=0.21
      Dose 2  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.93, P(Imm>0.20)=0.24
      Dose 3  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.94, P(Imm>0.20)=0.25
      Dose 4  : P(Tox<0.30)=1.00, P(Eff>0.25)=0.99, P(Imm>0.20)=0.26
      Dose 5  : P(Tox<0.30)=0.63, P(Eff>0.25)=1.00, P(Imm>0.20)=0.27

  Completed Trials Analysis:
    Mean sample size: 75.0 patients (SD: 0.0)
    PoC validated: 274 trials (36.0% of completed trials)

================================================================================
4. RECOMMENDATIONS
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Based on the calibration results:

1.   Type I Error Control Status: NOT ACHIEVED
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   Selected C_poc = 0.95 (largest tested)
     WARNING: This still exceeds the 10% target!
   Achieved Type I error rate: 27.4% (target:  10%)
   RECOMMENDATION: Test higher C_poc values (e.g., 0.96, 0.97, 0.98, 0.99)

2. Expected Trial Characteristics:
   - Early termination rate: 23.9%
   - Trial completion rate: 76.1%

3. Next Steps:
   - Validate calibration with alternative scenarios
   - Test performance in signal scenarios
   - Consider sensitivity analysis for key parameters

================================================================================
                            END OF REPORT
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... (see full report file for complete details) ...
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