

Automatically Labeling \$200B Life-Saving Datasets: A Large Clinical Trial Outcome Benchmark

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Abstract

The global cost of drug discovery and development exceeds \$200 billion annually. The main results of drug discovery and development are the outcomes of clinical trials, which directly influence the regulatory approval of new drug candidates and ultimately affect patient outcomes. Despite their significance, large-scale, high-quality clinical trial outcome data are not readily available to the public. Suppose a large clinical trial outcome dataset is provided; machine learning researchers can potentially develop accurate prediction models using past trials and outcome labels, which could help prioritize and optimize therapeutic programs, ultimately benefiting patients. This paper introduces Clinical Trial Outcome (CTO) dataset, the largest trial outcome dataset with around 479K clinical trials, aggregating outcomes from multiple sources of weakly supervised labels, minimizing the noise from individual sources, and eliminating the need for human annotation. These sources include large language model (LLM) decisions on trial-related documents, news headline sentiments, stock prices of trial sponsors, trial linkages across phases, and other signals such as patient dropout rates and adverse events. CTO's labels show unprecedented agreement with supervised clinical trial outcome labels from test split of the supervised TOP dataset [11], with a 91 F1.

1 Introduction

A clinical trial is an indispensable step toward developing a new drug, involving human participants to test the drug's efficacy and safety for treating target diseases. In 2022, drug discovery and development spending reached 244 billion dollars globally [38]. Among which, the clinical trial market reached \$44.3 billion in 2020 and is expected to grow to \$69.3 billion by 2028 [33]. Low efficacy, safety issues, and poor trial protocol design can lead to trial failures [10, 37, 25]. Eroom's

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Law² shows that the number of new FDA-approved drugs per billion US dollars of R&D spending has halved approximately every nine years since 1950, even with inflation adjustment [35]. Given these challenges, predicting trial outcomes in silico—using computational methods—could significantly enhance drug discovery efficiency.

Surprising challenge: Despite the significant effort and resources invested in clinical trials, it is surprising that trial outcomes are not readily available for all trials. While some trial results have been published, many do not have publications available, and connecting the trials across different phases is also challenging. This lack of high-quality trial outcome labels presents a major obstacle in creating predictive models related to trial outcomes, which could potentially optimize the drug development process and improve patient outcomes. Furthermore, the FDA does not release the clinical trial ID (NCTID) in documents of approved drug applications.

Public data sources, such as the ClinicalTrials.gov database with more than 400,000 historical trials [34, 46, 47], provide vital information for identifying trial outcome labels. Other valuable resources include the Food and Drug Administration (FDA) National Drug Code (NDC) directory [9], which offers a comprehensive set of drug approvals and their codes, and the DrugBank [44, 23] database, which contains biochemical descriptions of many drugs and their indications. However, these resources are not connected, and the lack of direct links between clinical trials, drug application processes, and different phases of drug interventions makes it difficult to obtain clear trial outcome labels. The absence of a centralized, easily accessible database that consolidates clinical trial outcomes, drug approvals, and intervention phases poses a significant challenge for researchers and drug developers. This fragmented landscape of information hinders the development of accurate predictive models and can slow down the drug discovery and development process.

Trial Outcome Definitions Clinical trial outcomes are multifaceted and have diverse implications. These outcomes can involve meeting the primary endpoint as defined in the study, advancing to the next phase of the trial, obtaining regulatory approval, impacting the financial outcome for the sponsor (either positively or negatively), and influencing patient outcomes such as adverse effects and trial dropouts. Our paper follows the previous conventions [11, 41, 10, 24, 1] and defines the trial outcome as a binary indicator, showing whether the trial achieves its primary endpoints and can progress to the next stage of drug development. For Phase 1 and 2 trials, success may mean moving to the next phase, such as from Phase 1 to Phase 2, and from Phase 2 to Phase 3. In Phase 3, success is measured by regulatory approval.

Recently, initial efforts have been made to forecast specific aspects of clinical trials to enhance their outcomes. These efforts include employing electroencephalographic (EEG) measures to predict the effects of antidepressant treatments [30], optimizing drug toxicity predictions based on drug and target properties [16], and using phase II trial results to anticipate phase III trial outcomes [29]. Additionally, there is a growing interest in developing comprehensive methods for predicting trial outcomes. For example, predicting drug approvals for 15 disease groups by analyzing drug and clinical trial features using classical machine learning techniques [24], using multimodal drug structure and text information to predict outcomes based on a supervised set of data [11], an algorithm that computes the probability of technical success via asking experts a standardized questionnaire [43], and multimodal trial outcome prediction via omics, text, clinical trial design, and small molecule properties [1]. Despite these efforts, several limitations still impede the utility of existing trial outcome prediction models. Namely—the lack of transparency in the clinical trial labeling process. Fu et al. [11] is one example of a publicly available expert-curated clinical trial dataset. However, it is also quite limited because it only contains 17,538 human-labeled interventional small-molecule drug trials, out of around 400,000 total trials. To date, we are unaware of any other large-scale, publicly available, open-source (fully reproducible) effort to compute trial outcome labels.

We state our contributions as follows:

- We propose CTO, the first large-scale, publicly available, open-sourced, and fully reproducible dataset of clinical trial outcomes derived from multiple sources of weakly supervised labels, including trial phase linkages, LLM interpretations of trial-related publications, news headline sentiments, stock prices of trial sponsors, and other trial metrics.

²reverse of “Moore’s Law”

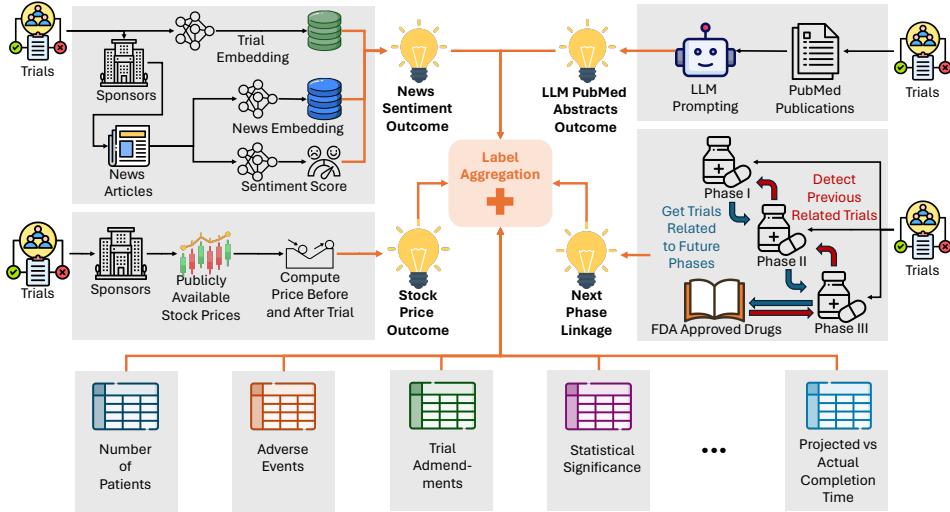


Figure 1: CTO integrates various data sources to generate labels for predicting clinical trial outcomes. Data sources include (1) News articles, from which trial embeddings and sentiment scores are derived; (2) Publicly available stock prices, used to compute price changes before and after trials; (3) PubMed abstracts, where LLMs are prompted to predict the trial outcome; and (4) trial phase linkage. Additional sources of outcomes include trial metrics such as the number of patients, adverse events, etc.

- CTO demonstrates significant agreement with published trial outcome results, achieving promising results with a 94 F1 score on Phase 3 trials and 91 F1 score on all phase trials compared to humanly annotated clinical trial outcomes.
- We provide all code³ and data in a reproducible and easily extendable format, allowing for calculating predicted labels for new trials. Additionally, we aggregate trial-related data, such as ICD coding, drug mapping, and publications, facilitating secondary applications and benchmarking current outcome prediction models.

1.1 Related Work

Table 1: This table describes an overview of selected recent trial outcome prediction work. All previous work relies on industry sponsors to obtain labels, and most are not easily accessible. We are the first to aggregate publicly available data sources on a large number of trials.

Dataset	Data Sponsor	Subset	# Trials	Labeling Method	Publicly Available
Lo et al. [24]	TrialTrove, Pharmaprojects	Phase II, III	19,136	Human Expert	✗
Feijoo et al. [7]	Biomedtracker	Industry Phase II, III	6,417	Manual linking	✗
Aliper et al. [1]	Insilico Medicine	Phase II	55,653	Biomedical KG, Trial stats	✗
Willigers et al. [43]	AstraZeneca	AstraZeneca Phase III	57	Human Expert	✗
TOP [11]	IQVIA	Small Molecule Drugs	17,538	Human Expert	✓
CTO (ours)	Publicly Collected	All	479,761	Publications, News, Trial linking, Stocks, Trial stats, Etc	✓

Predicting clinical trial outcomes is often led by industries with the capacity for extensive data curation. Informa’s TrialTrove [39] is widely used, containing around 20,000 trials [24]. AstraZeneca has developed structured feedback forms to improve Phase 3 trial success annotations [43]. Feijoo et al. [7] demonstrated that using Random Forest on Biomedtracker, a proprietary dataset aggregating company reports, results in strong outcome prediction performance.

Previous studies have tackled clinical trial outcome prediction using various methods. Early work employed statistical analysis [26] and ML models on limited private data sets (<500 samples) [6].

³<https://github.com/chufangao/CTOD/>

In drug toxicity prediction, Gayvert et al. [12] used Random Forest to predict outcomes based on chemical properties, while Artemov et al. [3] used Multilayer Perceptrons for Phase I/II trials. Lo et al. [24] applied KNN imputation and Random Forest on features from Pharmaprojects and TrialTrove. Additionally, Phase 2 to Phase 3 prediction was explored by Qi et al. [29] through clinical trials and by Aliper et al. [1] using experts, GPT-3.5, and a biomedical knowledge graph.

Fu et al. [11] released the first publicly available clinical trial outcome dataset based on manual curation. Train and test data splits were selected as all trials completed before 2014 and afterward respectively. After preprocessing and cleaning, the final number of trials in train, validation, and test datasets was reduced to $17,538 \rightarrow 12,465$ trials, which was only around 4% of all available trials at the time of publication⁴. Table 1 summarizes recent trial outcome work.

2 CTO Overview

Our main methodology is outlined in Figure 1. We overview our primary sources of outcome predictors—LLM prediction on Pubmed Abstracts, Trial Linkage, News Headlines, Stock Price, and finally, Trial Metrics computed from clincialtrials.gov. These metrics are computed independently and are aggregated via weakly supervised label aggregation.

2.1 LLM Predictions on PubMed Abstracts

PubMed abstracts have been automatically linked to trials by the Clinical Trials Transformation Initiative (CTTI)[5, 40, 2] as well as other efforts [17]. First, We extracted all PubMed abstracts for each trial through the NCBI API⁵ and the statistics of the extracted abstracts are given in the supplementary D.3. These abstracts can be categorized into 1) Background, 2) Derived, and 3) Results. Since we are interested in clinical trial outcomes, we only utilized abstracts in the Derived and Results categories. As many trials had multiple abstracts, we selected the top 2 abstracts based on their title similarity to the trial’s official title to provide the most relevant information.

Given these abstracts, we prompted the ‘gpt-3.5-turbo’ model to summarize important trial-related statistical tests and predict the outcome. Additionally, we prompted the LLM to generate QA pairs about the trial, which are provided as a supplement B.3 to our benchmark. The prompts are provided in the supplementary F.

2.2 Trial Linkage

The journey of a drug from discovery to FDA approval involves several stages, beginning with Phase 1 trials to assess safety and dosage. Subsequent Phase 2 and 3 trials evaluate efficacy and compare the new drug to existing therapies. Upon completing Phase 3, a drug may be submitted for FDA approval. A key limitation of the CITI dataset is the lack of connectivity between trial phases, which could significantly enhance the ability to analyze trial progression and outcomes based on advancement to subsequent phases. Moreover, linking trials across phases is not straightforward due to challenges, including unstructured data, inconsistent reporting standards, missing information, data noise, and discrepancies in intervention details across phases. Despite these challenges, linking trials can be invaluable, particularly as a source of weak labels in clinical trial outcome prediction tasks. This section presents our novel trial-linking algorithm, which, to our knowledge, is the first attempt to systematically connect different phases of clinical trials. The trial linkage extraction process consists of two primary steps: 1) Linking trials across different phases, as illustrated in Figure 2B, and 2) Matching phase 3 trials with FDA approvals, as shown in Figure 2C.

Linking of Clinical Trials Across Phases The progression of clinical trials through phases are not all strictly sequential from Phase 1 to Phase 3, as some studies may combine multiple phases. Many trials were categorized as ‘Not Applicable’ or were missing phase information entirely; these were excluded from our analysis. We created a phase connection map, illustrated in Figure 2A, that covers all phase categories present in the dataset. Our linking algorithm begins with the later phases and traces back to earlier phases. This approach is based on the assumption that a trial in a subsequent

⁴and around 3% as of June 2024

⁵<https://ncbi.nlm.nih.gov/>

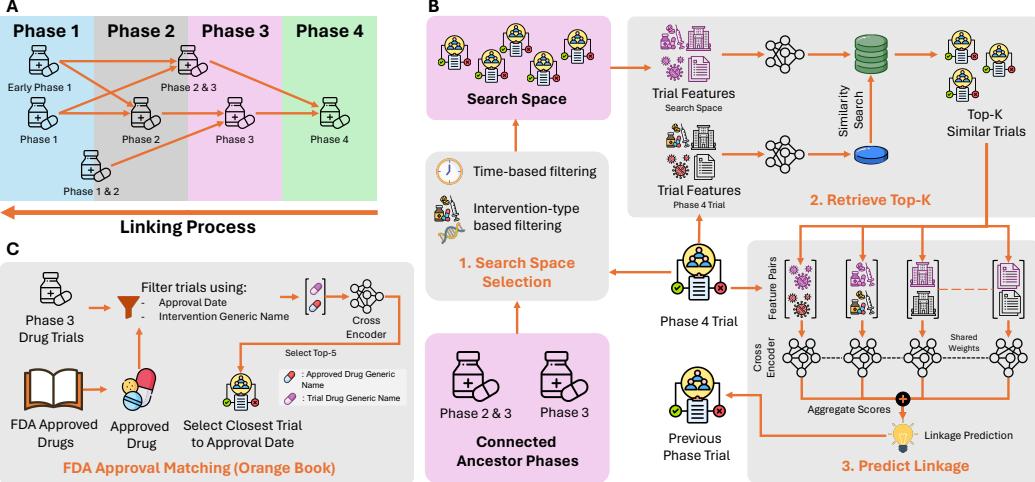


Figure 2: Overview of trial linkage algorithm. A) Illustrates the phase connection map, covering all the phase categories present in the dataset. B) Linking trials across phases based on completion dates and intervention types, disease, and other trial data. We 1) constraint the search space, then 2) retrieve top-K most similar past trials using embeddings similarity. Finally, 3) a cross-encoder re-ranking strategy predicts linkages by scoring likely pairs. C) Matching FDA-approved drugs from FDA orange book to Phase 3 and Phase 2 & 3 drug trials.

phase implies the success and existence of a corresponding trial in a preceding phase. Phase 3 trials are considered a success if a Phase 4 trial is found or if it is linked to an FDA new drug application.

The trial linkage process consists of three main steps: 1) Selection of the search space, 2) Retrieval of the top K most similar past trials, and 3) Prediction of linkage. In Figure 2B, we illustrate an example of linking a Phase 4 trial to its preceding phases. For a given trial x , the objective is to identify its predecessor among trials in its directly linked earlier phases. For instance, the directly linked earlier phases of Phase 4 are Phase 3 and Phase 2&3.

1. Search space selection: We filter the trials based on their completion dates relative to the start date, ensuring that any linkage candidate must have concluded before the start of x . Furthermore, we also consider intervention types such as ‘Drug’, ‘Biological’, ‘Device’, etc.

2. Retrieve top-K: From the filtered search space Z , we retrieve top-32 most similar past trials to x . We extract key features and encode them into dense embedding using PubMedBERT [14] to represent both x and trials in the search space ($z^i \in Z$) as follows: $x = \{x_I, x_C, x_T, x_S, x_E\}$, $z^i = \{z_I^i, z_C^i, z_T^i, z_S^i, z_E^i\}$. Where the subscript I denotes intervention or drug, C denotes condition or targeted disease, T denotes official trial title, S denotes trial summary, and E denotes eligibility criteria. We calculate similarity as: $\text{similarity}(x^i, z^i) = \sum_{j \in F} \frac{x^i \cdot z_j^i}{\|x^i\| \|z_j^i\|}$, where $F = \{I, C, T, S, E\}$.

We excluded the lead sponsor as a feature since the sponsor often changes depending on funding and performs worse empirically (Appendix E).

3. Predict linkage Given the large search space, we employ a re-ranking strategy using a cross-encoder pre-trained on MS-MARCO [4]. We provide feature pairs as input to the cross-encoder as follows: $\text{Cross-encoder score}(x^i, z^i) = \sum_{j \in F} g_\theta(x^i, z_j^i)$. Based on the cross-encoder scores, we predict the linkage by considering the trials with the highest positive cross-encoder scores as the most probable previous phase trials of x .

We apply this process for all trials in Phase 4, Phase 3, Phase 2 & 3, and Phase 2 to extract the trial linkages. To extract the outcome labels, we start with trials in the earlier phases and label them based on the existence of linked trials in the subsequent phases. However, trials in Phase 3 and Phase 4 have some exceptions to this process. For Phase 4 trials, there are no following trial phases, so we exclude them from the extracted weak labels. As for Phase 3 trials, they can be successful even without the existence of a subsequent Phase 4 trial. This highlights the importance of matching Phase 3 trials with their corresponding FDA approvals if they exist.

Matching Phase 3 trials with FDA approvals After establishing connections across different phases of clinical trials, we focus on matching the Phase 3 trials to drug approvals to obtain their outcome labels. We utilize the FDA Orange Book⁶ version as of April 2024. Specifically, we use the approval date and drug name provided in the ‘product.txt’ file, as the other files do not contain the relevant information required for the matching process. In this process, we only consider drug-related trials in Phase 3 and Phase 2 & 3 since the Orange Book solely comprises FDA-approved drugs. For a given FDA-approved drug, we first filter Phase 3 and Phase 2 & 3 trials based on the approval date and intervention generic name, retaining trials completed between 2 years and 2 months prior to the approval date to align with the FDA approval process timeline. Similar to trial linkage prediction, we provide the drug’s generic name and the trial’s intervention generic name as input pairs to a cross-encoder, predicting their similarity. We select the top 5 trials based on cross-encoder scores and match the FDA approval to the trial with the completion date closest to the approval date. We then update the previously extracted outcomes for Phase 3 and Phase 2 & 3 trials, labeling them as successful if matched to an FDA approval or having a linked Phase 4 trial.

2.3 News Headlines

News headlines were obtained via the following steps: **1. Web Scraping:** We sent requests to Google News for headlines regarding the top 1000 industry sponsors, which accounted for around 80% of the industry-sponsored trials (27,720 trials). Due to rate limitations, we limit our requests to a rate of around 1 query every 3-5 seconds. To obtain the widest range of news, we search each sponsor’s name and obtain up to 100 articles for every month, starting from the sponsor’s earliest clinical trial to the current day. We retrieved a total of 1,115,017 news articles. **2. News Sentiment Classification:** We utilize FinBERT [45] to obtain financial news sentiment (‘Positive’ or ‘Negative’ with a confidence score between 0 and 1) for every headline. We drop the ‘Neutral’ sentiment as it is irrelevant for our task. **3. News / Trial Matching:** Similar to Trial Linkage, we adopt a similar strategy of filtering using a top-K retriever and reranking using a cross-encoder. Trials are encoded with $x = \{x_1, x_C, x_T, x_S\} \rightarrow z^i$, and headlines are encoded as h^i . We use PubMedBERT to encode both trials and headlines and follow the steps in trial linkage to obtain relevancy scores. We consider all headline sentiments with relevance scores larger than the mean score and take the mode of the sentiment predictions.

2.4 Stock price

The stock price of a pharmaceutical or biotech company often reflects market expectations. If investors expect positive results, the stock may rise in anticipation of the trial’s completion. Conversely, if expectations are low or if previous trials have been unsuccessful, the stock may not perform as well. We utilized Yahoo finance⁷ to collect historical stock market data for companies that have publicly available tickers for completed trials. By averaging the stock prices over a specified time frame, the moving average reduces the noise caused by random, short-term price movements, making it easier to identify the underlying trend [19, 36]. A 5-day simple moving average (SMA) of a stock’s price is calculated by taking the average of the closing prices for the last 5 trading days. As shorter periods reveal shorter-term trends, we selected a 5-day SMA to capture the immediate short-term impact of the completion of clinical trials. A positive slope indicates an uptrend, while a negative slope indicates a downtrend in the SMA line [36]. The absolute value of the slope represents the steepness of the trend. We calculated the slope for a 7-day window starting at a clinical trial’s ‘completion date’.

2.5 Clinical Trial Metrics

We utilize the CTTI dataset to obtain preprocessed tables of trial details (e.g. eligibility criteria, statistics, linked references⁸) [5, 40, 2]. Specifically, we utilize the following information. (1) Whether results were reported, (2) The number of sponsors, (3) The number of patients, (4) The patient dropout rate, (5) The number of sites or locations for the trial, (6) Whether the P-value < 0.05, (7) The date at which the trial was last updated vs its completion date, (8) Number of deaths,

⁶<https://fda.gov/drugs/drug-approvals-and-databases/orange-book-data-files>

⁷<https://pypi.org/project/yfinance/>

⁸<https://aact.ctti-clinicaltrials.org>

(9) Number of serious adverse events, (10) Number of *any* adverse events, (11) The status of the trial e.g. terminated/withdrawn/completed/etc, and finally, (12) The number of amendments made to the trial page. Please see Appendix C.2 for in-depth discussions for a discussion on how trial outcomes are linked to these metrics.

Each of these metrics is treated as a weakly supervised Labeling Function (LF). For most of these metrics, we consider the "good" outcome as having greater or less than the median of that metric. For example, in the *Serious Adverse Events LF*, we predict "1" if a trial's number of serious adverse events is less than the overall median number of serious adverse events. Otherwise, we predict "0". While choosing a highly specific threshold could be better than choosing the median, we note that LFs in the data programming framework (as we describe in the next section) do not have to be perfect, only better than random for data programming to work well.

2.6 Weakly Supervised Label Aggregation

We integrate multiple sources of weak supervision to select highly confident predictions from the previous step of relation prompting. Data programming is a framework designed to create denoised pseudo-labels from various weak supervision sources via labeling functions and matrix completion [32, 31].

A labeling function (LF) is a noisy heuristic that either assigns labels to unlabeled data or abstains from making a prediction. For example, `f(text) = return SPAM if "HTTP" in-text else ABSTAIN` is a labeling function used for spam detection. The main idea is that LFs that agree more with other LFs should be weighted higher, and given more weight in the final label prediction. Further details are introduced in Appendix C.1. To demonstrate the superiority of this approach, we also compare with *Majority Vote* baseline, where it simply takes the mode prediction of non-abstaining label prediction on any given data point. Finally, since we have train/test splits on TOP data, we can utilize these ground truth labels to enable a classification-like approach to weakly supervised label aggregation i.e. training a classifier to predict true labels from weakly supervised output. We use the Random Forest classifier for this task and ensure that no data leakage occurs by only training on the training set of TOP.

In total, we have more than 450k trials with automatically labeled outcomes. However, to enable comparison with the supervised labels in TOP, we analyze our trial labels on the interventional small-drug trials (However, we still release the full set of predicted trials).

3 Results

3.1 Agreement with Human Annotations

Table 2: Agreement of aggregated weak labels with TOP Test. CTO_{MV} denotes Majority Vote, CTO_{DP} denotes Data Programming [32], and CTO_{RF} denotes Random Forest. Note that RF *actively* trained on the training human labels, whereas MV and DP are not.

Phase	CTO_{MV}				CTO_{DP}				CTO_{RF}			
	I	II	III	All	I	II	III	All	I	II	III	All
F1	0.726	0.689	0.904	0.793	0.870	0.856	0.921	0.884	0.913	0.878	0.941	0.909
PRAUC	0.741	0.688	0.891	0.793	0.819	0.755	0.858	0.807	0.856	0.792	0.894	0.843
ROCAUC	0.751	0.717	0.805	0.775	0.848	0.802	0.743	0.804	0.889	0.838	0.815	0.847
κ	0.490	0.430	0.606	0.529	0.700	0.623	0.582	0.646	0.790	0.693	0.710	0.729

We compare our aggregated labels, sourced from various weak labeling methods, against the TOP test set, which is annotated by human experts. The primary goal is to assess the agreement between our labels and the human-annotated labels. To ensure the validity of our analysis, we exclude any trials with a mismatch status between our current dataset and the TOP dataset, as the TOP dataset was annotated using trial data as of 2022. For instance, some trials were labeled as 'Unknown status' during that period, whereas in our updated data, they have been marked as 'completed.' This also highlights that the trial data changes more often, and annotating them manually each time is not feasible.

Table 2 shows that Data Programming completely beats Majority Vote in terms of agreement with the TOP dataset. Random Forest obtains the highest scores with a Cohen kappa κ on all phases of 0.729, indicating substantial agreement [27]. Additionally, the F1 score of 0.909 is much higher than any previous SOTA trial outcome prediction model [11, 41]. Figure 3 also shows that models trained on CTO data performs just as well as those trained on ground truth human annotations.

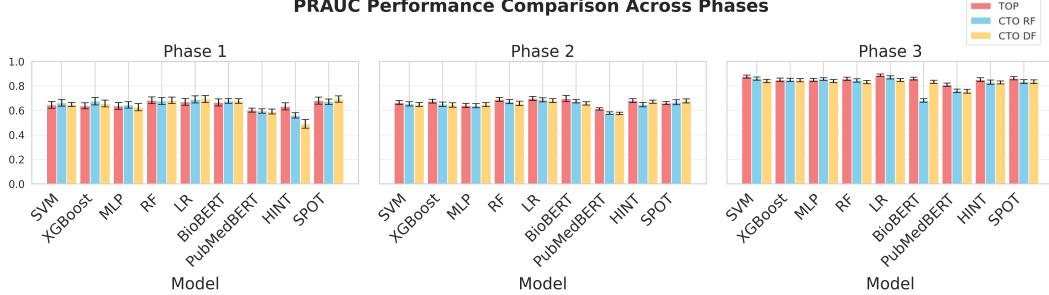


Figure 3: Comparison of PRAUC performance on the TOP test set with models trained on CTO_{RF} , CTO_{DP} , and ground truth, respectively. We see that the quality of the models using both of our labeling strategies performs similarly to TOP’s training labels, and even occasionally exceeds them.

3.2 Which Labeling Method to Use?

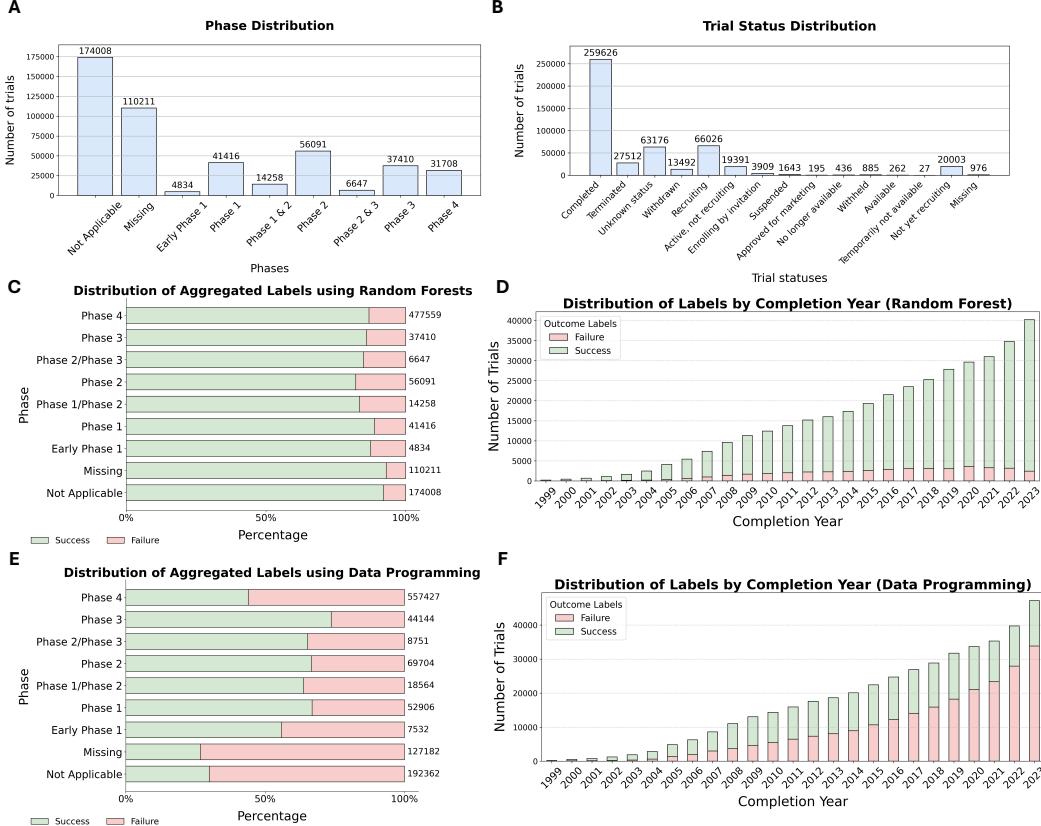


Figure 4: Overview of the phases, statuses and labels of CTO dataset. A) illustrates the distribution of phases within the dataset, highlighting the proportion of each phase. B) presents the distribution of trial statuses, showing how different statuses are represented in the dataset. C) and E) depict the distributions of labels per phase, using random forests and data programming as labeling functions, respectively. D) and F) display the distributions of labels by completion year, also utilizing random forests and data programming as labeling functions. Trials <2000 due to their small number.

Determining the better labeling method is subjective and depends on various factors. Figure 4 illustrates the distribution of labels generated by the random forest and data programming labeling functions, showing a significant distribution difference from that of Data Programming (RF predicts almost all trials to be successful). This discrepancy can be attributed to the nature of the random forest labeling function, which relies on a small-scale, human-annotated set that might not capture the overall trial distribution. However, this leads to better agreement with the TOP test set than with data programming.

On the other hand, data programming is an unsupervised approach that generates labels by considering the agreement and relationships between all weak labeling functions across the entire dataset. This approach allows data programming to more accurately learn the trial outcome label distribution. Due to this challenge, we provide both labels from the random forests and the data programming labeling function in our dataset release. Additionally, Figure 4 A and B illustrate the distribution of labels across phases and trial statuses in our proposed CTO dataset. This highlights the sheer quantity of the dataset compared to previous methods.

4 Discussion

We present the first attempt to utilize weak signals to automatically label a large-scale, reproducible dataset specifically designed for clinical trial outcome prediction. Our dataset and labels facilitate the development of prediction models not only for drug interventions but also for biologics and medical devices, broadening the scope of clinical trial outcome research. Our models consistently perform comparably to baseline models across all phases and metrics when benchmarked against TOP, underscoring the effectiveness of weak supervision and the reliability of our approach. We recognize that automatically created labels will never be a substitute for human ones. However, for data-hungry new ML methods in clinical trial optimization, we assert that this could be a good first step before obtaining human labels, due to our high agreement. In addition, our open-source nature means that any customization to specific tasks can be made quickly and reproducible. Our dataset will be made available at <https://github.com/chufangao/CTOD>.

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Checklist

1. For all authors...
 - (a) Do the main claims made in the abstract and introduction accurately reflect the paper's contributions and scope? **[Yes]**
 - (b) Did you describe the limitations of your work? **[Yes]** See Conclusion
 - (c) Did you discuss any potential negative societal impacts of your work? **[Yes]**
 - (d) Have you read the ethics review guidelines and ensured that your paper conforms to them? **[Yes]**
2. If you are including theoretical results...
 - (a) Did you state the full set of assumptions of all theoretical results? **[N/A]**
 - (b) Did you include complete proofs of all theoretical results? **[N/A]**
3. If you ran experiments (e.g. for benchmarks)...
 - (a) Did you include the code, data, and instructions needed to reproduce the main experimental results (either in the supplemental material or as a URL)? **[Yes]**
 - (b) Did you specify all the training details (e.g., data splits, hyperparameters, how they were chosen)? **[Yes]**
 - (c) Did you report error bars (e.g., with respect to the random seed after running experiments multiple times)? **[Yes]**
 - (d) Did you include the total amount of compute and the type of resources used (e.g., type of GPUs, internal cluster, or cloud provider)? **[Yes]**
4. If you are using existing assets (e.g., code, data, models) or curating/releasing new assets...
 - (a) If your work uses existing assets, did you cite the creators? **[Yes]**
 - (b) Did you mention the license of the assets? **[Yes]**
 - (c) Did you include any new assets either in the supplemental material or as a URL? **[Yes]**
 - (d) Did you discuss whether and how consent was obtained from people whose data you're using/curating? **[N/A]** We are using public data.
 - (e) Did you discuss whether the data you are using/curating contains personally identifiable information or offensive content? **[N/A]**
5. If you used crowdsourcing or conducted research with human subjects...
 - (a) Did you include the full text of instructions given to participants and screenshots, if applicable? **[N/A]**
 - (b) Did you describe any potential participant risks, with links to Institutional Review Board (IRB) approvals, if applicable? **[N/A]**
 - (c) Did you include the estimated hourly wage paid to participants and the total amount spent on participant compensation? **[N/A]**

A Ethics and Broader Impacts

Using a weakly supervised dataset for clinical trial outcome prediction with large language models (LLMs) can potentially decrease the reliability of the model’s predictions if not correctly instantiated with proper labeling functions. Weak supervision may result in incomplete or imprecise labeling, leading to the model learning incorrect associations and missing crucial factors, which can introduce or exacerbate biases. This lack of precise guidance can also cause the model to overfit to noise or incorrect patterns in the training data, reducing its ability to generalize effectively to new, unseen data. In diverse clinical scenarios, one must take care to independently verify model predictions to prevent potentially jeopardizing patient safety with inaccurate predictions. To mitigate these issues, it’s essential to improve the quality of the training data through better labeling techniques, supplementary high-quality data, or advanced methods like semi-supervised or active learning.

Furthermore, we use publicly available data, so the risk of identification is minimized. However, we recognize that LLMs on public data inherently still pose some privacy risks.

Reproducibility We utilized an AMD EPYC 7513 32-core Processor with 100 GB of RAM to run our experiments. Running Data Programming with less or more powerful systems may impact speed. For us, obtaining the labels took around 25 hours in experiments and prototyping. Additionally, we made use of ChatGPT for writing as well as obtaining trial outcome prediction on the PubMed abstracts. Total cost was around \$200 US dollars.

Contents

A Datasheet for Datasets	14
B Additional Results and Contributions	18
B.1 Results on TOP test data	18
B.2 Results on Pre-2020 Split vs Post-2020 Split	18
B.3 Additional Contributions	20
C Label Creation Continued	20
C.1 Data Programming	20
C.2 Weakly Supervised Labeling Functions	21
C.3 Phase-Specific Thresholding	22
D CTO Statistics	23
D.1 Labeling Function Statistics	23
D.2 Statistics on Trial Linkage	25
D.3 Statistics on LLM Predictions	25
D.4 Pair-wise Agreement Between Labeling Functions	26
E Ablation on Features for Trial Linkage	28
F Prompts for LLM Predictions on PubMed Abstracts	29
G Case studies	32
G.1 Case study 1	32
G.2 Case study 2	32
H User Manual: Instructions to Generate and Use CTO	32
H.1 Instructions to Generate Clinical Trial Linkage	32
H.2 Instructions to Obtain LLM Predictions on PubMed Abstracts	33
H.3 News Headlines	34
H.4 Stock Price	35
H.5 Running Baselines	35

A Datasheet for Datasets

A.1 Motivation

- **For what purpose was the dataset created?**

We created CTO to democratize clinical trial outcome prediction, which was previously only available to industry-sponsored researchers. Furthermore, we attempt to expand the previous labeling efforts (which were primarily focused on small drug interventions) and predict labels on all trials.

- **Who created the dataset (e.g., which team, research group) and on behalf of which entity (e.g., company, institution, organization)?**

The authors of this paper.

- **Who funded the creation of the dataset? If there is an associated grant, please provide the name of the grantor and the grant name and number.**

This work was supported by NSF award SCH-2205289, SCH-2014438, and IIS-2034479.

A.2 Composition

- **What do the instances that comprise the dataset represent (e.g., documents, photos, people, countries)?**

CTO contains molecule SMILES strings, eligibility criteria, ICD Codes, drug names, diseases, study status, phase information, and our automatically created labels. Furthermore, we also have additional QA tasks as extracted by GPT 3.5 Turbo 0125, news articles mined for the top 1000 industry sponsors, and stock prices.

- **How many instances are there in total (of each type, if appropriate)?**

There is a total of 479,761 trials, each with multiple types of predicted labels via random forest and data programming, as well as each phase-optimized threshold. For small-molecule drug interventions, we also have SMILES and ICD Codes. We release all such labels to not limit any downstream use. Furthermore, there are a total of 1,115,017 news articles we extracted and 105,570 trials with corresponding QA pairs.

- **Does the dataset contain all possible instances or is it a sample (not necessarily random) of instances from a larger set?**

We provide all possible trial labels up to the beginning of May 2024.

- **What data does each instance consist of?**

CTO contains molecule eligibility criteria, drug names, diseases, study status, phase information, and our automatically created labels.

- **Is there a label or target associated with each instance?**

The automatically predicted label is provided for each question.

- **Is any information missing from individual instances? If so, please provide a description, explaining why this information is missing (e.g., because it was unavailable). This does not include intentionally removed information, but might include, e.g., redacted text.**

No.

- **Are relationships between individual instances made explicit (e.g., users' movie ratings, social network links)?**

No.

- **Are there recommended data splits (e.g., training, development/validation, testing)?**

See Table 4 and Figure 4.

- **Are there any errors, sources of noise, or redundancies in the dataset?**

Automatically created labels inherently come with an element of noise. However, our high agreement with TOP's human labels (up to 0.91 F1), implies that our labels are of high quality.

- **Is the dataset self-contained, or does it link to or otherwise rely on external resources (e.g., websites, tweets, other datasets)?**

CTO depends on multiple open source datasets.

1. CTTI: <https://ctti-clinicaltrials.org/>
2. DrugBank <https://drugbank.com/>
3. PubMed <https://pubmed.ncbi.nlm.nih.gov/>

- **Does the dataset contain data that might be considered confidential (e.g., data that is protected by legal privilege or by doctor-patient confidentiality, data that includes the content of individuals' non-public communications)?**

No. We obtained all data sources via open-source methods.

- Does the dataset contain data that, if viewed directly, might be offensive, insulting, threatening, or might otherwise cause anxiety?
No.
- Does the dataset relate to people?
Yes.
- Does the dataset identify any subpopulations (e.g., by age, gender)?
Yes, but only in the eligibility criteria of the trials, which are public.
- Does the dataset contain data that might be considered sensitive in any way (e.g., data that reveals race or ethnic origins, sexual orientations, religious beliefs, political opinions or union memberships, or locations; financial or health data; biometric or genetic data; forms of government identification, such as social security numbers; criminal history)?
No. There is no reference to individuals.

A.3 Collection process

- How was the data associated with each instance acquired?
We automatically mined each LLM prediction, trial linkage, news headline, and stock price as an overview in Section 2.
- What mechanisms or procedures were used to collect the data (e.g., hardware apparatuses or sensors, manual human curation, software programs, software APIs)?
We mainly used Google Sheets and Python to collect, process, and label the data. In addition, we used OpenAI's ChatGPT (GPT-3.5-turbo 0125) to generate QA and GPT outcome predictions.
- If the dataset is a sample from a larger set, what was the sampling strategy (e.g., deterministic, probabilistic with specific sampling probabilities)?
Some data splitting was done according to previous data splits from TOP <https://github.com/futianfan/clinical-trial-outcome-prediction>. Additionally, we also split the data according to the following dates: $(-\infty, 2018, 2020, \infty)$
- Who was involved in the data collection process (e.g., students, crowd workers, contractors) and how were they compensated (e.g., how much were crowd workers paid)?
The authors of the paper collected and processed the data.
- Over what timeframe was the data collected?
We collected the data between December 2023 and April 2024.
- Were any ethical review processes conducted (e.g., by an institutional review board)?
N/A.
- Does the dataset relate to people?
Yes.
- Did you collect the data from the individuals in question directly, or obtain it via third parties or other sources (e.g., websites)?
N/A.
- Were the individuals in question notified about the data collection?
N/A.
- Did the individuals in question consent to the collection and use of their data?
N/A.
- If consent was obtained, were the consenting individuals provided with a mechanism to revoke their consent in the future or for certain uses?
N/A.
- Has an analysis of the potential impact of the dataset and its use on data subjects (e.g., a data protection impact analysis) been conducted?
The dataset does not have individual-specific information.

A.4 Preprocessing/cleaning/labeling

- Was any preprocessing/cleaning/labeling of the data done (e.g., discretization or bucketing, tokenization, part-of-speech tagging, SIFT feature extraction, removal of instances, processing of missing values)?
N/A.
- Was the “raw” data saved in addition to the preprocess/cleaned/labeled data (e.g., to support unanticipated future uses)?
N/A.
- Is the software that was used to preprocess/clean/label the data available?
Preprocessing, cleaning, and labeling are done via Google Sheets and Python.

A.5 Uses

- Has the dataset been used for any tasks already?
No.
- Is there a repository that links to any or all papers or systems that use the dataset?
No.
- What (other) tasks could the dataset be used for?
Our dataset is designed to promote research primarily in clinical trial outcome prediction. The dataset can also be used for stock price/trend prediction B.3, question answering B.3, etc.
- Is there anything about the composition of the dataset or the way it was collected and preprocessed/cleaned/labeled that might impact future uses?
N/A.
- Are there tasks for which the dataset should not be used?
N/A.

A.6 Distribution

- Will the dataset be distributed to third parties outside of the entity (e.g., company, institution, organization) on behalf of which the dataset was created?
No.
- How will the dataset be distributed?
Since clinical trial data is frequently updated, we provide the code for generating our CTO dataset at <https://github.com/chufangao/CTOD>. The current version of the dataset can be accessed at <https://zenodo.org/doi/10.5281/zenodo.11535960>.
- Will the dataset be distributed under a copyright or other intellectual property (IP) license, and/or under applicable terms of use (ToU)?
The dataset is released under MIT License.
- Have any third parties imposed IP-based or other restrictions on the data associated with the instances?
No.
- Do any export controls or other regulatory restrictions apply to the dataset or to individual instances?
No.

A.7 Maintenance

- Who will be supporting/hosting/maintaining the dataset?
The authors of this paper.
- How can the owner/curator/manager of the dataset be contacted(e.g., email address)?
Contact the corresponding authors (chufan2@illinois.edu & jp65@illinois.edu & trishad2@illinois.edu & jimeng@illinois.edu).

- **Is there an erratum?**
No.
- **Will the dataset be updated (e.g., to correct labeling errors, add new instances, delete instances)?**
If any corrections are needed, we plan to upload an updated version of the dataset along with detailed explanations of the changes.
- **If the dataset relates to people, are there applicable limits on the retention of the data associated with the instances (e.g., were the individuals in question told that their data would be retained for a fixed period of time and then deleted)?**
N/A
- **Will older versions of the dataset continue to be supported/hosted/maintained?**
Primarily, we aim to keep only the latest version of the dataset. However, in specific cases like major updates to the dataset or the necessity to validate previous research with older versions, we will exceptionally retain past versions of the dataset for up to one year.
- **If others want to extend/augment/build on/contribute to the dataset, is there a mechanism for them to do so?**
Contact the authors of this paper or raise a github issue.

B Additional Results and Contributions

B.1 Results on TOP test data

We run standard ML baselines [11], namely Support Vector Machine (SVM), XGBoost, Multilayer Perceptron (MLP), Random Forest (RF), and Logistic Regression (LR). For these models, we model the trial outcome prediction task as a natural language classification task for maximum flexibility without requiring the need for molecular structure. TF-IDF is used to obtain features—the concatenated trial phase, disease indication, ICD codes, drugs, and eligibility criteria $\{x_P, x_I, x_C, x_T, x_S, x_E\}$. Essentially, we use the trial linkage features with the addition of Phase x_P . We additionally utilize PubMedBERT and BioBERT as additional baselines by adding an MLP classification head to the encoder output of the concatenated text. The sizes of our train, validation, and test splits are 47080, 901, and 3165 respectively, with training and validation mined from CTO (trials completed < 2014 as per TOP [11]). We tested on the TOP test data. We demonstrate F1, PR-AUC, and ROC-AUC scores for all baseline models in Table 3.

We observe that models trained on CTO’s labels perform similarly, and even occasionally outperform those trained on supervised TOP. We hypothesize that this is due to a couple of factors. This demonstrates the effectiveness and reliability of our approach in predicting clinical trial outcomes. First, we combine highly diverse sources of LFs, the final predicted labels may serve as additional insights that the human annotators may have otherwise gleaned from fewer sources. Additionally, data programming enforces a level of self-regularization of the LFs, potentially smoothing the labels to allow for improved learning, much like in knowledge distillation’s teacher pseudo-labels [13, 15].

B.2 Results on Pre-2020 Split vs Post-2020 Split

Since Covid changed the landscape of clinical trials due to its disruptive nature, the trial distribution before and after 2020 are quite different (See empirical performance in Table 4). Note that we choose CTO_{DP}, since despite its lower performance on TOP, we believe it has stronger generalizability to all trials, as shown by its proportion of positive and negative outcome label prediction in Figure 4.

The *Pre-2020 Split* consists of trials where their completion dates are before 2018. The test completion dates start in 2018 but are within 2020. This split has 27,245, 6,828, and 6,151 samples in the training, validation, and test sets, respectively. We have another data split, the *Post-2020 Split*. The completion dates of the training trials are before 2020, while the test completion dates are after 2020 but before 2024. This split has 32,200, 8,024, and 12,525 samples in the training, validation, and test sets, respectively.

Note that for post-2020, the training set includes all trials that were completed before 2020 and therefore the entire Pre-2020 dataset.

Table 3: Comparison of baseline models trained on TOP vs CTO labels.

Phase	Model	TOP			CTO_{RF}			CTO_{DP}		
		F1	PRAUC	ROCAUC	F1	PRAUC	ROCAUC	F1	PRAUC	ROCAUC
I	SVM	0.632 \pm 0.019	0.645 \pm 0.028	0.592 \pm 0.023	0.713 \pm 0.015	0.661 \pm 0.027	0.626 \pm 0.021	0.720 \pm 0.010	0.648 \pm 0.017	0.614 \pm 0.013
	XGBoost	0.630 \pm 0.020	0.637 \pm 0.025	0.596 \pm 0.021	0.706 \pm 0.017	0.675 \pm 0.030	0.645 \pm 0.021	0.719 \pm 0.016	0.656 \pm 0.027	0.606 \pm 0.023
	MLP	0.589 \pm 0.023	0.636 \pm 0.028	0.575 \pm 0.022	0.661 \pm 0.019	0.645 \pm 0.026	0.600 \pm 0.018	0.655 \pm 0.020	0.626 \pm 0.030	0.581 \pm 0.024
	RF	0.641 \pm 0.024	0.682 \pm 0.028	0.623 \pm 0.024	0.715 \pm 0.015	0.676 \pm 0.020	0.624 \pm 0.021	0.716 \pm 0.015	0.682 \pm 0.026	0.631 \pm 0.022
	LR	0.656 \pm 0.018	0.669 \pm 0.028	0.631 \pm 0.021	0.715 \pm 0.016	0.690 \pm 0.029	0.656 \pm 0.023	0.726 \pm 0.016	0.693 \pm 0.029	0.660 \pm 0.021
	BioBERT	0.627 \pm 0.022	0.665 \pm 0.029	0.612 \pm 0.023	0.713 \pm 0.015	0.676 \pm 0.019	0.641 \pm 0.020	0.716 \pm 0.016	0.677 \pm 0.019	0.649 \pm 0.015
	PubMedBERT	0.646 \pm 0.014	0.602 \pm 0.017	0.588 \pm 0.015	0.715 \pm 0.014	0.595 \pm 0.018	0.579 \pm 0.013	0.719 \pm 0.015	0.591 \pm 0.020	0.571 \pm 0.012
II	HINT	0.621 \pm 0.022	0.633 \pm 0.029	0.590 \pm 0.025	0.611 \pm 0.020	0.559 \pm 0.022	0.520 \pm 0.031	0.607 \pm 0.021	0.490 \pm 0.035	0.545 \pm 0.026
	SPOT	0.652 \pm 0.025	0.679 \pm 0.029	0.624 \pm 0.028	0.600 \pm 0.016	0.670 \pm 0.022	0.635 \pm 0.016	0.625 \pm 0.029	0.693 \pm 0.026	0.646 \pm 0.027
	SVM	0.672 \pm 0.011	0.664 \pm 0.017	0.626 \pm 0.013	0.715 \pm 0.010	0.653 \pm 0.017	0.617 \pm 0.012	0.720 \pm 0.010	0.648 \pm 0.017	0.614 \pm 0.013
	XGBoost	0.659 \pm 0.013	0.675 \pm 0.016	0.627 \pm 0.014	0.706 \pm 0.011	0.650 \pm 0.018	0.609 \pm 0.014	0.710 \pm 0.012	0.644 \pm 0.018	0.607 \pm 0.014
	MLP	0.615 \pm 0.014	0.640 \pm 0.017	0.599 \pm 0.014	0.671 \pm 0.011	0.638 \pm 0.017	0.601 \pm 0.015	0.673 \pm 0.012	0.647 \pm 0.017	0.599 \pm 0.013
	RF	0.675 \pm 0.011	0.690 \pm 0.016	0.643 \pm 0.014	0.715 \pm 0.010	0.671 \pm 0.017	0.628 \pm 0.013	0.712 \pm 0.011	0.657 \pm 0.018	0.623 \pm 0.014
	LR	0.674 \pm 0.013	0.697 \pm 0.017	0.648 \pm 0.012	0.714 \pm 0.010	0.686 \pm 0.017	0.640 \pm 0.015	0.718 \pm 0.010	0.679 \pm 0.016	0.642 \pm 0.014
III	BioBERT	0.672 \pm 0.016	0.696 \pm 0.025	0.648 \pm 0.015	0.715 \pm 0.007	0.674 \pm 0.014	0.642 \pm 0.014	0.718 \pm 0.007	0.657 \pm 0.014	0.627 \pm 0.014
	PubMedBERT	0.682 \pm 0.010	0.612 \pm 0.010	0.601 \pm 0.009	0.705 \pm 0.009	0.578 \pm 0.010	0.545 \pm 0.010	0.713 \pm 0.009	0.575 \pm 0.010	0.540 \pm 0.006
	HINT	0.654 \pm 0.013	0.680 \pm 0.016	0.632 \pm 0.013	0.708 \pm 0.010	0.647 \pm 0.018	0.627 \pm 0.014	0.713 \pm 0.007	0.670 \pm 0.013	0.635 \pm 0.016
	SPOT	0.681 \pm 0.009	0.660 \pm 0.012	0.617 \pm 0.010	0.601 \pm 0.014	0.666 \pm 0.020	0.625 \pm 0.014	0.608 \pm 0.015	0.677 \pm 0.017	0.622 \pm 0.014
	SVM	0.813 \pm 0.010	0.876 \pm 0.012	0.700 \pm 0.018	0.853 \pm 0.009	0.859 \pm 0.013	0.674 \pm 0.017	0.854 \pm 0.007	0.840 \pm 0.014	0.653 \pm 0.018
	XGBoost	0.813 \pm 0.010	0.849 \pm 0.015	0.674 \pm 0.017	0.852 \pm 0.009	0.848 \pm 0.014	0.666 \pm 0.018	0.855 \pm 0.008	0.846 \pm 0.013	0.659 \pm 0.018
	MLP	0.762 \pm 0.011	0.848 \pm 0.012	0.650 \pm 0.017	0.824 \pm 0.011	0.856 \pm 0.011	0.666 \pm 0.016	0.833 \pm 0.009	0.839 \pm 0.013	0.642 \pm 0.021
III	RF	0.830 \pm 0.009	0.858 \pm 0.013	0.675 \pm 0.015	0.857 \pm 0.008	0.844 \pm 0.014	0.656 \pm 0.018	0.857 \pm 0.009	0.831 \pm 0.014	0.639 \pm 0.017
	LR	0.828 \pm 0.008	0.887 \pm 0.010	0.725 \pm 0.014	0.855 \pm 0.008	0.870 \pm 0.013	0.705 \pm 0.017	0.857 \pm 0.008	0.847 \pm 0.013	0.677 \pm 0.019
	BioBERT	0.838 \pm 0.009	0.859 \pm 0.012	0.696 \pm 0.016	0.854 \pm 0.010	0.681 \pm 0.015	0.848 \pm 0.014	0.855 \pm 0.010	0.833 \pm 0.013	0.650 \pm 0.015
	PubMedBERT	0.850 \pm 0.008	0.809 \pm 0.014	0.650 \pm 0.013	0.852 \pm 0.010	0.759 \pm 0.015	0.531 \pm 0.008	0.855 \pm 0.010	0.756 \pm 0.016	0.522 \pm 0.004
	HINT	0.825 \pm 0.009	0.850 \pm 0.016	0.696 \pm 0.017	0.872 \pm 0.006	0.830 \pm 0.017	0.592 \pm 0.020	0.871 \pm 0.006	0.828 \pm 0.012	0.606 \pm 0.014
	SPOT	0.832 \pm 0.008	0.862 \pm 0.013	0.676 \pm 0.020	0.676 \pm 0.015	0.834 \pm 0.016	0.665 \pm 0.018	0.653 \pm 0.013	0.834 \pm 0.016	0.638 \pm 0.016

We additionally show results from both pre- and post-2020 splits in Table 4. The pre-2020 split shows generally higher performance across all metrics and phases compared to the post-2020 split, indicating that the pre-2020 data is easier to predict. The decline in performance post-2020 can be attributed to the complexities and disruptions introduced by the COVID-19 pandemic, which affected clinical trial operations and outcomes. Overall, these observations suggest that the pre-2020 data offers a more stable and predictable environment for clinical trial outcome prediction and that post-2020 data should require additional consideration.

 Table 4: Performance of baselines on both data splits of CTO for CTO_{DP} . The average difference for pre- and post-2020 is 0.035 F1, 0.056 PRAUC, and 0.029 ROCAUC.

Phase	Model	Pre			Post		
		F1	PRAUC	ROCAUC	F1	PRAUC	ROCAUC
I	SVM	0.744 \pm 0.008	0.632 \pm 0.015	0.556 \pm 0.012	0.664 \pm 0.007	0.516 \pm 0.012	0.528 \pm 0.010
	XGBoost	0.731 \pm 0.008	0.656 \pm 0.013	0.561 \pm 0.012	0.646 \pm 0.007	0.532 \pm 0.012	0.545 \pm 0.009
	MLP	0.673 \pm 0.010	0.614 \pm 0.016	0.545 \pm 0.015	0.583 \pm 0.009	0.518 \pm 0.011	0.532 \pm 0.009
	RF	0.744 \pm 0.008	0.591 \pm 0.014	0.502 \pm 0.011	0.662 \pm 0.006	0.468 \pm 0.009	0.458 \pm 0.009
	LR	0.740 \pm 0.008	0.628 \pm 0.015	0.548 \pm 0.012	0.651 \pm 0.007	0.505 \pm 0.011	0.519 \pm 0.009
	PubMedBERT	0.743 \pm 0.005	0.623 \pm 0.017	0.538 \pm 0.016	0.664 \pm 0.006	0.511 \pm 0.008	0.527 \pm 0.005
	BioBERT	0.743 \pm 0.005	0.613 \pm 0.014	0.522 \pm 0.014	0.664 \pm 0.006	0.476 \pm 0.009	0.490 \pm 0.008
II	SVM	0.862 \pm 0.005	0.795 \pm 0.011	0.574 \pm 0.012	0.849 \pm 0.003	0.781 \pm 0.007	0.569 \pm 0.009
	XGBoost	0.843 \pm 0.005	0.810 \pm 0.009	0.582 \pm 0.012	0.820 \pm 0.004	0.775 \pm 0.008	0.559 \pm 0.008
	MLP	0.784 \pm 0.006	0.790 \pm 0.010	0.569 \pm 0.012	0.750 \pm 0.005	0.765 \pm 0.007	0.545 \pm 0.008
	RF	0.863 \pm 0.005	0.799 \pm 0.009	0.574 \pm 0.011	0.850 \pm 0.004	0.762 \pm 0.008	0.532 \pm 0.009
	LR	0.856 \pm 0.006	0.797 \pm 0.009	0.579 \pm 0.010	0.835 \pm 0.004	0.779 \pm 0.007	0.568 \pm 0.008
	PubMedBERT	0.865 \pm 0.004	0.812 \pm 0.009	0.583 \pm 0.012	0.849 \pm 0.004	0.741 \pm 0.005	0.508 \pm 0.005
	BioBERT	0.865 \pm 0.004	0.829 \pm 0.010	0.603 \pm 0.012	0.849 \pm 0.004	0.779 \pm 0.007	0.563 \pm 0.008
III	SVM	0.910 \pm 0.005	0.863 \pm 0.011	0.560 \pm 0.020	0.912 \pm 0.003	0.864 \pm 0.007	0.563 \pm 0.011
	XGBoost	0.901 \pm 0.006	0.867 \pm 0.010	0.574 \pm 0.020	0.894 \pm 0.004	0.858 \pm 0.009	0.552 \pm 0.015
	MLP	0.841 \pm 0.008	0.851 \pm 0.012	0.551 \pm 0.017	0.825 \pm 0.005	0.846 \pm 0.010	0.523 \pm 0.014
	RF	0.910 \pm 0.005	0.856 \pm 0.011	0.536 \pm 0.019	0.912 \pm 0.003	0.854 \pm 0.007	0.529 \pm 0.014
	LR	0.906 \pm 0.006	0.870 \pm 0.013	0.576 \pm 0.017	0.904 \pm 0.004	0.860 \pm 0.008	0.561 \pm 0.013
	PubMedBERT	0.911 \pm 0.004	0.878 \pm 0.009	0.598 \pm 0.016	0.911 \pm 0.003	0.836 \pm 0.004	0.497 \pm 0.006
	BioBERT	0.911 \pm 0.004	0.892 \pm 0.011	0.631 \pm 0.019	0.911 \pm 0.003	0.870 \pm 0.005	0.585 \pm 0.012

B.3 Additional Contributions

Additional Feature Collection To run the baselines, we needed to collect ICD codes for diseases and SMILES strings [42] for drugs. We collected **ICD10 codes** for the diseases from the NIH Clinical Table Search Service⁹[11]. We additionally collected **SMILES** (Simplified Molecular Input Line Entry System) strings for drugs from DrugBank. We also used NIH PubChem¹⁰ [22, 21, 20] to collect the SMILES we could not find in DrugBank.

Stock Trend Prediction The trend of a stock price is the overall direction in which the price of the stock is moving over a specified period, derived from the historical price data [8]. As discussed in 2.4, we calculated the slope of stock prices. We define trend as the direction of the slope, i.e., positive slope refers to positive trend, and negative slope refers to negative trend. We tried to predict the trend of stock price in the 7-day window starting from a clinical trial’s completion date. Table 5 shows the scores for different ML models for stock trend prediction. We utilized phase, eligibility criteria, diseases, and drugs as features for predicting trend. We get embeddings of the features using BioBERT and use the embeddings as input to the different baseline methods of Table 5.

Table 5: Comparison of model performance metrics for stock trend prediction

Model	Accuracy	ROCAUC	F1
LR	0.5121	0.5314	0.5531
MLP	0.5418	0.5202	0.6620
SVM	0.5441	0.4878	0.6860
RF	0.5040	0.5103	0.5377
XGBoost	0.5013	0.5077	0.5340

QA Dataset In addition to the weak trial outcome labels, we provide a QA dataset on trial publications as an additional contribution. While obtaining LLM predictions on PubMed abstracts, we prompted the model to generate question-answer pairs from the given abstracts. The prompts for generating the QA pairs are provided in the supplementary material (Figure 10). The answers are provided in both short-answer and multiple-choice formats. Examples can be found in the supplementary material (Fig 11 and 12). This QA dataset offers valuable information about the trials, complementing the weak outcome labels. It can be used for various downstream tasks, such as question answering, information extraction, and knowledge base construction related to clinical trials.

C Label Creation Continued

C.1 Data Programming

The full data programming framework is detailed by Ratner et al. [31]. We introduce a small aspect of the framework below. At a high level, the aggregation of weakly supervised labeling functions (LFs) is framed as a dependency graph G_{source} where each LF λ_i is dependently conditioned on the true label Y . In our case, we assume conditional independence of all $\lambda_i|Y$. For this case, the dependency graphs will have observable cliques $O = \{\lambda_i, i \in n_{lf}\} \subset C$, where n_{lf} is the number of labeling functions.

From here, the covariance matrix of an observable subset of the cliques in G_{source} is analyzed, leading to a matrix completion approach for recovering estimated accuracies μ (used in the final label model to predict $P(Y|\lambda)$).

Let $\mu = \mathbb{E}(\psi(C))$ where $\psi(C)$ is a vector of indicator random variables for all combinations of all but one of the labels emitted by each variable in clique C.

The norm of the covariance of observed LFs cliques O and separator set S cliques $Cov(\psi(O) \cup \psi(S))$ can be used to recover μ .

⁹<https://clinicaltables.nlm.nih.gov/>

¹⁰PubChemPy API <https://pubchempy.readthedocs.io/en/latest/>

$$\mathbf{Cov}(\psi(O) \cup \psi(S)) = \Sigma = \begin{bmatrix} \Sigma_O & \Sigma_{OS} \\ \Sigma_{OS}^T & \Sigma_S \end{bmatrix} \quad (1)$$

Its inverse is:

$$K = \Sigma^{-1} = \begin{bmatrix} K_O & K_{OS} \\ K_{OS}^T & K_S \end{bmatrix} \quad (2)$$

Applying block matrix inversion, we get:

$$\begin{aligned} K_O &= \Sigma_O^{-1} + c \Sigma_O^{-1} \Sigma_{OS} \Sigma_{OS}^T \Sigma_O^{-1} \\ c &= (\Sigma_S - \Sigma_{OS}^T \Sigma_O^{-1} \Sigma_{OS}) \end{aligned}$$

Let $z = \sqrt{c} \Sigma_O^{-1} \Sigma_{OS}$, then

$$K_O = \Sigma_O^{-1} + zz^T$$

Solving for z can directly recover estimated accuracies from μ via Algorithm 1 in Ratner et al. [31].

C.2 Weakly Supervised Labeling Functions

In this section, we report all of our LFs and their implementations.

- `results_reported`: 1 if results were reported for a trial. Otherwise, it predicts 0.
- `num_sponsors`: The number of sponsors for a trial. Can be thresholded. It is important to study the impact of single sponsors, multiple sponsors, collaborative partnerships, and public funding. The number and type of sponsors will have a significant impact on the clinical trial process and the overall path of bringing the new drug to market. Sponsors affect all parts of the trial, from funding and resources, regulatory guidance, global reach, operational support, supply chain management, market access and distribution, and risk management.
- `num_patients`: The number of patients for a trial. Can be thresholded. As the clinical trials are conducted with strong statistical power to detect the true effect of the drug and to minimize the risk of committing Type II error (failing to detect the treatment effect that is present or false negatives), number of participants in each respective trial is key aspect of trial success.
- `patient_drop`: The number of patients that drop out during the trial. Can be thresholded. Patients drop out from the clinical trial due to lack of efficacy unintended adverse events or other reasons that could result in unanticipated trial outcomes.
- `sites`: The number of total sites during the trial. Can be thresholded. This also indirectly measures the funding capabilities of the sponsors, much like `num_sponsors`.
- `pvalues`: The total sum of occurrences where the P-value < 0.05 . Can be thresholded in the number of occurrences (the 0.05 threshold remains the same). Most of the p-value < 0.05 suggests the observed effect is statistically significant and helpful to reject the null hypothesis.
- `update_more_recent`: The difference in the date at which the trial was last updated vs its completion date. Can be thresholded. The time gap can provide critical insights into the trials' post-completion process and transparency. Identifying delays is helpful for trial success, as it could be due to data analysis and validation, regulatory review, and publication process. A highly amended trial could indicate success due to the large amount of publications.
- `death_ae`, `serious_ae`, `all_ae`: Represents the number of deaths, serious adverse events, and total adverse events, respectively. Can be thresholded. The total number of adverse events (AEs), serious adverse events (SAEs), and deaths in a clinical trial can provide important safety information about the investigational treatment. However, the significance of these numbers depends on various factors, including the size and duration of the trial, the nature of the treatment, and the characteristics of the study population.
- `status`: The status of the trial. We say that a trial is not successful if the status is '*Terminated*', '*Withdrawn*', '*Suspended*', '*Withheld*', '*No longer available*', or '*Temporarily not available*'. However, if it is '*Approved for marketing*', then we say it is successful. Otherwise, we abstain from predicting either. Having this information incorporated serves to enhance the transparency, regulatory compliance, and ethical conduct of clinical trials. I.e. "*Terminated: The study has stopped early and will not start again. Participants are no longer being examined or treated.*" usually occurs when the trial causes significant negative side-effects in several patients.

- **amendments**: Represents the number of trial amendments. Can be thresholded. Clinical trials must follow approved protocols [18, 28], but amendments may be required after regulatory approval to adjust protocols according to new requirements or insights. We scraped record histories for each trial from <https://clinicaltrials.gov/> and calculated the total number of times a clinical trial has been amended. The number of amendments to a clinical trial protocol can provide some insights into the trial’s progress and potential success, but it’s not necessarily a direct indication of success or failure. Therefore, we consider the total number of amendments of trial as a weak label. Sometimes, amendments to trial protocols are crucial for adapting to emerging data from ongoing clinical trials, addressing safety concerns, or optimizing study design to yield better outcomes.
- **stock_price**: Is positive if the sponsor stock price’s 5-day moving average has a positive or negative slope. See Section 2.4.
- **linkage**: Is positive if a trial was found to have any later-stage trials linked to it. See Section 2.2.
- **news_headlines**: Is positive or negative depending on sentiment from any news headline related to the trial. See Section 2.3.
- **gpt**: Represents GPT3.5-turbo-0125’s decisions on PubMed abstracts. See Section 2.1.

C.3 Phase-Specific Thresholding

For Phases 1, 2, and 3, we find specific quantile thresholds from $(0.1, 0.2, \dots, 0.9)$ for all LFs that have tunable thresholds, fine-tuned on each respective phase on the TOP training dataset.

To reiterate our final labeling process, we utilize both an unsupervised aggregation approach—data programming—and a supervised random forest to obtain our estimated labels and ground our weakly supervised signals on the humanly annotated TOP training data. For data programming, we add TOP training labels to all of our other weakly supervised LFs. We duplicate TOP labels 3 times to obtain high agreement and therefore high weight in the matrix completion step.

For our supervised approach, we train a Random Forest model on all other weakly supervised LF outputs to predict the ground truth. Both approaches automatically create predictions for all of the trials (more than 400k trials). For the final prediction, trials are first segmented by their phase, where the respective phase threshold-tuned predicted labels are matched.

D CTO Statistics

D.1 Labeling Function Statistics

Table 7 and Table 6 show statistics of all tunable and static labeling functions for the TOP training and validation data splits. We see that most LFs cover more than 50% of the data, although this is not true of news headlines and status. Additionally, each individual accuracy scores and kappa values are generally not stellar on their own, with the highest kappa being status (which suffers from low coverage). In terms of kappa values, p-values from the tunable LFs and GPT decisions stand out from the static LFs as the highest, which makes sense as studies with more significant results may be one of the original annotator’s primary signals and would also be referred to in the publications. The highest accuracy is status and GPT. Since status predicts all negative, it is clear that terminated, withdrawn, and incomplete trials in general are considered unsuccessful.

Table 6: Table of all *static* (*i.e. not thresholded*) statistics of the different labeling functions that we consider for CTO. Pos. Prop. refers to the positive percentage of all valid labels (*i.e.* $\frac{\#1}{\#1 + \#0}$). Coverage indicates the proportion of TOP trials for that phase that the LF has predictions on. Acc. indicates raw accuracy compared to TOP train and valid split, and κ denotes cohen kappa as well.

Phase	Labeling Function	Abstain	Predict 0	Predict 1	Pos. Prop.	Coverage	Acc	κ
1	status	814	347	0	0.000	0.217	0.954	0.000
	gpt	179	41	198	0.828	0.150	0.890	0.678
	linkage	0	496	573	0.536	0.670	0.516	0.035
	stock_price	0	95	130	0.578	0.141	0.540	-0.021
	results_reported	0	800	361	0.311	0.727	0.455	-0.059
2	status	3296	1155	0	0.000	0.228	0.968	0.000
	gpt	683	338	913	0.730	0.247	0.875	0.707
	linkage	0	2125	2027	0.488	0.820	0.576	0.150
	stock_price	0	457	447	0.494	0.178	0.504	0.008
	results_reported	0	2058	2393	0.538	0.879	0.524	0.050
3	status	2999	439	0	0.000	0.121	0.954	0.000
	gpt	605	276	1389	0.834	0.460	0.908	0.717
	linkage	0	1284	1929	0.600	0.888	0.626	0.209
	stock_price	0	438	528	0.547	0.267	0.550	0.057
	results_reported	0	1399	2039	0.593	0.951	0.619	0.199

Table 7: Table of all statistics of the different *tunable (by varying the quantile threshold)* labeling functions that we consider for CTO. Pos. Prop. refers to the positive percentage of all valid labels (i.e. $\frac{\#1}{\#1+\#0}$). Coverage indicates the proportion of TOP trials for that phase that the LF has predictions on. Acc. indicates raw accuracy compared to TOP train and valid split, and κ denotes cohen kappa as well.

Phase	Labeling Function	Best Quantile	Abstain	0	1	Pos. Prop.	Coverage	Acc	κ
I	update_more_recent	0.8	88	665	408	0.380	0.672	0.564	0.153
	sites	0.1	0	588	491	0.455	0.676	0.543	0.092
	serious_ae	0.9	0	22	339	0.939	0.226	0.490	-0.045
	pvalues	0.5	0	33	23	0.411	0.035	0.585	0.256
	patient_drop	0.9	0	4	220	0.982	0.140	0.530	0.013
	num_sponsors	0.7	0	1064	97	0.084	0.727	0.446	-0.017
	num_patients	0.2	0	126	235	0.651	0.226	0.723	0.441
	news_headlines	0.7	637	16	48	0.750	0.040	0.610	0.009
	death_ae	0.1	0	37	324	0.898	0.226	0.553	0.086
	amendments	0.1	0	30	195	0.867	0.141	0.715	-0.076
II	update_more_recent	0.8	290	2897	1264	0.304	0.822	0.530	0.051
	sites	0.9	0	2723	1398	0.339	0.814	0.537	0.059
	serious_ae	0.9	0	211	2179	0.912	0.472	0.488	-0.031
	pvalues	0.5	0	418	341	0.449	0.150	0.683	0.384
	patient_drop	0.9	0	100	1614	0.942	0.338	0.533	0.003
	num_sponsors	0.9	0	4328	123	0.028	0.879	0.515	-0.007
	num_patients	0.3	0	869	1524	0.637	0.472	0.699	0.398
	news_headlines	0.9	2678	24	68	0.739	0.018	0.608	-0.007
	death_ae	0.1	0	155	2235	0.935	0.472	0.515	0.023
	amendments	0.1	0	57	847	0.937	0.178	0.633	-0.026
III	update_more_recent	0.9	217	1431	1790	0.556	0.891	0.513	-0.012
	sites	0.8	0	1091	1902	0.635	0.827	0.527	-0.017
	serious_ae	0.9	0	708	1322	0.651	0.561	0.597	0.060
	pvalues	0.5	0	449	896	0.666	0.372	0.768	0.450
	patient_drop	0.9	0	587	1210	0.673	0.497	0.609	0.053
	num_sponsors	0.1	0	2505	933	0.271	0.951	0.367	-0.124
	num_patients	0.2	0	80	1959	0.961	0.564	0.759	0.182
	news_headlines	0.9	2734	26	72	0.735	0.027	0.696	0.077
	death_ae	0.9	0	61	1969	0.970	0.561	0.720	0.029
	amendments	0.1	0	55	911	0.943	0.267	0.717	-0.001
	all_ae	0.9	0	876	1154	0.568	0.561	0.540	0.015

D.2 Statistics on Trial Linkage

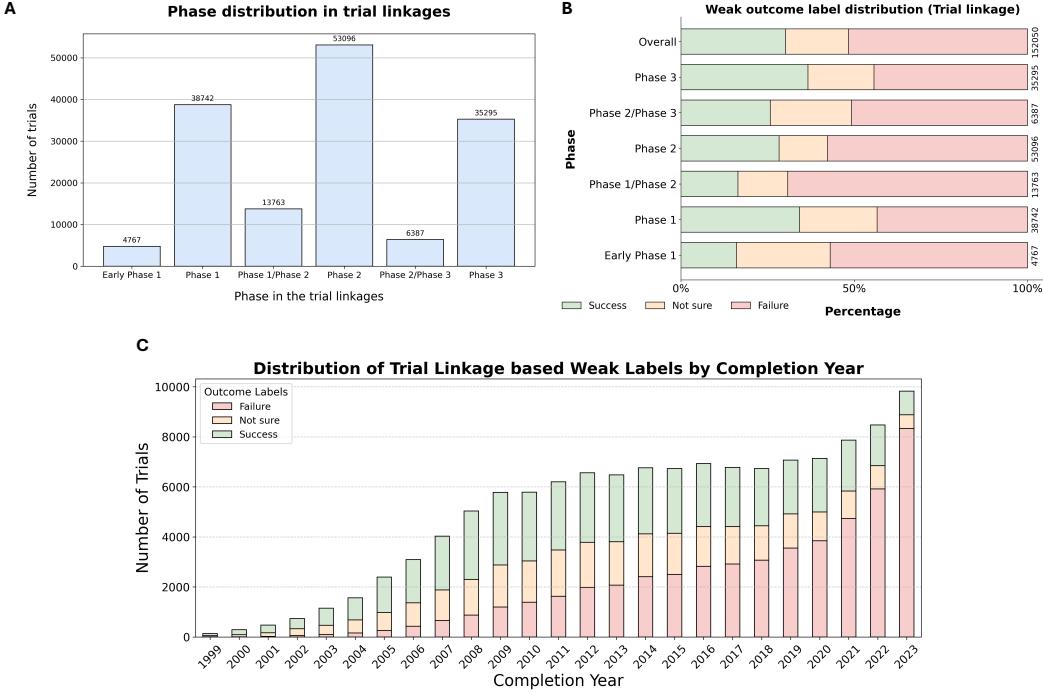


Figure 5: Overview of the weak labels extracted from the trial linkage.

We present statistics on the weak trial outcome labels extracted from the clinical trial linkages in Figure 5. Figure 5 A shows the phase distribution of these weak labels, excluding trials with missing phase information or labeled as 'Not Applicable', as they are omitted from our linking algorithm. Additionally, outcomes for Phase 4 are not included because there are no subsequent trials for Phase 4. The criteria for extracting labels for trial linkage are defined as follows:

$$\text{Trial outcome} = \begin{cases} \text{Success} & \text{if next phase trial exists} \\ \text{Not Sure} & \text{if there is a weakly connected next phase trial} \\ \text{Failure} & \text{if no next phase trial found} \end{cases} \quad (3)$$

Here, a "weakly connected next phase trial" refers to a trial link found during the retrieval stage that received a negative cross-encoder score during the predict linkage stage. Figure 5 B and C illustrate the distribution of weak labels across different phases and over time (years).

D.3 Statistics on LLM Predictions

In Figure 6, we present the statistics of LLM predictions on PubMed abstracts, including a histogram showing the number of publications per trial. Figure 6 A illustrates the phase distribution of the extracted weak labels, including rare phases such as terminated, recruiting, and completed. The LLM is prompted to predict the trial outcome based on the provided abstracts as 'Success', 'Failure', or 'Not Sure'. The distribution of weak labels over time (years) and across phases is shown in Figure 6 B and C, respectively. The number of 'Failure' labels is relatively low compared to others, as trials with multiple publications are more likely to be successful. Additionally, Figure 6 D presents the histogram for background, derived, and result-type publications for the trials.

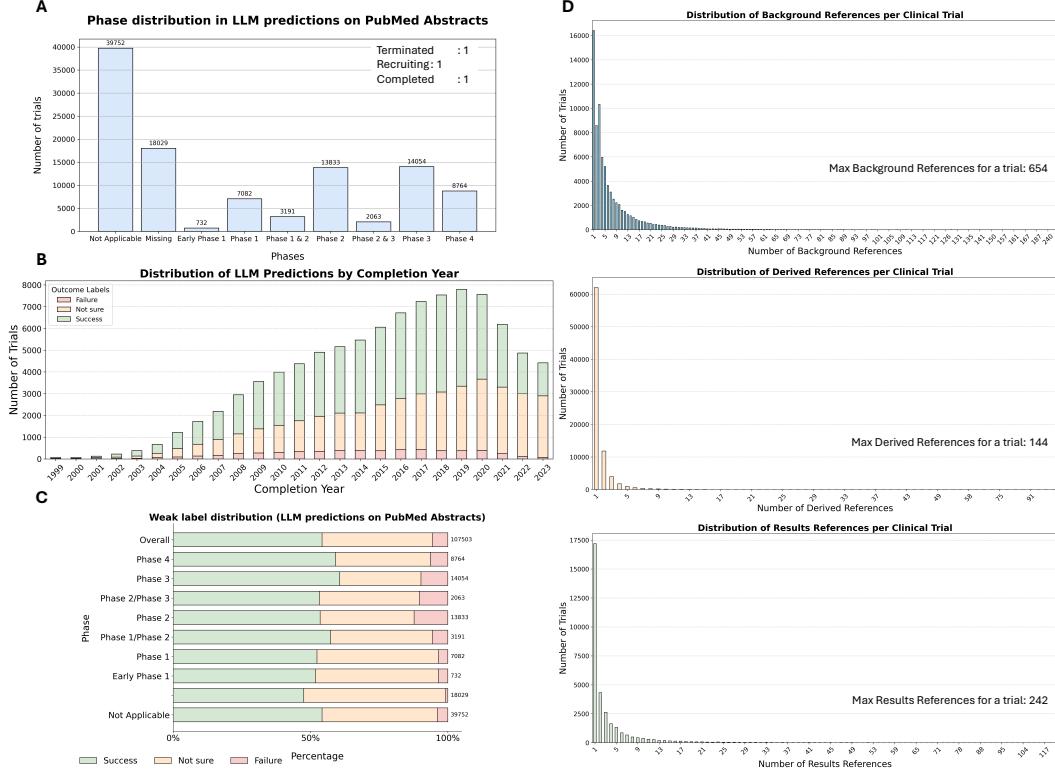


Figure 6: Overview of the weak labels from LLM predictions on PubMed abstracts.

D.4 Pair-wise Agreement Between Labeling Functions

To analyze the agreement between the labeling functions and the final aggregated labels, we calculated pairwise agreement scores using Cohen’s Kappa in the TOP data splits. These scores are shown in Figure 7 and 8 for random forest and data programming label aggregation, respectively. Each cell in the heatmap represents the agreement score between a pair of labeling functions. It is important to note that each labeling function does not cover all trials with weak labels. Therefore, while calculating Cohen’s Kappa, we only considered the trials common to both labeling functions. For instance, there are no common trials with weak labels from ‘status’ and ‘amendments,’ so the corresponding cell is left blank.

In the context of random forest label aggregation, LLM predictions on PubMed abstracts, p-values, trial linkage, number of sites, and number of patients showed higher agreement with the final aggregated labels. Similar patterns were observed with labels aggregated using data programming. Notably, LLM predictions had high agreement with p-values, likely because the LLM considered the p-values provided in the abstracts to predict trial outcomes. Additionally, there was good agreement between LLM predictions on PubMed abstracts and other factors such as trial linkage and number of patients.

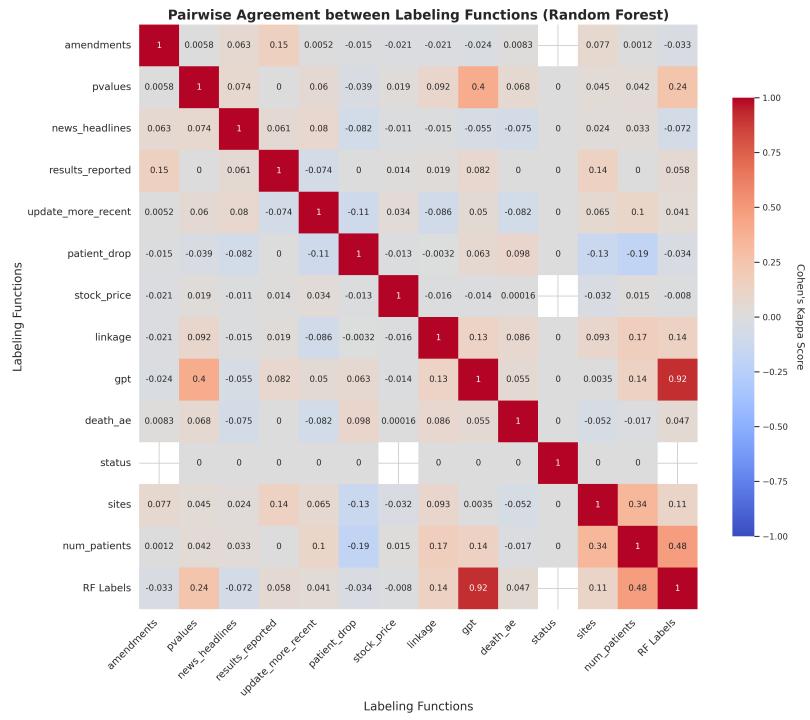


Figure 7: Pairwise agreement with the labeling functions (RF)

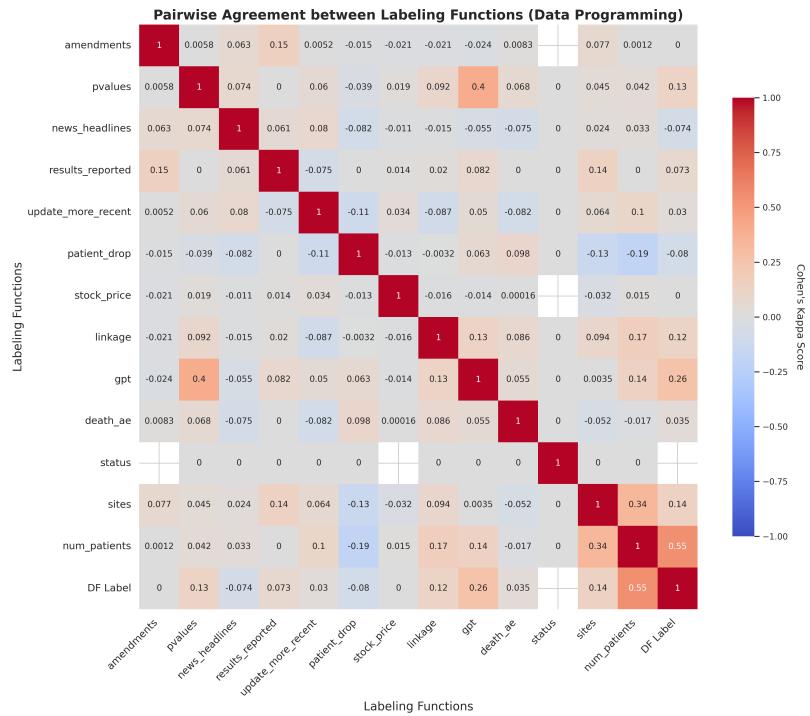


Figure 8: Pairwise agreement with the labeling functions (DP)

E Ablation on Features for Trial Linkage

This section focuses on the ablation study conducted on the trial features for the trial linking algorithm. Figure 9 presents the comparison results with TOP and the outcome labels from the trial linkage created using individual features. The features "intervention," "official title," "brief summary," and "eligibility criteria" consistently achieved better performance across all phases. In contrast, "lead sponsor" performed the worst, likely because trial sponsors often change based on funding capacity, even when a trial progresses to the next phase.

Additionally, Table 8 shows the performance of various combinations of trial features across phases. Combining all trial features except "lead sponsor" yielded better performance across all phases. Including "lead sponsor" features reduced the accuracy of the extracted weak outcome labels. However, adding "lead sponsor" improved performance for Phase 1 trials, as it is rare for a trial to change sponsors between Phase 1 and Phase 2.

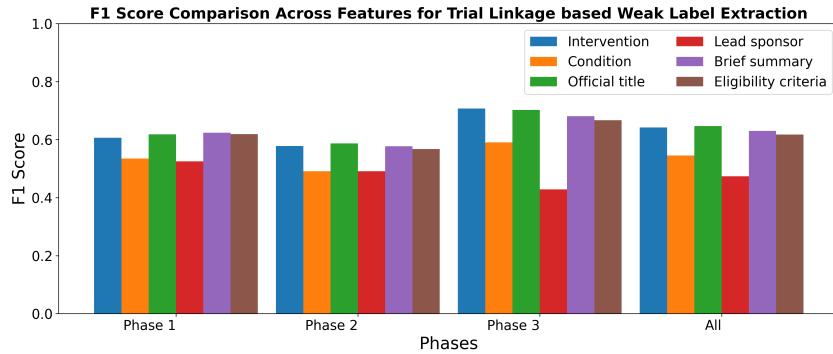


Figure 9: Ablation study on the use of different trial features to predict trial linkages and the agreement of their extracted weak labels with TOP human-annotated data labels using F1 scores.

Table 8: Results of the ablation study on the different combinations of trial features to predict trial linkages and the agreement of their extracted weak labels with TOP human-annotated data labels using F1 scores. ↓ indicates that adding the feature decreased the performance. ↑ indicates that adding the feature improved the performance.

Phase	Feature combination	F1
Phase 1	Official title + Intervention	0.645
	Official title + Intervention + Brief Summary	0.6426 ↓
	Official title + Intervention + Brief Summary + Eligibility	0.6447 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition	0.6532 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition + Lead Sponsor	0.6658 ↑
Phase 2	Official title + Intervention	0.6027
	Official title + Intervention + Brief Summary	0.6042 ↑
	Official title + Intervention + Brief Summary + Eligibility	0.608 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition	0.6196 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition + Lead Sponsor	0.6189 ↓
Phase 3	Official title + Intervention	0.7323
	Official title + Intervention + Brief Summary	0.7319 ↓
	Official title + Intervention + Brief Summary + Eligibility	0.7379 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition	0.7498 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition + Lead Sponsor	0.7384 ↓
All	Official title + Intervention	0.6686
	Official title + Intervention + Brief Summary	0.6687 ↑
	Official title + Intervention + Brief Summary + Eligibility	0.6737 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition	0.6842 ↑
	Official title + Intervention + Brief Summary + Eligibility + Condition + Lead Sponsor	0.6796 ↓

F Prompts for LLM Predictions on PubMed Abstracts

In this section, we describe the method used to obtain LLM predictions on PubMed abstracts, including the statistical test results and question-answer pairs. An example of such a prompt is shown in Figure 10. Additionally, we provide two examples of input abstracts given to the LLM and their resulting outputs, as shown in Figures 11 and 12.



Figure 10: LLM Prompts.

Provided Top 2 Abstract (Example 1)	Response from GPT-3.5
<p>Here is the list of PubMed abstracts in the format of Metadata followed by Abstract:</p> <p>NCT ID: NCT01845259 Trial Title: Does a GLP-1 Receptor Agonist Change Glucose Tolerance in Antipsychotic-treated Patients? A Randomized, Double-blinded, Placebo-controlled Clinical Trial</p> <p>Reference type: derived Title: Does a GLP-1 receptor agonist change glucose tolerance in patients treated with antipsychotic medications? Design of a randomised, double-blinded, placebo-controlled clinical trial. Journal: BMJ open Date of Publication: 2014 Mar 25 Abstract: BACKGROUND: Metabolic disturbances, obesity and life-shortening cardiovascular morbidity are major clinical problems among patients with antipsychotic treatment. Especially two of the most efficacious antipsychotics, clozapine and olanzapine, cause weight gain and metabolic disturbances. Additionally, patients with schizophrenia-spectrum disorders not infrequently consume alcohol. Glucagon-like peptide-1 (GLP-1) has shown to improve glycaemic control and reduce alcohol intake among patients with type 2 diabetes. OBJECTIVES: To investigate whether the beneficial effects of GLP-1 analogues on glycaemic control and alcohol intake, in patients with type 2 diabetes, can be extended to a population of pre-diabetic psychiatric patients receiving antipsychotic treatment. METHODS AND ANALYSIS: Trial design, intervention and participants: This study is a 16-week, double-blinded, randomised, parallel-group, placebo-controlled clinical trial, designed to evaluate the effects of the GLP-1 analogue liraglutide on glycaemic control and alcohol intake compared to placebo in patients who are prediabetic, overweight (body mass index >=27 kg/m²), diagnosed with a schizophrenia-spectrum disorder and on stable treatment with either clozapine or olanzapine. OUTCOMES: The primary endpoint is the change in glucose tolerance from baseline (measured by area under the curve for the plasma glucose excursion following a 4 h 75 g oral glucose tolerance test) to follow-up at week 16. The secondary endpoints include changes of dysglycaemia, body weight, waist circumference, blood pressure, secretion of incretin hormones, insulin sensitivity and beta cell function, dual-energy X-ray absorption scan (body composition), lipid profile, liver function and measures of quality of life, daily functioning, severity of the psychiatric disease and alcohol consumption from baseline to follow-up at week 16. Status: Currently recruiting patients. ETHICS AND DISSEMINATION: Ethical approval has been obtained. Before screening, all patients will be provided oral and written information about the trial. The study will be disseminated by peer-review publications and conference presentations. TRIAL REGISTRATION NUMBER: ClinicalTrials.gov: NCT01845259, EudraCT: 2013-000121-31.</p> <p>Reference type: derived Title: Effect of Liraglutide Treatment on Prediabetes and Overweight or Obesity in Clozapine- or Olanzapine-Treated Patients With Schizophrenia Spectrum Disorder: A Randomized Clinical Trial. Journal: JAMA psychiatry Date of Publication: 2017 Jul 1 Abstract: IMPORTANCE: Compared with the general population, patients with schizophrenia have a 2- to 3-fold higher mortality rate primarily caused by cardiovascular disease. Previous interventions designed to counteract antipsychotic-induced weight gain and cardiometabolic disturbances reported limited effects. OBJECTIVES: To determine the effects of the glucagon-like peptide-1 receptor agonist liraglutide added to clozapine or olanzapine treatment of schizophrenia spectrum disorders. DESIGN, SETTING, AND PARTICIPANTS: This randomized clinical double-blind trial enrolled participants at 2 clinical sites in Denmark. Of 214 eligible participants with a schizophrenia spectrum disorder, 103 were randomized to liraglutide or placebo. Participants received stable treatment with clozapine or olanzapine, were overweight or obese, and had prediabetes. Data were collected from May 1, 2013, through February 25, 2016. INTERVENTIONS: Treatment for 16 weeks with once-daily subcutaneous injection of liraglutide or placebo. Trial drug therapy was titrated during the first 2 weeks of the study. MAIN OUTCOMES AND MEASURES: The primary end point was change in glucose tolerance estimated by a 75-g oral glucose tolerance test result. Secondary end points included change in body weight and cardiometabolic parameters. RESULTS: Of the 103 patients undergoing randomization (60 men [58.3%] and 43 women [41.7%]), 97 were included in the efficacy analysis, with a mean (SD) age of 42.5 (10.5) years and mean (SD) body mass index (calculated as weight in kilograms divided by height in meters squared) of 33.8 (5.9). The liraglutide and placebo groups had comparable characteristics (mean [SD] age, 42.1 [10.7] vs 43.0 [10.5] years; 30 men in each group; mean [SD] body mass index, 33.7 [5.1] vs 33.9 [6.6]). A total of 96 randomized participants (93.2%) completed the trial. Glucose tolerance improved in the liraglutide group compared with the placebo group ($P < .001$). Altogether, 30 liraglutide-treated participants (63.8%) developed normal glucose tolerance compared with 8 placebo-treated participants (16.0%) ($P < .001$; number needed to treat, 2). Body weight decreased with liraglutide compared with placebo (-5.3 kg; 95% CI, -7.0 to -3.7 kg). Reductions in waist circumference (-4.1 cm; 95% CI, -6.0 to -2.3 cm), systolic blood pressure (-4.9 mm Hg; 95% CI, -9.5 to -0.3 mm Hg), visceral fat (-250.19 g; 95% CI, -459.9 to -40.5 g), and low-density lipoprotein levels (-15.4 mg/dL; 95% CI, -23.2 to -7.7 mg/dL) occurred with liraglutide compared with placebo. Adverse events with liraglutide affected mainly the gastrointestinal tract. CONCLUSIONS AND RELEVANCE: Liraglutide significantly improved glucose tolerance, body weight, and cardiometabolic disturbances in patients with schizophrenia spectrum disorders treated with clozapine or olanzapine. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01845259.</p>	<p>{description}: 'The clinical trial NCT01845259 is a randomized, double-blinded, placebo-controlled trial designed to investigate the effects of the GLP-1 analogue liraglutide on glucose tolerance in antipsychotic-treated patients. The primary endpoint of the trial is the change in glucose tolerance from baseline to week 16. Secondary endpoints include changes in dysglycaemia, body weight, waist circumference, blood pressure, incretin hormone secretion, insulin sensitivity, beta cell function, body composition, lipid profile, liver function, quality of life, daily functioning, severity of psychiatric disease, and alcohol consumption.'</p> <p>'extracted features': [{'description': 'Study Design', 'value': 'Randomized, double-blinded, placebo-controlled clinical trial'}, {'description': 'Number of Participants', 'value': '103'}, {'description': 'Primary Endpoint', 'value': 'Change in glucose tolerance from baseline to week 16'}, {'description': 'Secondary Endpoints', 'value': 'Changes in dysglycaemia, body weight, waist circumference, blood pressure, incretin hormone secretion, insulin sensitivity, beta cell function, body composition, lipid profile, liver function, quality of life, daily functioning, severity of psychiatric disease, and alcohol consumption'}],</p> <p>'questions': [{'question': 'What is the study design of the clinical trial NCT01845259?', 'answer': 'Randomized, double-blinded, placebo-controlled clinical trial', 'options': ['Observational study', 'Retrospective study', 'Randomized, double-blinded, placebo-controlled clinical trial', 'Case-control study', 'Cross-sectional study'], 'correct_option': 'Randomized, double-blinded, placebo-controlled clinical trial'}, {'question': 'How many participants were included in the clinical trial NCT01845259?', 'answer': '103', 'options': ['50', '75', '100', '103', '125'], 'correct_option': '103'}, {'question': 'What is the primary endpoint of the clinical trial NCT01845259?', 'answer': 'Change in glucose tolerance from baseline to week 16', 'options': ['Change in body weight', 'Change in waist circumference', 'Change in glucose tolerance from baseline to week 16', 'Change in blood pressure', 'Change in lipid profile'], 'correct_option': 'Change in glucose tolerance from baseline to week 16'}, {'question': 'What are the secondary endpoints of the clinical trial NCT01845259?', 'answer': 'Changes in dysglycaemia, body weight, waist circumference, blood pressure, incretin hormone secretion, insulin sensitivity, beta cell function, body composition, lipid profile, liver function, quality of life, daily functioning, severity of psychiatric disease, and alcohol consumption', 'options': ['Changes in body weight and waist circumference', 'Changes in blood pressure and lipid profile', 'Changes in incretin hormone secretion and insulin sensitivity', 'Changes in body composition and liver function', 'Changes in quality of life and daily functioning'], 'correct_option': 'Changes in dysglycaemia, body weight, waist circumference, blood pressure, incretin hormone secretion, insulin sensitivity, beta cell function, body composition, lipid profile, liver function, quality of life, daily functioning, severity of psychiatric disease, and alcohol consumption'}, {'question': 'outcome': 'success', 'outcome reasoning': 'The trial is currently recruiting patients and the primary endpoint is the change in glucose tolerance from baseline to week 16. If the GLP-1 analogue liraglutide shows a significant improvement in glucose tolerance compared to placebo, it is likely that the trial will be successful.'}</p>

Figure 11: Example response from GPT-3.5.

Provided Top 2 Abstract (Example 2)	Response from GPT-3.5
<p>Here is the list of PubMed abstracts in the format of Metadata followed by Abstract: NCT ID: NCT01846273</p> <p>Trial Title: A 24-month, Phase IV, Randomized, Double Masked, Multi-center Study of Ranibizumab Monotherapy or Ranibizumab in Combination With Verteporfin Photodynamic Therapy on Visual Outcome in Patients With Symptomatic Macular Polypoidal Choroidal Vasculopathy</p> <p>Reference type: derived</p> <p>Title: Efficacy and Safety of Ranibizumab With or Without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: A Randomized Clinical Trial.</p> <p>Journal: JAMA ophthalmology Date of Publication: 2017 Nov 1</p> <p>Abstract: IMPORTANCE: Polypoidal choroidal vasculopathy (PCV) is a common subtype of exudative age-related macular degeneration among Asian individuals. To our knowledge, there are no large randomized clinical trials to evaluate intravitreal ranibizumab, with and without verteporfin photodynamic therapy (vPDT), for the treatment of PCV. OBJECTIVE: To compare the efficacy and safety of combination therapy of ranibizumab and vPDT with ranibizumab monotherapy in PCV. DESIGN, SETTING, AND PARTICIPANTS: A double-masked, multicenter randomized clinical trial of 322 Asian participants with symptomatic macular PCV confirmed by the Central Reading Center using indocyanine green angiography was conducted between August 7, 2013, and March 2, 2017. INTERVENTIONS: Participants were randomized 1:1 to ranibizumab, 0.5 mg, and sham PDT ($n = 154$; monotherapy group). All participants received 3 consecutive monthly ranibizumab injections, followed by a pro re nata regimen. Participants also received vPDT/sham PDT on day 1, followed by a pro re nata regimen based on the presence of active polypoidal lesions. MAIN OUTCOMES AND MEASURES: Step 1 assessed whether combination therapy was noninferior (5-letter margin) to monotherapy for change in best-corrected visual acuity from baseline and superior in complete polyp regression. If noninferiority was established, step 2 assessed whether combination therapy was superior to monotherapy measured by best-corrected visual acuity change at month 12. RESULTS: Baseline demographics of the 322 participants were comparable between the treatment groups. Mean (SD) age of the patients was 68.1 (8.8) years, and overall, 69.9% of the patients were men. At baseline, the overall mean best-corrected visual acuity and mean central subfield thickness were 61.1 letters and 413.3 μm, respectively. At 12 months, mean improvement from baseline was 8.3 letters with combination therapy vs 5.1 letters with monotherapy (mean difference, 3.2 letters; 95% CI, 0.4–6.1), indicating that combination therapy met the predefined criterion for noninferiority as well as being superior to monotherapy ($P = .01$). Combination therapy was also superior to monotherapy in achieving complete polyp regression at month 12 (69.3% vs 34.7%; $P < .001$). Over 12 months, the combination therapy group received a median of 4.0 ranibizumab injections compared with 7.0 in the monotherapy group. Vitreous hemorrhage was the only ocular serious adverse event (combination therapy group, 1 [0.6%]; monotherapy group, 3 [2.0%]). CONCLUSIONS AND RELEVANCE: After 12 months, combination therapy of ranibizumab plus vPDT was not only noninferior but also superior to ranibizumab monotherapy in best-corrected visual acuity and superior in complete polyp regression while requiring fewer injections. Combination therapy should be considered for eyes with PCV. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01846273.</p> <p>Reference type: derived</p> <p>Title: Comparison of Ranibizumab With or Without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: The EVEREST II Randomized Clinical Trial.</p> <p>Journal: JAMA ophthalmology Date of Publication: 2020 Sep 1</p> <p>Abstract: IMPORTANCE: The 2-year efficacy and safety of combination therapy of ranibizumab administered together with verteporfin photodynamic therapy (vPDT) compared with ranibizumab monotherapy in participants with polypoidal choroidal vasculopathy (PCV) are unclear. OBJECTIVE: To compare treatment outcomes of ranibizumab, 0.5 mg, plus prompt vPDT combination therapy with ranibizumab, 0.5 mg, monotherapy in participants with PCV for 24 months. DESIGN, SETTING, AND PARTICIPANTS: This 24-month, phase IV, double-masked, multicenter, randomized clinical trial (EVEREST II) was conducted among Asian participants from August 7, 2013, to March 2, 2017, with symptomatic macular PCV confirmed using indocyanine green angiography. INTERVENTIONS: Participants ($N = 322$) were randomized 1:1 to ranibizumab, 0.5 mg, plus vPDT (combination therapy group; $n = 168$) or ranibizumab, 0.5 mg, plus sham PDT (monotherapy group; $n = 154$). All participants received 3 consecutive monthly ranibizumab injections, followed by a pro re nata regimen. Participants also received vPDT (combination group) or sham PDT (monotherapy group) on day 1, followed by a pro re nata regimen based on the presence of active polypoidal lesions. MAIN OUTCOMES AND MEASURES: Evaluation of combination therapy vs monotherapy at 24 months in key clinical outcomes, treatment exposure, and safety. Polypoidal lesion regression was defined as the absence of indocyanine green hyperfluorescence of polypoidal lesions. RESULTS: Among 322 participants (mean [SD] age, 68.1 [8.8] years; 225 [69.9%] male), the adjusted mean best-corrected visual acuity (BCVA) gains at month 24 were 9.6 letters in the combination therapy group and 5.5 letters in the monotherapy group (mean difference, 4.1 letters; 95% CI, 1.0–7.2 letters; $P = .005$), demonstrating that combination therapy was superior to monotherapy by the BCVA change from baseline to month 24. Combination therapy was superior to monotherapy in terms of complete polypoidal lesion regression at month 24 (81 of 143 [56.6%] vs 23 of 86 [26.7%] participants; $P < .001$). Participants in the combination group received fewer ranibizumab injections (median, 6.0 [interquartile range (IQR), 4.0–11.0]) than the monotherapy group (median, 12.0 [IQR, 7.0–17.0]) up to month 24. The combination group required a median of 2.0 (IQR, 1.0–3.0) vPDT treatments for 24 months, with 75 of 168 participants (44.6%) requiring only 1 vPDT treatment. CONCLUSIONS AND RELEVANCE: The 24-month data findings confirm that ranibizumab therapy, given as monotherapy or in combination with vPDT, is efficacious and safe for treatment of PCV. Combination therapy with vPDT added to ranibizumab achieved superior BCVA gain, increased odds of complete polypoidal lesion regression, and fewer treatment episodes compared with ranibizumab monotherapy. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT01846273.</p>	<p>{description}: The combination therapy of ranibizumab and verteporfin photodynamic therapy (vPDT) was found to be superior to ranibizumab monotherapy in terms of best-corrected visual acuity (BCVA) improvement and complete polypoidal lesion regression. The combination therapy required fewer injections and treatment episodes compared to monotherapy;</p> <p>{extracted features}: [{description}: 'Number of participants', value: 322.0, {description}: 'Treatment groups', value: 'Combination therapy group (ranibizumab + vPDT): 168 participants, Monotherapy group (ranibizumab): 154 participants', {description}: 'Baseline mean best-corrected visual acuity (BCVA)', value: '61.1 letters', {description}: 'Mean BCVA improvement at 12 months', value: 8.3, {description}: 'Mean BCVA improvement with monotherapy at 12 months', value: 5.1, {description}: 'Mean difference in BCVA improvement between combination therapy and monotherapy at 12 months', value: 3.2,]</p> <p>{questions}: [{question}: 'What was the primary outcome measure of the trial?', answer: 'Change in best-corrected visual acuity (BCVA) from baseline', options: ['Change in central subfield thickness from baseline', 'Number of ranibizumab injections received', 'Percentage of participants achieving complete polyp regression', 'Presence of vitreous hemorrhage', 'Change in intraocular pressure from baseline'], correct_option: 'Change in best-corrected visual acuity (BCVA) from baseline', </p> <p>{question}: 'What was the treatment regimen for the participants?', answer: 'Participants received 3 consecutive monthly ranibizumab injections, followed by a pro re nata regimen. They also received verteporfin photodynamic therapy (vPDT) or sham PDT based on the presence of active polypoidal lesions.', options: ['Participants received monthly vPDT treatments', 'Participants received only ranibizumab injections', 'Participants received only sham PDT', 'Participants received vPDT regardless of the presence of active polypoidal lesions', 'Participants received vPDT only if they had vitreous hemorrhage'], correct_option: 'Participants received 3 consecutive monthly ranibizumab injections, followed by a pro re nata regimen. They also received verteporfin photodynamic therapy (vPDT) or sham PDT based on the presence of active polypoidal lesions.', </p> <p>{question}: 'Which treatment group showed superior best-corrected visual acuity (BCVA) improvement at 12 months?', answer: 'Combination therapy group (ranibizumab + vPDT)', options: ['Monotherapy group (ranibizumab)', 'Combination therapy group (ranibizumab + sham PDT)', 'Combination therapy group (ranibizumab + vPDT)', 'Combination therapy group (ranibizumab + vPDT + sham PDT)', 'Monotherapy group (sham PDT)', correct_option: 'Combination therapy group (ranibizumab + vPDT)', </p> <p>{question}: 'What was the mean difference in best-corrected visual acuity (BCVA) improvement between combination therapy and monotherapy at 12 months?', answer: '3.2 letters', options: ['1.0 letters', '4.1 letters', '6.1 letters', '8.3 letters', '9.6 letters'], correct_option: '3.2 letters', </p> <p>{question}: 'What was the percentage of participants achieving complete polyp regression at 12 months with combination therapy?', answer: '69.3%', options: ['26.7%', '34.7%', '44.6%', '56.6%', '81.0%'], correct_option: '69.3%', </p> <p>{outcome}: 'success', </p> <p>{outcome reasoning}: The combination therapy of ranibizumab and verteporfin photodynamic therapy (vPDT) was found to be superior to ranibizumab monotherapy in terms of best-corrected visual acuity (BCVA) improvement and complete polypoidal lesion regression. The combination therapy met the predefined criterion for noninferiority and was also superior to monotherapy ($P = .01$). Therefore, based on the primary outcome measures and statistical significance, the trial outcome is predicted to be successful.'</p>

Figure 12: Example response 2 from GPT-3.5.

G Case studies

We utilized our random forest labels for the following case studies.

G.1 Case study 1

We conducted a case study on clinical trial NCT01213160¹¹. This trial was completed in 2013. Five different weak labels (GPT decision, trial linkage, stock price, sites, and amendment) suggest that the trial was successful. The link to the PubMed article for this trial is <https://ncbi.nlm.nih.gov/pmc/articles/PMC5502072/>, which also suggests that "*AZD4547 was well tolerated in Japanese patients, with the best response of stable disease ≥ 4 weeks.*" Therefore, we believe NCT01213160 was successful, as our CTO label suggests. We believe the TOP label for this trial is incorrect.

G.2 Case study 2

Another clinical trial we examined in detail is NCT01111188¹². This trial was terminated. Therefore, our label for this trial is Failure (label: 0). However, its TOP label is Success (label: 1), which is unlikely as the trial was not completed. Additionally, the GPT decision for the trial was 0, which means it thinks the PubMed abstract we collected suggests that the trial failed. "...*all patients required dose delays during cycle 2 due to cytopenias, and the study team decided to stop the trial...with the primary toxicity being myelosuppression*".

H User Manual: Instructions to Generate and Use CTO

We provide documentation to use CTO as of June 2024, and we will attempt to update this document over time as our sources update. However, the most up-to-date information can be seen in our GitHub <https://github.com/chufangao/CTOD>. The current version of the dataset can be accessed at <https://zenodo.org/doi/10.5281/zenodo.11535960>.

H.1 Instructions to Generate Clinical Trial Linkage

The code to reproduce clinical trial linkages in the CTO dataset from the CITI dataset is provided in the GitHub repository under the /clinical_trial_linkage folder. The step-by-step instructions to generate the clinical trials linkages are as follows:

Prerequisites:

- Download the FDA orange book and save it to ./FDA_approvals/. Currently, we provide the downloaded version as of 2024-04, which was used to create our dataset. Refer to <https://fda.gov/drugs/drug-approvals-and-databases/orange-book-data-files> for additional details on the FDA orange book.
- Download the trial dataset from CITI <path>. If it has already been downloaded, provide the path to the data in the scripts.
- Download the National Drug Code Directory /drug/ndc: <https://open.fda.gov/data/downloads/>
- Download the DrugBank full database for researchers:
e.g. <https://go.drugbank.com/releases/latest>

1. Extract trial info and save trial embeddings: First, we extract trial features from the CITI dataset. Provide the <data_path> for downloaded CITI data in the command below:

```
cd clinical_trial_linkage  
python extract_trial_info.py --data_path <CTI dir>
```

¹¹<https://clinicaltrials.gov/study/NCT01213160>

¹²<https://clinicaltrials.gov/study/NCT01111188>

Run the following command to extract and save the embeddings for the trial features using Pub-MedBERT. Make sure to provide the path to save the embeddings. Feel free to make changes to num_workers and gpu_ids as necessary.

```
python get_embedding_for_trial_linkage.py  
--root_folder <saved embeddings dir>  
--num_workers 2 --gpu_ids 0,1
```

2. Linking of clinical trials across phases: Based on the extracted embeddings, we link the trials across different phases, as shown in the above figure. Run the following command to link the trials across phases. Provide the root_folder path to save the extracted linkages and embedding_path with the saved embeddings. Since we link from the latter phase to the initial phases, provide the starting later phase to target_phase. Also, we need only to consider the following phases to create the trial linkage: ['Phase 2', 'Phase 2/Phase 3', 'Phase 3', 'Phase 4']

```
# Phase 4  
python create_trial_linkage.py --root_folder <created linkages dir>  
--target_phase 'Phase 4' --embedding_path <saved embeddings dir>  
--num_workers 2 --gpu_ids 0  
  
# Phase 3  
python create_trial_linkage.py --root_folder <created linkages dir>  
--target_phase 'Phase 3' --embedding_path <saved embeddings dir>  
--num_workers 2 --gpu_ids 0  
  
# Phase 2/Phase 3  
python create_trial_linkage.py --root_folder <created linkages dir>  
--target_phase 'Phase 2/Phase 3' --embedding_path <saved embeddings dir>  
--num_workers 2 --gpu_ids 0  
  
# Phase 2  
python create_trial_linkage.py --root_folder <created linkages dir>  
--target_phase 'Phase 2' --embedding_path <saved embeddings dir>  
--num_workers 2 --gpu_ids 0
```

3. Extract outcome labels: Run the following command to extract clinical trial outcome weak labels from clinical trial linkages. Provide the path with saved trial linkages.

```
python extract_outcome_from_trial_linkage.py  
--trial_linkage_path <trial linkage dir>
```

4. FDA approval matching: Run the following command to match the FDA approvals from the orange book to phase 3 trials and update the outcome labels for phase 3 trials.

```
python match_fda_approvals.py --trial_linkage_path <matched trials path>
```

The final outcome labels extracted from the clinical trial linkages and matching FDA approvals will be saved at:

```
<trial linkage dir>/outcome_labels/Merged_(ALL)_trial_linkage_outcome_df.csv
```

H.2 Instructions to Obtain LLM Predictions on PubMed Abstracts

The code to obtain LLM predictions on the PubMed abstracts as of in the CTO dataset from the CITI dataset is provided in the GitHub repository under the /llm_prediction_on_pubmed folder. The step-by-step instructions are as follows:

Prerequisites:

- Download the trial dataset from CITI. If it has already been downloaded, provide the path to the data in the scripts.

- To extract all the PubMed abstracts linked to the clinical trials, we use the NCBI API. Follow the instructions on this page to create an NCBI account and obtain the API key.

1. Extract PubMed Abstracts: Run the following commands for the extraction algorithm to retrieve all linked PubMed abstracts. Provide the NCBI API key, the path to the CITI data, and the path to save the extracted abstracts.

```
cd llm_prediction_on_pubmed
python extract_pubmed_abstracts.py --data_path <CITI dir>
--NCBI_api_key <API key> --save_path <Path to save extracted abstracts>
```

2. Retrieve the Top 2 Abstracts: To make the process efficient, we initially retrieve the top 2 most relevant abstracts (as shown in the figure above) and save them in a data frame.

```
python retrieve_top2_abstracts.py --data_path <Path to CITI data>
--pubmed_path <extracted pubmed dir>
```

The resultant data frame will be saved at <pubmed_path>/top_2_extracted_pubmed_articles.csv

3. Get LLM Predictions: To get the LLM prediction on PubMed abstracts, provide the OpenAI API key to the get_llm_predictions.py script and run the following. Also, provide the path to the above top_2_extracted_pubmed_articles.csv and the path to save LLM predictions. Along with the LLM predictions, extracted statistical features from the abstracts and the QA pairs are saved in the JSON files.

```
python get_llm_predictions.py
--top_2_pubmed_path <top_2_extracted_pubmed_articles.csv path>
--save_path <LLM predictions dir>
```

Finally, run the following code to combine all the outcomes. Also, provide the path to the above top_2_extracted_pubmed_articles.csv and the path to saved LLM predictions.

```
python clean_and_extract_final_outcomes.py
--gpt_decisions_path <LLM predictions dir>
--top_2_pubmed_path <top_2_extracted_pubmed_articles.csv path>
```

Final outcome predictions from LLM saved in <top_2_pubmed_path>/pubmed_gpt_outcomes.csv

H.3 News Headlines

Prerequisites:

- We use GNews to scrap Google News for the news headlines.

1: Scrape Google News First, we extract trial features from the CITI dataset. Provide the <data_path> for downloaded CITI data in the command below:

Run the following command to start the scraping for the top 1000 industry sponsors (NOTE: This will take a long time, i.e. on the scale of multiple weeks.) We share our scraped headlines in the Zenodo supplementary.

```
python get_news.py --mode=get_news
```

2: Obtaining Sentiment Embeddings from News Headlines and Study Titles

Running this command also saves the news title embeddings and a dataframe of the news as news.csv.

```
python get_news.py --mode=process_news
```

3 Corresponding News and Trials: We encode trial study title embeddings and obtain TopK Similarity. Running this command also saves study title embeddings.

```
python get_news.py --mode=correspond_news_and_studies
```

H.4 Stock Price

Prerequisites:

- Download the trial dataset from CTTI. If it has already been downloaded, provide the path to the data in the scripts.
- Create a csv file ‘tickers.csv’ that contains the names and corresponding tickers of sponsors in ‘name’ and ‘ticker’ columns respectively.
- Install yfinance from <https://pypi.org/project/yfinance/>

1: Obtain Stock Prices: Run `tickers_2_history.ipynb` to get historical stock prices for the sponsors in `tickers.csv` if those are available publicly. The stock price data will be stored in `stock_prices_historical.csv`.

2: Calculate Slope: Use `studies.txt` and `sponsors.txt` from CTTI with `stock_prices_historical.csv` and `tickers.csv` to calculate the slope of the stock prices using `slope_calculation.ipynb`.

H.5 Running Baselines

Here are the steps to run different baselines for clinical trial outcome prediction:

SPOT: Update the train, test, and validation data paths in `run_spot.py`. Execute the Python file:

```
python run_spot.py
```

BioBERT: Modify the train, test, and validation data paths in `biobert_trial_outcome.py`. Run the Python file:

```
python biobert_trial_outcome.py
```

PubMedBERT: Change the train, test, and validation data paths in `pubmedbert_trial_outcome.py`. Execute the Python file:

```
python pubmedbert_trial_outcome.py
```

SVM, XGBoost, MLP, RF, or LR: Ensure that the paths in `baselines.py` are correct. Run the Python file:

```
python baselines.py
```