Artificial Intelligence Applications for Clinical Trial Matching: A Scoping Review Protocol

Sarah Jenkins[1,2], Aaron Vance[2], Chloe Lin[1,3]

[1]Department of Medical Informatics, Meridian Health Institute, Metropolis, USA
[2]Synapse AI Labs, Nexa Research Park, Austin, USA
[3]Center for Clinical Innovation, Vertex Health Systems, Boston, USA

Contact: s.jenkins@meridianhealth.org

Abstract

Background: Identifying eligible participants for clinical trials remains a primary bottleneck in clinical research, causing significant delays in pharmaceutical development and therapeutic validation. Recently, artificial intelligence (AI) technologies—specifically natural language processing (NLP), machine learning (ML), and large language models (LLMs)—have been deployed to automate the parsing of clinical protocols and patient electronic health records (EHRs). However, a comprehensive mapping of these technologies, their deployment contexts, and their evaluation metrics has not been performed.
Objective: This scoping review aims to map the literature on AI applications for clinical trial matching, highlighting the specific machine learning methodologies, clinical domains, types of matched data, and operational outcomes reported.
Methods: The proposed scoping review will follow the Joanna Briggs Institute (JBI) methodology for scoping reviews. We will search MEDLINE (PubMed), Embase, IEEE Xplore, and Scopus for articles published from January 2018 to August 2026. Two independent reviewers will screen titles and abstracts, followed by full-text screening, with conflicts resolved by a third reviewer. Data will be extracted using a pre-tested charting form, and results will be presented descriptively and in tabular formats.
Keywords: Artificial Intelligence, Clinical Trial Matching, Natural Language Processing, Patient Recruitment, Scoping Review Protocol.

1 Introduction

1.1 Background and Rationale

Clinical trial matching is the process of aligning individual patients with trials for which they meet the precise inclusion and exclusion criteria. Historically, this matching has relied on manual review by clinical research coordinators, which is slow, labor-intensive, and prone to oversight [4]. Given the rapid expansion of trial protocols globally, manual matching cannot scale, resulting in up to 80% of trials failing to meet their recruitment timelines [2].

To address this, clinical investigators and data scientists have turned to Artificial Intelligence (AI). AI techniques, particularly Natural Language Processing (NLP), can extract key clinical concepts (such as diagnoses, lab values, and genomic markers) from unstructured clinical trial descriptions and patient electronic health records (EHRs) [1]. While several proprietary systems (such as Nexa TrialMatch and Synapse Cohort) claim high accuracy, academic literature showcases a heterogeneous landscape of methodologies ranging from rule-based parsers to modern generative transformers and large language models (LLMs).

A preliminary search of the Cochrane Database of Systematic Reviews, MEDLINE, and the JBI Evidence Synthesis database revealed no existing systematic reviews or scoping reviews on this

specific topic. A scoping review is uniquely suited here as it will map the broad, interdisciplinary literature across computer science and clinical medicine, establishing a taxonomy of existing tools and identifying key research gaps in evaluation methods and ethnic or demographic bias.

1.2 Objectives and Research Questions

The objective of this scoping review is to systematically map and analyze the literature on AI applications in clinical trial matching. Specifically, we seek to answer the research questions outlined in Box 1.2.

Box 1: Primary Research Questions

RQ1: What artificial intelligence methodologies (e.g., machine learning, deep learning, NLP, LLMs) are currently deployed for matching patients to clinical trials?

RQ2: What clinical domains (e.g., oncology, cardiology, rare diseases) are most frequently represented in AI-driven matching literature?

RQ3: How is patient data structured and integrated (e.g., EHR structured data, unstructured physician notes, genomic profiles, patient-reported outcomes)?

RQ4: What evaluation metrics (e.g., precision, recall, F1-score, time-to-match, screen-fail rates) are used to assess the performance and clinical utility of these systems?

RQ5: What challenges, limitations, and ethical considerations (e.g., algorithmic bias, data privacy, model explainability) are discussed in the literature?

2 Methodology

The scoping review will be conducted in accordance with the Joanna Briggs Institute (JBI) methodology for scoping reviews [3]. The reporting will align with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines [5].

2.1 Eligibility Criteria

We will apply the Population (or participants), Concept, and Context (PCC) framework to define the eligibility criteria for our review. These criteria are summarized in Table 1.

Table 1: PCC Eligibility Criteria Framework

PCC Dimension	Inclusion Criteria	Exclusion Criteria
Population	Human patient cohorts of any age, gender, or clinical diagnosis eligible or evaluated for clinical trial inclusion.	Animal models, purely synthetic cohorts without reference clinical validation.
Concept	Computerized or algorithmic systems utilizing AI (including machine learning, NLP, rule-based systems, and hybrid frameworks) specifically designed or evaluated for patient-to-trial matching.	Non-algorithmic recruitment strategies (e.g., manual screening, poster campaigns, digital advertising, simple keyword search without clinical context parsing).
Context	All clinical environments (hospitals, multi-center trials, primary care, clinical research organizations) or secondary analysis of public clinical registries (e.g., ClinicalTrials.gov).	Non-clinical trial registries, general-purpose cohort building tools not evaluated for trial eligibility matching.
Study Types	Peer-reviewed journal articles, conference papers (IEEE, ACM, etc.), and preprints (arXiv, bioRxiv) containing empirical evaluations.	Systematic reviews, letters, commentaries, editorials, and book reviews. Only English-language articles published from Jan 2018 to Aug 2026.

2.2 Search Strategy

A comprehensive search strategy will be executed across the following databases: MEDLINE (via PubMed), Embase, IEEE Xplore, and Scopus. The search strategy will be developed by the research team in collaboration with a medical librarian.

A sample search string designed for MEDLINE is shown in Box 2.2. This search strategy was validated using test records from peer-reviewed literature in August 2026.

Box 2: Draft MEDLINE (PubMed) Search Strategy

Search Query Block:

```
("Artificial Intelligence"[Mesh] OR "Natural Language
Processing"[Mesh] OR "Machine Learning"[Mesh] OR "Deep
Learning"[Mesh] OR "large language model*"[Title/Abstract] OR
"NLP"[Title/Abstract] OR "neural network*"[Title/Abstract] OR
"AI"[Title/Abstract])
AND
("Clinical Trials as Topic"[Mesh] OR "Patient Selection"[Mesh] OR
"clinical trial*"[Title/Abstract] OR "trial eligibility"[Title/Abstract]
OR "patient recruitment"[Title/Abstract])
AND
("match*"[Title/Abstract] OR "select*"[Title/Abstract] OR
"screen*"[Title/Abstract] OR "cohort identification"[Title/Abstract]
OR "automated parsing"[Title/Abstract])
```

Filters: English language, Publication date: January 1, 2018 – August 31, 2026.

2.3 Study Selection and Screening

Following the search, all identified citations will be uploaded to Covidence (or a similar screening software) and duplicates will be removed automatically.

The screening process will consist of two distinct phases:

1. **Title and Abstract Screening:** Two reviewers (SJ and AV) will independently screen the titles and abstracts of all retrieved studies against the predefined inclusion and exclusion criteria.
2. **Full-Text Review:** Studies that pass the first phase will undergo full-text review by the same two reviewers independently.

Any discrepancies or disagreements between the reviewers at either stage will be discussed and resolved through consensus. If consensus cannot be reached, a third reviewer (CL) will make the final decision. The results of the search and study screening process will be reported in full in the final scoping review and presented using a PRISMA 2020 flow diagram.

3 Data Charting and Extraction

Data extraction (also referred to as data charting) will be performed by two independent reviewers using a standardized extraction form. This form will be piloted on a random sample of five included studies to ensure consistency and completeness.

3.1 Data Extraction Variables

The draft data charting form covers bibliographic data, technical methodology, clinical contexts, and operational findings. The variables to be extracted are detailed in Table 2.

Table 2: Draft Data Extraction Variables and Classification

Category	Specific Fields	Description / Examples
Study Identification	Publication Year, Author(s), Journal/Conference, Study Location	Basic metadata to identify the paper, geographic distribution, and publication trends.
AI Technology	Core AI Paradigm, Model Architecture, Training Framework	Categorization of techniques (e.g., Classical ML, Deep Learning, Transformer-based LLM, Rule-based systems) and specific models used (e.g., BERT, GPT-4, proprietary engines).
Data Modality	Input Data Type, Unstructured Text Extraction, Clinical Coding	Types of clinical data parsed (e.g., EHR demographics, ICD-10 codes, lab measurements, genomic variants) and NLP techniques (e.g., Named Entity Recognition, Negation detection).
Clinical Context	Therapeutic Area, Trial Phase, Matching Scope	The clinical focus (e.g., Oncology, Infectious Disease) and trial characteristics (e.g., Phase I–IV, single-center vs. multi-center).
Performance Metrics	Technical Performance, Operational Metrics	Performance indicators such as Precision, Recall, F1-score, AUC-ROC, alongside real-world metrics like time saved or reduction in screening failures.
Ethical & Bias Audits	Demographic Reporting, Bias Mitigation, Privacy Safeguards	Assessment of whether the study evaluated model performance across gender, race, or age groups, and techniques used to preserve privacy.

3.2 Charting Process Flow

During extraction, reviewers will extract data into a shared spreadsheet hosted on a secure cloud platform. Discrepancies will be resolved through discussion, and any modifications to the charting form during the review will be documented and reported in the final publication.

To visualize our extraction workflow, Figure 1 illustrates the iterative charting cycle between initial pilots, full extraction, and validation.

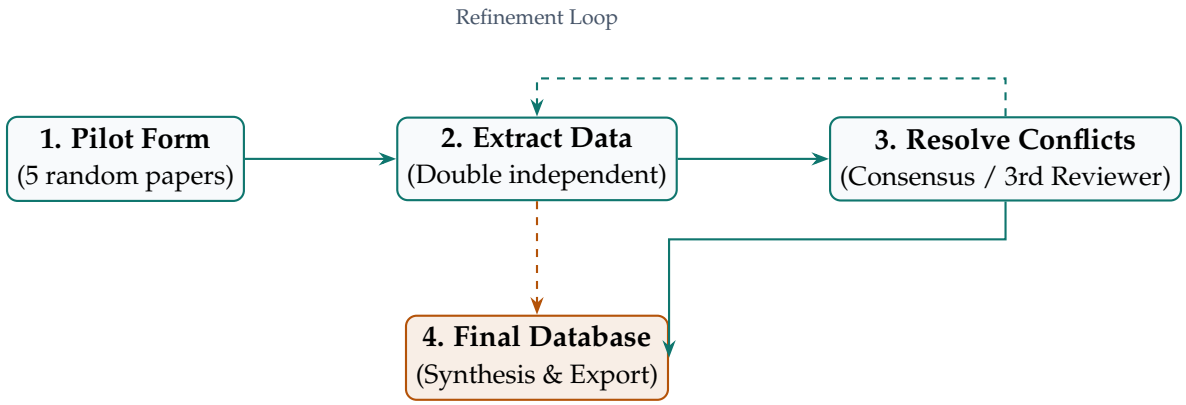

Figure 1: Iterative data extraction and validation workflow.

4 Data Synthesis and Presentation

The synthesis and presentation of results will follow the PRISMA-ScR guidelines to ensure systematic and transparent reporting. We will combine quantitative mapping with qualitative thematic analysis to provide a comprehensive landscape of AI-driven trial matching.

4.1 Quantitative Mapping and Analysis

Basic descriptive statistics will be compiled for all included studies. We will analyze and present:

- The chronological distribution of publications from 2018 to 2026.
- The frequency of clinical specialties (e.g., oncology, cardiology, rare diseases) using AI matching.
- The proportion of studies utilizing open-source versus proprietary models (such as Meridian Clinical Matcher or Nexa Clinical Suite).
- Technical metrics (accuracy, F1-score, AUC-ROC) summarized by model architecture class.

4.2 Qualitative and Thematic Synthesis

We will conduct a thematic analysis of the qualitative text extracted from the discussion sections of the papers, focusing on the following areas:

- **Implementation Barriers:** Issues regarding integration with legacy Electronic Health Record (EHR) databases, data cleansing requirements, and system latency.
- **Algorithmic Bias:** The extent to which systems are evaluated for bias against minority populations, and whether demographic features are handled ethically.
- **Explainability:** Methods utilized to explain matching decisions to clinicians (e.g., SHAP/LIME values, highlighted text segments, or LLM-generated rationales).

4.3 Scoping Review Timeline

The projected timeline for the scoping review is summarized in Table 3, detailing the stages and institutional responsibilities.

Table 3: Scoping Review Project Timeline

Phase / Milestone	Target Completion	Institutional Lead
Protocol Registration	October 2026	Meridian Health Institute
Database Search & Deduplication	November 2026	Meridian Informatics Library
Title & Abstract Screening	January 2027	Synapse AI Labs & Meridian
Full-Text Screening	March 2027	Synapse AI Labs & Vertex Systems
Data Charting & Extraction	May 2027	Vertex Systems & Meridian
Synthesis & Manuscript Draft	July 2027	Meridian Health Institute
Submission for Peer Review	September 2027	All Collaborating Authors

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