ICI - GEARBOx - Final Report
UC_PI S. Volchenboum-AWD102895
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Executive Summary

The **GEARBOx platform** (Genomic Eligibility Algorithm for Better Outcomes) was conceived and developed at the University of Chicago in partnership with the Leukemia & Lymphoma Society and the Data for the Common Good (D4CG) program. Fueled by generous support from ICI, GEARBOx has evolved to become a transformative, patient-centric platform for efficiently and accurately matching children with cancer to the clinical trials most appropriate for their unique diagnostic and molecular profiles.

GEARBOx overcomes the fundamental barriers of clinical trial matching, including the complexity and variability of eligibility criteria presented in free-text formats. Our platform has grown from a focused pediatric AML tool to a scalable multi-disease system, significantly broadening impact while streamlining trial identification for pediatric, adolescent, and young adult oncology patients.

Platform Overview

GEARBOx comprises four integrated components:

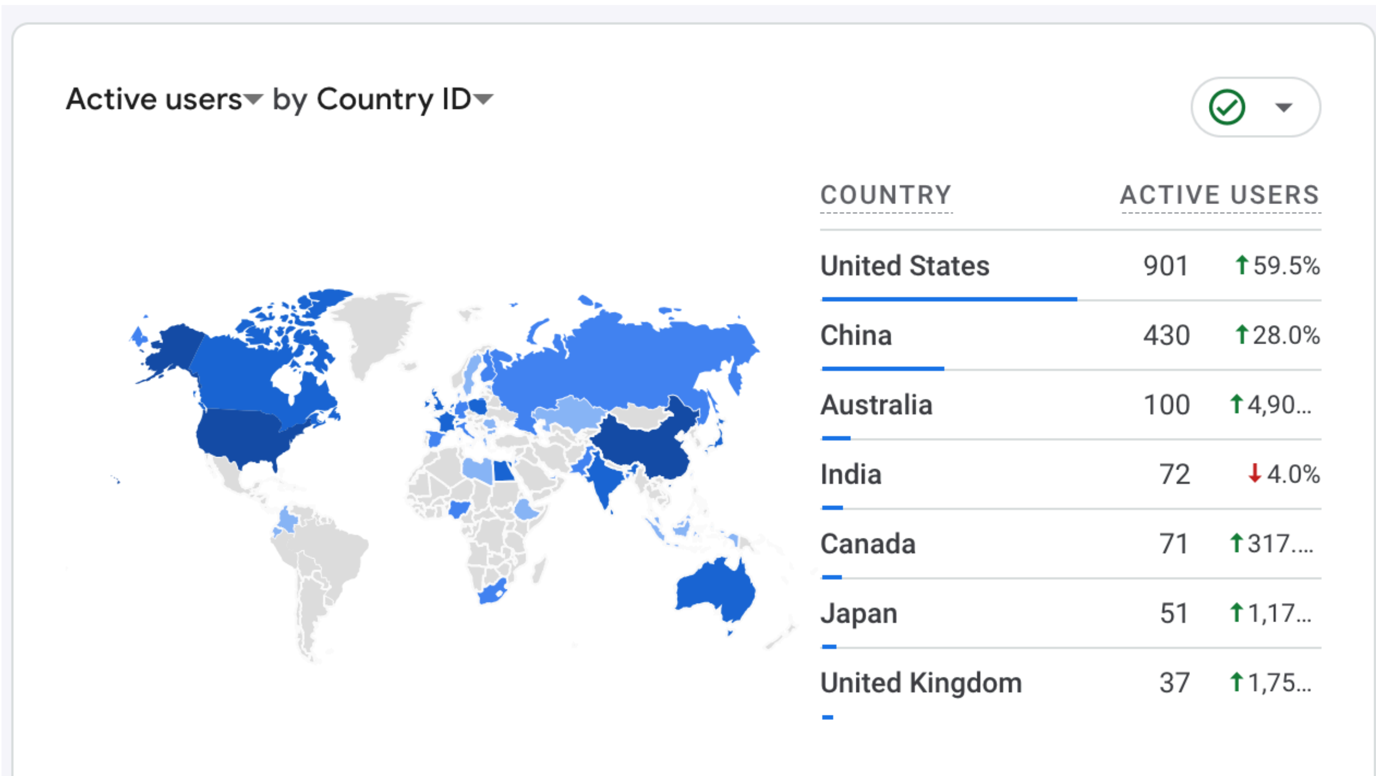
1. **Clinical Trial Matching Ecosystem**: A scalable system supporting multi-disease trial matching for childhood cancers.
2. **AI Technology Stack**: Automated ingestion, parsing, and mapping of trial eligibility criteria into computable logic, using cutting-edge natural language processing (NLP) and machine learning (ML) approaches.
3. **Administrative UI**: Expert-driven review, annotation, and boolean logic assembly for complex eligibility criteria.
4. **Clinician UI**: Streamlined interface for entering patient data, generating match results, and reviewing trial eligibility, optimized for decision support.

Expansion and Achievements

Disease Coverage and Clinical Reach

- **Initial Focus**: Launched with seven relapsed/refractory AML clinical trials.
- **Progressive Expansion**: Added multiple malignancies including neuroblastoma, germ cell tumors, rhabdomyosarcoma, Ewing sarcoma, and osteosarcoma.

- **Variable Harmonization**: Developed and harmonized new variables, supporting disease- and trial-specific requirements across cancer types.
- **Global Usage**: Enabled by 325 unique users, predominantly physicians and researchers from 165 institutions, with trials representing 1,472 recruiting sites globally.
- **Integration into Tumor Boards**: GEARBOx is actively used in international tumor boards, strengthening global collaborative care.



Automation and Technical Innovation

- **End-to-End NLP Pipeline**: Robust, automated pipeline for ingesting clinicaltrials.gov protocols, extracting and labeling eligibility criteria, and converting free-text requirements into structured computable logic.
- **Reduced Annotation Burden**: Time required for manual trial extraction and annotation dropped drastically, while annotation accuracy increased through continuous expert feedback integration and NLP model retraining.
- **LLM Deployment**: Successfully incorporated large language models (e.g., GPT-4, GPT-4o) with structured frameworks (Instructor) for improved mapping accuracy, consistency, and mitigation of hallucinations.

- **NLP Components**:
    - Context-free grammar (CFG) parsing for quantitative/ordinal criteria (e.g., age, lab values)
    - Biomedical named entity recognition (scispaCy) with UMLS and NCIt mapping
    - Word embeddings (k-nearest neighbors) for semantic mapping
    - Binary classifiers for identifying "soft" exclusion criteria (washout periods, reproductive health requirements)

User Interface & Usability

- **Administrative Enhancements**: Advanced modules for reviewing extracted criteria, assembling eligibility logic with boolean operators, and organizing label sets via Doccano (now supporting bulk operations, robust metadata, soft deletes, and user roles).
- **Clinician-Facing Improvements**: Data entry, branching questions, and match result explanations are now more compact, intuitive, and actionable—enabling clinicians to quickly discern matched, unmatched, or undetermined results, with expandable rationale categories.
- **Ongoing Stakeholder Feedback**: Continuous input from multi-site clinicians and researchers iteratively refines UI workflow, annotation processes, and question knowledgebase.

Interoperability and Integration

- **EHR Integration**: Proof-of-concept for connecting directly to Epic EHR, with focus on mapping Epic fields to GEARBOx variables. Determined that OAuth-based integration or internal system development offers the most control and security.
- **Molecular Data Sharing**: Governance-aligned collaborations with Children's Oncology Group (COG), Hematologics, Inc., and international consortia could enable future secure molecular assay data exchange.
- **Deployment Options**: Architecture transitioned for Red Hat OpenShift compatibility (on-prem), supporting hospital security/governance requirements while maintaining robust AWS cloud deployments.

Aims and Progress

Aim 1: Expand Tumor Types

- Expanded platform from AML to major pediatric solid tumors.

- Manual abstraction with expert clinicians ensured high standardization and the creation of gold-standard annotation sets for evaluating NLP model performance.
- Feedback-driven simplification of question sets and knowledgebase to improve usability and engagement.

Aim 2: Refine Criteria Extraction

- Developed and optimized end-to-end NLP pipeline.
- Integrated CFG, word embeddings, binary classifiers, and NER for robust free-text-to-computable mapping.
- LLM experiments pushed boundaries on mapping accuracy and output reliability.
- Maintained high performance in criteria extraction through constant SME (subject matter expert) annotation, review, and model feedback loops.

Aim 3: Enhance Interface and Functionality

- Created a UI for admins and improved clinician interface, streamlining workflows and supporting flexible logic construction (react-awesome-query-builder).
- New features: grouping, nesting, priority assignment, metadata extension, robust error handling, and real-time eligibility logic assembly.

Aim 4: Integrate and Deploy with Third-Party Sources

- Explored manual, agreement-based, and OAuth EHR integration pathways, determining OAuth as optimal for control, security, and scalability.
- Adapted platform for seamless data flow with research partners within institutional governance frameworks.

Measured Impact

- **Clinical and Research Utility**: GEARBOx has directly powered advances in childhood cancer care, improving match efficiency and data-driven decision-making for international clinicians and research teams.
- **Platform Scalability**: Broad disease coverage and flexible architecture support global, multi-institutional collaborations in real-time.
- **Positive Feedback Loop**: Annotation accuracy and workflow efficiency continue to improve as model retraining incorporates expert corrections rapidly.

Next Steps and Funding Request

GEARBOx is **well-positioned for further transformative advances**:

- **Deepening Automation**: Additional investment will allow for full EHR integration, streamlined clinician onboarding, and the expansion of AI-powered eligibility mapping to cover the entire clinical trial landscape.
- **Broadening Disease and Modalities**: Funding will drive faster inclusion of new tumor types and molecular markers, empowering rare cancer research and precision medicine.
- **Accelerating Impact**: More resources will enable proactive trial identification, enhanced analytics for clinical support, and deeper partnerships with global research consortia.

Recommendation:
Renewed and increased support for GEARBOx will translate directly into more efficient, equitable, and precise matching for children and families facing cancer. Our platform has delivered on ambitious goals, thanks to prior investment, on the precipice of revolutionizing pediatric clinical trial access and cancer informatics for the future.