Improving Medication Safety: Predicting Potential Drug-Drug Interactions Using Machine Learning

David Forson, Mohammed Moidul Hassan, Chiara Zheng

Health Information Systems (94-706)
Heinz College, Carnegie Mellon University
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H. John Heinz III College
Carnegie Mellon University

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ABSTRACT

Drug interactions pose a significant challenge in modern healthcare, contributing to a substantial number of adverse drug events (ADEs) that range from mild discomfort to life-threatening conditions. The increasing prevalence of polypharmacy, particularly among elderly patients and individuals managing chronic diseases, has made it even more difficult for healthcare providers to manually track and prevent potential drug interactions. Although physicians and pharmacists rely on their expertise and existing drug interaction databases, the sheer volume of new medications and emerging research makes it nearly impossible to stay fully updated on all possible risks. This gap in knowledge and real-time detection has led to preventable medication errors, hospital readmissions, and increased healthcare costs.

PROBLEM, CONTEXT, STAKEHOLDER ANALYSIS

Drug-drug interactions (DDIs) are complex clinical issues that have been a longstanding concern for stakeholders working to mitigate their burdens on both patients and the healthcare system at large. Stakeholders can be categorized in different ways. In one framework, they form a triad consisting of the patient, the prescriber, and the pharmacist, all of whom are directly involved in addressing the risks posed by DDIs. In another framework, the stakeholders can be classified as a pentad: prescribers and pharmacists, drug development companies, regulatory bodies, payers, and publishers of health-related journals. Regardless of the classification, the shared goals among

stakeholders are clear: to identify leadership that can drive initiatives addressing DDIs, to increase patient involvement in the care process through education and

self-advocacy, and to institutionalize principles of conservative prescribing in medical education and practice while promoting high-quality DDI metrics (Beninger, 2023).

Given the potentially devastating effects of DDIs, eHealth solutions have become essential in addressing their impact. These digital tools have been shown to improve medication therapy management by providing critical services to physicians across healthcare settings (Hammar et al., 2021). Clinical Decision Support Systems (CDSS) in particular have proven effective at alerting prescribers to common drug interactions, with ongoing research aiming to further advance these systems.

We believe that integrating a Clinical Decision Support System into a Computerized Physician Order Entry (CPOE) system offers a valuable opportunity to enhance patient safety by proactively identifying potential drug interactions before prescriptions are finalized. The ability to predict and prevent ADEs not only improves patient outcomes but also reduces the cognitive burden on physicians and pharmacists, allowing them to focus on delivering high-quality care. Furthermore, advancements in AI-driven models and natural language processing techniques can enhance these systems by incorporating the latest research findings, ensuring that healthcare professionals have access to the most up-to-date information.

As healthcare systems increasingly adopt Electronic Health Records (EHRs) and CPOE systems, the limitations of traditional drug interaction alerts have become more apparent. Many existing systems rely on static, rule-based databases, often generating excessive and non-specific alerts that contribute to clinician alert fatigue. This

phenomenon reduces the effectiveness of alerts, as critical warnings may be dismissed due to frequent false positives.

We have developed a DSS system which can potentially be integrated into the CPOE system to proactively identify potential drug-drug interactions. This works by using Machine Learning (ML) based models trained on drug interaction datasets from the past decade. To enhance predictions and enable the use of the latest data, this DSS can be augmented with Retrieval-Augmented Generation (RAG) models to allow for inclusion of information from the latest literature. This will help provide proactive support for identification of drug-drug interactions directly within clinical workflow, reducing clinician alert fatigue and improving patient safety.

POLICY AND MANAGEMENT ISSUES

The Duke-Margolis Center for Health Policy identifies the prevalence of harmful drug-drug interactions as a major problem in the United States, attributing approximately 26% of drug-related hospitalizations to this cause (Harrison et al., n.d.). The Center emphasizes that fragmented healthcare systems—spanning multiple stakeholders such as drug developers, the FDA, and third-party publishers—contribute to this issue by generating data with inconsistencies, which inadvertently leads to drug-drug interactions. A key policy concern is that while FDA oversight is effective in approving drugs, it is less effective in the standardization of post-approval guidelines. The lack of centralized systems and consistent updates further exacerbates the problem. To address these challenges, the proposed solution involves standardizing

drug-drug interaction information, improving health IT integration, and enhancing post-marketing drug updates to minimize incidences of drug-drug interactions.

Another policy issue arises from poor stakeholder coordination. Vendors, Electronic Health Record (EHR) developers, and healthcare organizations often use different methods to curate and display DDI alerts, leading to repetitive and non-specific warnings that contribute to 'alert fatigue.' In low-resource health facilities, the lack of advanced customization in Clinical Decision Support Systems (CDSS) may cause drug-drug interactions due to insufficient pharmacy support capabilities (Malone et al., n.d.). To mitigate these risks, improving alert design by implementing tiered alerts and adopting context-aware filtering—integrating patient-specific data to suppress unnecessary alerts—will be critical in minimizing drug-drug interactions.

CURRENT UNDERLYING PROCESS MODEL

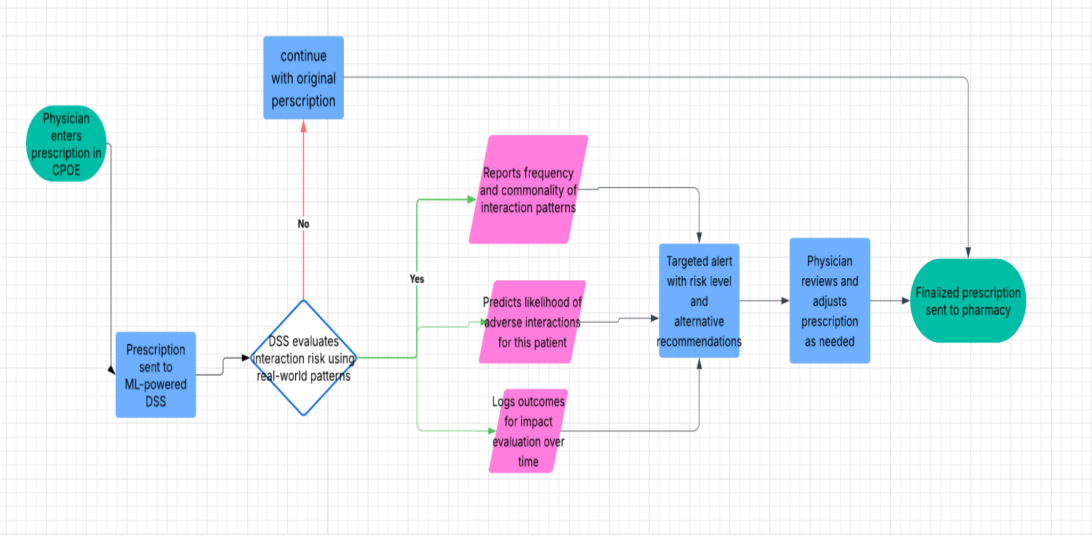

Figure 1: Process Model

The key activities associated with our drug-drug interaction (DDI) decision support process begin with when a physician logs into the system with their username and password, with authorization then they can select their purpose of using the system (e.g patient data intake, lab test order, etc). Once they choose “drug prescribing” they have entered our system. Physicians will select the drug they plan to subscribe into the Physician Order Entry (CPOE) system. Once submitted, the prescription is automatically sent to the machine learning (ML)-powered Decision Support System (DSS) for evaluation. The DSS analyzes the prescribed drugs for potential interaction risks by leveraging real-world patterns and predictive modeling trained on drug chemical properties and historical interaction data. At the decision point, if the DSS finds no significant interaction risk, the prescription continues as originally intended without interruption. However, if a risk is detected, the system initiates several key activities. For now it generates the likelihood (with percentages and identified as high, moderate or low risk) of the drugs entered having an interaction, along with all drug info related to the entered drug. In the future with more development with our DSS, It will generate reports that summarize the frequency and commonality of identified interaction patterns, predict the likelihood of adverse drug interactions for the specific patient context, and logs these outcomes for ongoing impact evaluation. Based on this analysis, the DSS issues a targeted alert to the physician, indicating the risk level and suggesting alternative drug recommendations if appropriate. The physician then reviews this information and, if needed, adjusts the prescription accordingly before finalizing and sending it to the pharmacy. Throughout this process, the DSS not only supports

immediate decision-making but also continuously learns from logged outcomes to enhance its predictive capabilities over time. This workflow ensures that critical alerts are provided in a timely, clinically relevant manner, integrating seamlessly into the prescription workflow without overwhelming physicians with unnecessary warnings.

GAPS BETWEEN EXISTING SOLUTION AND OUR APPROACH

IBM Watson Health Has developed a tool known as the IBM Micromedex tool which uses the MONAHAN algorithm - a deterministic rule-based approach - to identify drug-drug interaction. The algorithm uses data on pharmacokinetics and pharmacodynamics of drugs as well as evidence from clinical trials and curated literature to accurately determine known interactions, which can identify - to a large extent- the drug-drug interactions our DSS can. However, it fails to identify drug-drug interactions for novel or emerging drugs unless there's a manual update, which may not be always available until a significant period of pharmacovigilance. However, our DSS model employs language-based molecular embeddings that capture structural and contextual features of drugs making drug-drug interactions possible for even new or emerging drugs, which in turn, provides better patient safety outcomes and health, overall.

IT ARCHITECTURE OF DSS

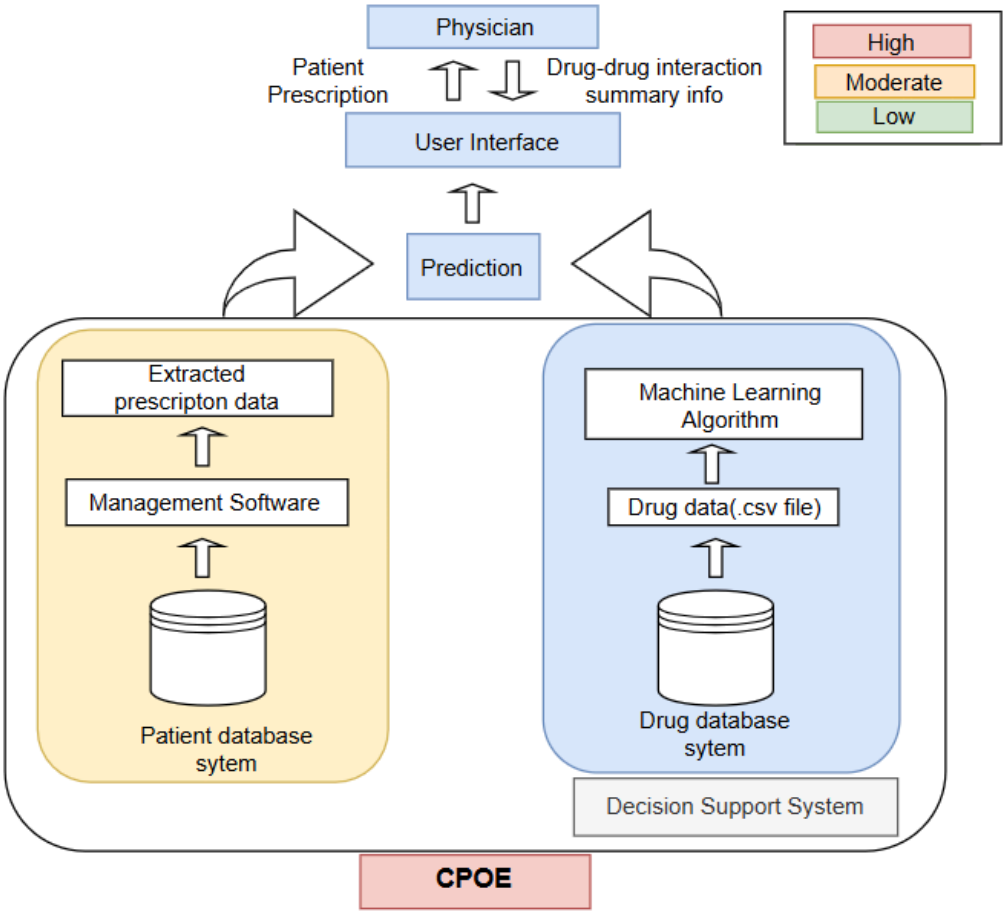

Figure 2: Workflow of Drug Prescription and DSS Drug-Drug Interaction Check.

A. DEVELOPMENT OF THE DRUG DATABASE SYSTEM

1. Data from the Higher-Order Drug-Drug Interaction Dataset was converted from a .xml file to a .csv file.

2. Data wrangling was done appropriately to have unique drug records by checking for duplicates and to also rename columns for easy identification.

3. The dataset was then split into six different .csv files based on unique drug components. The six different tables were drugs, drug_indications, drug_properties,

drug_pharmacodynamics, drug_timestamp and drug_regulatory_info.

4. The data was further cleaned and a final view was created capturing all features of the final of all six tables and exported as a .csv file.

5.Using streamlit and other libraries, the resulting file was connected to the saved trained machine learning model, which makes the prediction based on the drug names entered into the Decision-support system found in the final .csv file. If the resulting percentage lies between 0% and 29% inclusive, the interaction is said to be low. If the likelihood lies between 30% and 70% inclusive, the interaction is said to be moderate. Beyond 70%, the interaction is said to be significant.

6.The final view(.csv file) also contains other drug information such as the general drug description, half-life, clearance, dosage form etc.. which can be accessed to inform further clinical decisions.

B. HOW THE DRUG-DRUG INTERACTION DSS WORKS WITH THE PATIENT DATABASE SYSTEM

1. The Drug Interaction Decision Support System is designed to be integrated into a Computerized Decision Support System to access drugs that are prescribed to determine the likelihood of interaction.

2. The model employed is trained via language-based molecular embeddings that capture structural and contextual features of drugs.

3. Using this technique, drug-drug interactions can be captured proactively for drugs -even for newly developed ones- to ensure better decisions, patients safety and better clinical outcomes.

DATA SOURCES USED

1. The Higher-Order Drug-Drug Interaction Dataset was used for this project. This dataset is derived from the United States Food and Drugs Administration(FDA) Adverse Event Reporting System records.

2. The dataset consists of 109,744 records including 2506 unique drugs and 4,569 unique side effects. The dataset captures multi-drug interactions.

3. The data elements captured include the drugs, drug properties, drug indications, drug regulatory information, drug timestamp and drug pharmacodynamics.

4. The drugs element captures the drug_id, the drug_name, drug_description, drug_type,drug_state(dosage form), Chemical Abstract Service Number (cas_number) and the Unique Ingredient Identifier(unii code). The drug_properites element uniquely identifies the average_mass, the monoisotopic mass, synthesis_reference, volume of distribution, clearance, half-life and protein-binding. The drug_indications element uniquely captures the indication for the captured drugs. The drug_pharmacodynamics element uniquely captures the pharmacodynamics,mechanism of action, toxicity, metabolism, absorption and route of administration. The drug_timestamp element uniquely identifies the time the drug data was first entered(created) and the last time it was updated. The drug_regulatory_info element provides data on the fda_label as well as the Material Safety Data Sheet (msds).

DATA FLOW FOR THE DATABASE:

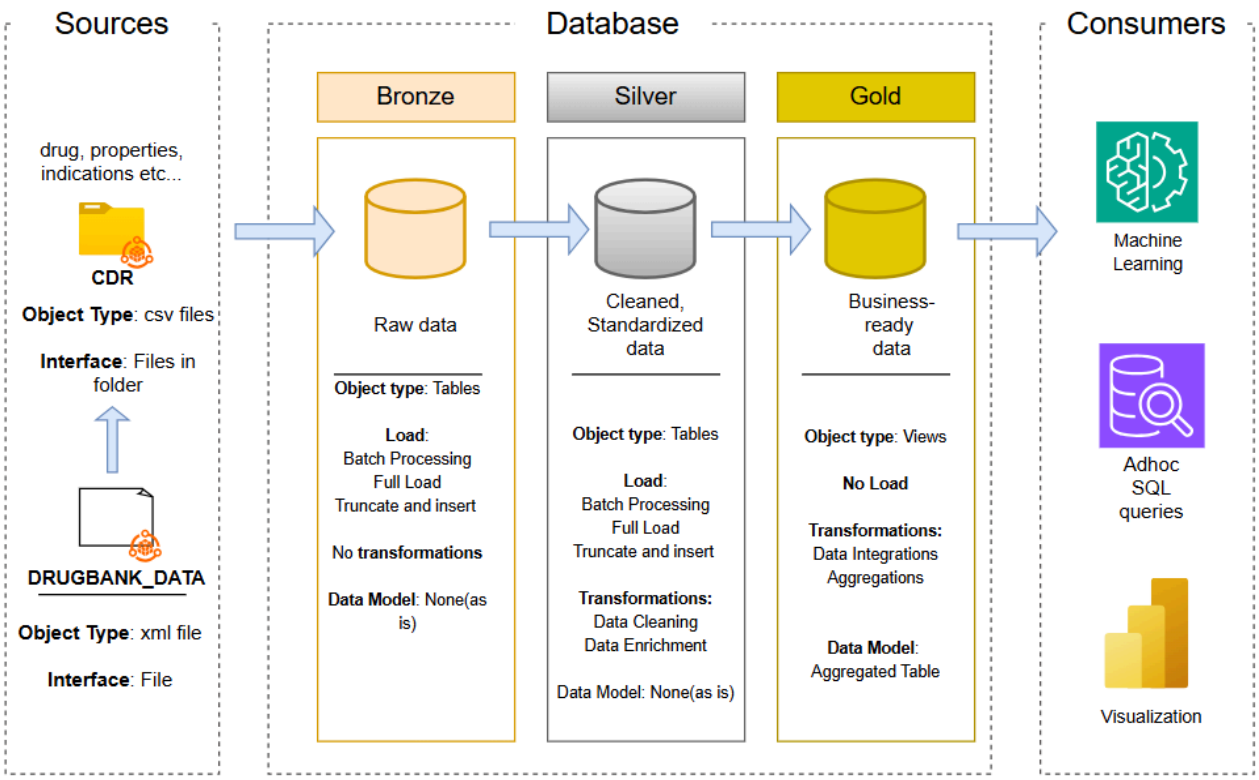

Figure 3: Data Flow Diagram for DSS Drug Database Integration.

FINAL STRUCTURE OF THE DATABASE:

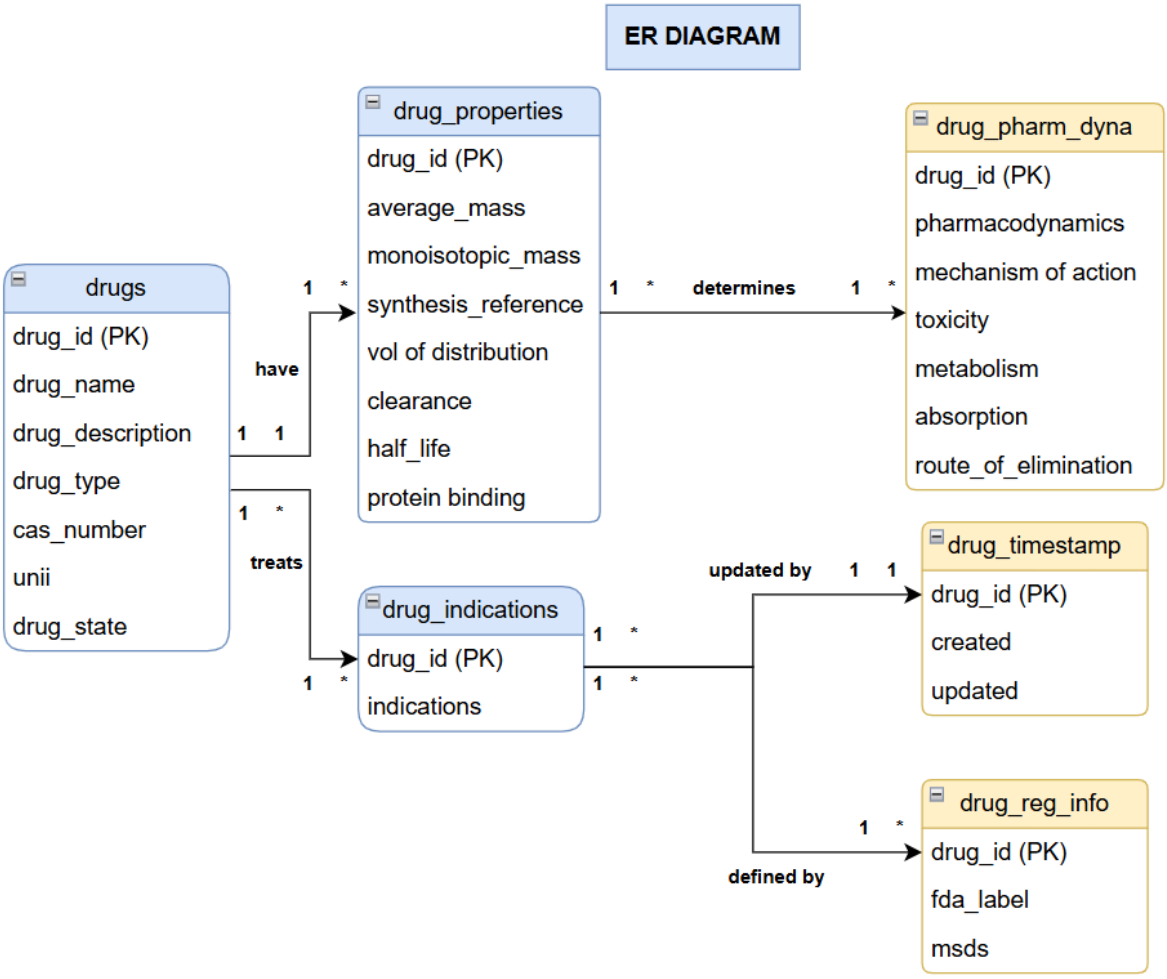

Figure 4: Entity-Relationship (ER) Diagram of Drug-Drug Interaction Database.

STANDARDS AND HIPAA REQUIREMENTS.

Our Decision Support System(DSS) will be using the RxNorms Standard, a normalized drug vocabulary, to standardize drug names across the database for querying for both brand and generic drugs. The National Council for Prescription Drug Products(NCPDP)standard - a messaging standard- is also needed for our DSS product since drug-drug interactions will still be evaluated for drugs that are electronically prescribed. The incorporation of the ICD 9/10 - a terminology standard for

classification of symptoms and diagnosis- is important for our DSS as the drugs captured in the database are mapped onto their respective indications. The Health Level Seven (HL7) standard will be vital to ensure that there is Electronic Health Record Interoperability. The HIPAA standard is also needed to ensure patient privacy and security as our DSS will access patient's medication information and flag them accordingly.

APPLYING THE PEIT FRAMEWORK

We applied the PEIT (Process-Enabling Information Technology) framework to guide the implementation and deployment of our Drug-Drug Interaction (DDI) Decision Support System (DSS). Our strategy addresses key PEIT elements: Process, People, Groups, Technology, Pitfalls, and Strategies.

Predictive modeling of drug-drug interactions is relatively novel for most clinicians. To address the associated complexity, we incorporated initial training sessions and designed a user interface that uses a simple risk categorization system (High, Moderate, Low) to promote intuitive understanding. Although the DSS introduces new predictive capabilities, it does not overhaul existing clinical workflows; rather, it integrates into them with a moderate volume of change, minimizing operational disruption and allowing clinicians to adapt without major workflow interruptions.

Clinicians maintain full discretion to accept or override DSS alerts, ensuring that the tool supports but does not dictate clinical decisions. Since familiarity with pharmacology and health IT systems varies among users, we prepared comprehensive user guides,

onboarding tutorials, and live demonstrations to enhance system understanding and adoption. By equipping clinicians with adequate training, we hope to promote confidence and consistency in DSS usage across different levels of technical and clinical expertise.

The system impacts multiple professional groups, particularly physicians and pharmacists, and is designed to integrate directly into critical clinical workflows, notably prescribing and medication reconciliation processes. Recognizing the different degrees of autonomy across clinical departments, we have planned for an incremental deployment strategy. The rollout will initially focus on specific departments such as cardiology or oncology, allowing for department-specific customization before broader institutional adoption.

Technologically, the DSS is designed as a flexible tool, providing predictive insights without enforcing rigid new workflows. This ensures that clinical autonomy is preserved while enhancing clinical decision-making. The system integrates seamlessly alongside existing Computerized Physician Order Entry (CPOE) systems, avoiding major IT infrastructure changes and reducing barriers to implementation.

Potential pitfalls include initial user distrust of predictive alerts and the possibility of discretionary use leading to low adoption rates. To mitigate these risks, we plan to use a Rational-Empirical Approach by demonstrating the system's predictive accuracy through case studies and emphasizing its real-world impact on improving safety outcomes. A phased rollout strategy will be employed, starting with a small pilot group to gather feedback and refine the system. Furthermore, we plan to establish a governance-level

steering committee composed of physicians, pharmacists, and IT personnel to oversee deployment, monitor adoption trends, and guide system iteration. Finally, live technical support and dedicated user feedback channels will be provided during the initial post-deployment period to ensure continuous user engagement and rapid troubleshooting.

WHAT-IF SCENARIO ANALYSIS.

The DDI DSS was specifically designed to support "what-if" analysis during the drug prescribing process. By allowing clinicians to explore different drug combinations and immediately view predictive interaction risks, the system enhances clinical flexibility and safety. For example, if a clinician considers prescribing warfarin and ciprofloxacin, the system might flag a high-risk interaction likelihood of 74%, categorizing it as red, and suggesting the need for alternative therapy or heightened INR monitoring. Alternatively, prescribing simvastatin and amlodipine might result in a moderate-risk prediction (e.g., 38%), where the system advises dosage adjustments or patient counseling regarding potential side effects. In low-risk scenarios, such as acetaminophen and amoxicillin with a predicted interaction likelihood of 4%, the system reinforces clinician confidence that no significant action is required.

This ability to simulate various prescribing options empowers clinicians to test alternative therapies quickly within the DSS interface. It promotes more informed decision-making without the need for extensive manual cross-referencing or pharmacy consultations. By integrating predictive modeling with clinical intuition, the DSS not only

flags potential dangers but encourages proactive therapeutic adjustments tailored to patient needs.

POLICY IMPLICATIONS

From a health policy perspective, the DDI DSS aligns strongly with current regulatory efforts to enhance patient safety, minimize adverse drug events, and promote technology-enabled clinical decision support. Agencies such as the Centers for Medicare & Medicaid Services (CMS) and the Office of the National Coordinator for Health Information Technology (ONC) have emphasized the critical role of clinical decision support (CDS) tools in improving healthcare quality under initiatives like Meaningful Use and Promoting Interoperability. The DSS directly supports these goals by helping clinicians identify potentially harmful drug combinations before they result in patient harm, thus improving overall care outcomes and potentially reducing healthcare costs related to preventable adverse events.

In terms of IT policy, the system must strictly adhere to HIPAA regulations concerning the privacy and security of patient health information. All clinical inputs, model outputs, and usage logs must be protected by appropriate encryption and access control protocols. Interoperability is also a key consideration: the DSS is designed with compliance to HL7 FHIR standards to facilitate seamless integration with a wide range of EHR platforms. Furthermore, IT governance policies must mandate regular model retraining, validation, and bias audits to ensure the predictive outputs remain clinically relevant and equitable across diverse patient populations.

CONCLUSIONS AND RECOMMENDATIONS

The DDI DSS represents a transformative innovation in clinical decision support by delivering real-time, predictive insights into potential drug-drug interactions during the prescribing process. Its integration into clinical workflows enhances the clinician's ability to make safer, more informed therapeutic decisions while preserving provider autonomy. By categorizing interaction risks into intuitive green, orange, and red flags, and offering clear action recommendations, the system complements rather than disrupts existing clinical judgment.

Based on our implementation analysis,We propose several key reccomandations. First, a pilot deployment within select clinical departments should be prioritized to gather performance metrics and clinician feedback. Second, comprehensive training programs explaining model functionality and limitations are essential to foster clinician trust and adoption. Third, a robust feedback mechanism should be incorporated into the user interface to capture real-world input for model improvement. Fourth, institutions must maintain strict data security standards and regularly reassess model performance to prevent drift or emerging biases. Finally, expansion of the system's capabilities to include pharmacogenomic interactions,alternative drugs, renal dosing alerts, or patient-specific factors could further enhance clinical utility over time.

Ultimately, the DDI DSS is positioned not merely as a technological innovation, but as a vital partner in promoting safer prescribing practices and advancing patient-centered care delivery.

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APPENDIX

Example DSS interface output

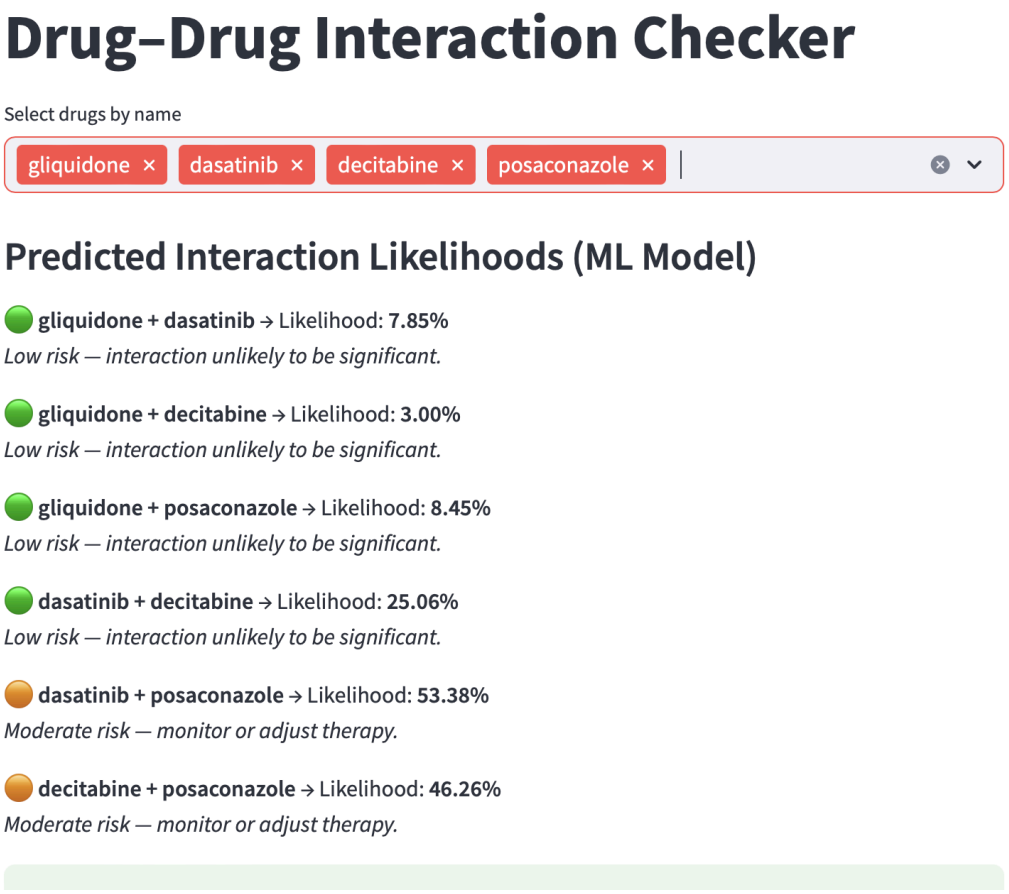

Figure 5: Sample Interface Output of Drug-Drug Interaction DSS.