Improving Medication Safety with Pharmacogenomics-Enhanced Clinical Decision Support Systems (PGx-CDSS)

Executive Summary:

Project Title: Improving Medication Safety with Pharmacogenomics-Enhanced Clinical Decision Support Systems (PGx-CDSS)

Overview:
Medication errors and adverse drug events (ADEs) are major challenges in hospital settings, leading to increased patient harm, prolonged hospital stays, and higher healthcare costs. Traditional Clinical Decision Support Systems (CDSS) provide standardized medication recommendations but fail to account for individual genetic differences that impact drug metabolism and efficacy. This project aims to implement and evaluate a Pharmacogenomics-Enabled Clinical Decision Support System (PGx-CDSS) that integrates patient genetic data with electronic health records (EHRs) to provide personalized medication recommendations in real time.

Objectives:

- Reduce medication errors and ADEs by providing personalized dosing recommendations.
- Improve clinical decision-making by integrating pharmacogenomic data into existing EHR workflows.
- Enhance provider adoption and usability by minimizing alert fatigue and optimizing system design.
- Validate the impact of PGx-CDSS on patient safety, medication efficacy, and healthcare outcomes.

Strategic Importance:
Precision medicine is the future of healthcare, and pharmacogenomics offers a data-driven approach to optimizing drug therapy. By integrating PGx into CDSS, this project aligns with national healthcare goals to improve patient safety, reduce costs, and enhance treatment effectiveness. The findings will inform future hospital-wide adoption strategies and contribute to advancing personalized medicine in clinical practice.

Implementation Approach:
The project will be executed in three phases:

1. System Development & Integration: Embed PGx-CDSS within the hospital's EHR system and ensure seamless data flow.
2. Pilot Study & Evaluation: Implement the system in select hospital departments, collecting data on medication safety, usability, and clinical outcomes.
3. Analysis & Scaling: Assess impact, refine system functionalities based on clinician feedback, and develop a roadmap for broader implementation.

Expected Outcomes:

- Reduction in medication errors and ADEs.
- Increased clinician confidence in pharmacogenomic-guided prescribing.
- Streamlined clinical workflows with minimal disruption.
- Data-driven insights to inform broader adoption of PGx-CDSS in healthcare systems.

Conclusion:

This project represents a critical step toward integrating precision medicine into everyday clinical practice. By leveraging pharmacogenomics and advanced decision support, we can improve medication safety, enhance patient outcomes, and set the foundation for more personalized healthcare. This initiative has the potential to serve as a model for hospitals nationwide seeking to adopt innovative, data-driven strategies for medication management.

Lay Language Summary:

Principal Investigator: Kevin Nguyen
IRB#: To be assigned
Study/Protocol Title: Improving Medication Safety with Pharmacogenomics-Enhanced Clinical Decision Support Systems (PGx-CDSS)

1. Purpose: This study will test a computer system called PGx-CDSS. This system helps doctors and pharmacists pick the right dose of medicine for patients by looking at their genes and health. The goal is to reduce mistakes and make treatments safer in hospitals.
2. Recruitment of participants: The study will include doctors, pharmacists, and nurses who use the PGx-CDSS system. It will also include patients who take certain medicines, like blood thinners, pain relievers, or antidepressants, that work differently based on their genes. Doctors and nurses will be invited to join, and patients will be chosen based on the medicines they take.
3. Procedures: Patients will receive normal medical care. If their genetic information is available, the PGx-CDSS system will use it to suggest better medicine doses. Doctors and nurses will follow the system's advice when giving medications. They will also share their experiences using the system through surveys or interviews.
4. Survey/interview instruments used: Doctors and nurses will answer surveys and participate in interviews. They will talk about how easy the system is to use, how helpful it is, and if it improves their work. Their feedback will help make the system better.
5. Experimental drug/device usage: This study is not testing a new drug or device. It is testing a tool that helps doctors and pharmacists choose safer medications for patients.
6. Data analysis: The study will compare patient safety before and after using the PGx-CDSS system. Researchers will check if there are fewer medication mistakes and if patients have better health outcomes. They will also look at feedback from doctors and nurses to see if the system is easy to use and helpful.

Purpose:

Medication errors remain a significant challenge in hospital settings, leading to adverse drug events (ADEs), increased healthcare costs, and poor patient outcomes. Clinical Decision Support Systems (CDSS) have been widely implemented to assist healthcare providers in medication

management; however, existing CDSS often rely on standardized dosing protocols that do not account for individual patient differences. Pharmacogenomics (PGx)-enhanced CDSS (PGx-CDSS) offers a promising solution by integrating genetic and clinical data to provide personalized dosing recommendations and improve medication safety.

The Need for PGx-CDSS

Despite the potential benefits of pharmacogenomics in precision medicine, its integration into real-world clinical workflows has been slow. Many healthcare providers lack easy access to patient genetic data, and even when available, interpreting this data requires specialized knowledge. PGx-CDSS bridges this gap by automating genetic data interpretation and delivering actionable recommendations at the point of care. This system aims to minimize medication errors, enhance treatment efficacy, and reduce adverse reactions through tailored prescribing.

Past Research and Gaps in Literature

A substantial body of research has explored the role of pharmacogenomics in medication management, demonstrating its ability to reduce adverse drug reactions and optimize therapeutic efficacy. However, several gaps remain:

1. Alert Fatigue and Workflow Integration: Traditional CDSS often contribute to alert fatigue, causing clinicians to override recommendations. Research has shown that context-aware alerts and better EHR integration can improve adherence to CDSS recommendations.
2. Limited Real-World Validation: While PGx-CDSS has been studied in controlled settings, real-world hospital implementations remain limited. There is a need to evaluate how PGx-CDSS performs in diverse clinical environments.
3. Usability and Adoption Barriers: Studies indicate that clinician adoption is critical for CDSS success. Understanding how providers interact with PGx-CDSS and what influences their trust in the system is essential for successful implementation.

Research Contribution and Significance

This project seeks to address these challenges by designing, implementing, and evaluating a PGx-CDSS in hospital settings. By focusing on real-time data integration, usability improvements, and workflow alignment, this study will provide valuable insights into the feasibility and impact of PGx-CDSS on medication safety and patient outcomes. Findings will contribute to ongoing efforts in precision medicine, informatics, and clinical decision support, ultimately guiding future adoption and policy decisions in healthcare.

Project Description:

Research Problem:
Medication errors and adverse drug events (ADEs) continue to be major issues in hospital settings. Traditional Clinical Decision Support Systems (CDSS) offer standardized medication recommendations that do not account for genetic variability in drug metabolism. This project

aims to develop and evaluate a Pharmacogenomics-Enabled Clinical Decision Support System (PGx-CDSS) that integrates genetic and clinical data to deliver personalized medication dosing recommendations, reducing medication errors and improving patient outcomes.

Subproblems:

1. Integration of Pharmacogenomic Data into CDSS:
    o How can genetic data be effectively incorporated into existing CDSS frameworks?
    o What are the challenges in integrating real-time pharmacogenomic insights into Electronic Health Records (EHRs)?
2. Development of Predictive Dosing Algorithms:
    o How can machine learning or statistical models predict optimal medication dosing based on genetic and clinical data?
    o What genetic and non-genetic factors should be included for precise dosing predictions?
3. Real-World Validation of PGx-CDSS:
    o How effective is PGx-CDSS in reducing medication errors compared to traditional CDSS?
    o What improvements in patient outcomes, such as reduced ADEs and hospital readmissions, can be observed?
4. Usability and Clinician Adoption:
    o How can the PGx-CDSS be designed to ensure seamless integration into clinical workflows without causing alert fatigue?
    o What training or educational tools are necessary for clinicians to confidently use the system?

Terms and Assumptions:

- Pharmacogenomics (PGx): The study of how genes affect a person's response to drugs.
- Clinical Decision Support System (CDSS): A technology that provides clinicians with knowledge and patient-specific information to enhance decision-making.
- Electronic Health Records (EHRs): Digital records that store patient health information, including medical history, treatments, and test results.
- Adverse Drug Events (ADEs): Harm caused by the use of medication, including side effects and medication errors.
- Assumption 1: Clinicians will adopt PGx-CDSS if it is seamlessly integrated into their workflow and reduces medication errors.
- Assumption 2: Patients with pharmacogenomic data available will benefit from more precise medication dosing recommendations.
- Assumption 3: Hospitals will support the adoption of PGx-CDSS if it leads to cost savings and improved patient safety.

Subproblem Interconnections:
These subproblems work together to form a holistic research approach. First, integrating pharmacogenomic data into CDSS (Subproblem 1) is crucial for generating meaningful

predictive dosing recommendations (Subproblem 2). Once developed, these recommendations must be validated through real-world clinical implementation (Subproblem 3) to assess their impact on medication safety and patient outcomes. Finally, for long-term success, the system must be designed for usability and clinician adoption (Subproblem 4), ensuring it is both effective and practical in a hospital setting. This interconnected approach ensures that the PGx-CDSS is both scientifically sound and clinically feasible.

Framework:

For this project, the best-fitting framework is Sittig and Singh's 8-Dimensional Sociotechnical Model, which is specifically designed to assess and optimize health information technology (HIT) interventions, including Clinical Decision Support Systems (CDSS). This model considers multiple dimensions such as technology, human-computer interaction, workflow integration, and organizational policies, all of which are crucial for implementing PGx-CDSS in hospital settings.

1. Comprehensive Analysis of HIT Implementation: Sittig and Singh's model provides a structured approach to evaluating how pharmacogenomics data can be effectively integrated into CDSS while addressing technical, organizational, and user-related factors. Given that PGx-CDSS requires real-time clinical data integration, this model ensures all critical dimensions are considered.
2. Addressing Usability and Adoption Challenges: One of the key barriers to PGx-CDSS adoption is clinician workflow disruption and alert fatigue. The 8-dimensional model incorporates human-computer interaction and social factors, making it a strong fit for designing an intuitive and effective system that encourages provider engagement.
3. Focus on Patient Safety and Clinical Outcomes: This framework emphasizes patient safety as a core component of HIT evaluation. Since the project's goal is to enhance medication safety and reduce adverse drug events through personalized dosing, this model provides the necessary structure to assess safety improvements at multiple levels.
4. Proven Application in Health Informatics Research: Sittig and Singh's model has been widely applied in evaluating and improving HIT interventions, making it a reliable and validated framework for guiding the implementation of PGx-CDSS in hospital settings.

This framework ensures a systematic approach to implementing and evaluating PGx-CDSS, addressing both technical feasibility and clinical usability while maintaining a strong focus on patient safety.

Design and Methods:

1. Design: A mixed-methods approach combining a quantitative quasi-experimental study with qualitative user feedback analysis.
2. Setting: A hospital setting where PGx-CDSS is implemented in inpatient and outpatient departments.
3. Subjects and Sampling:
    a. Physicians, pharmacists, and nurses using PGx-CDSS.
    b. Patients receiving medications that require pharmacogenomic consideration (e.g., warfarin, clopidogrel, antidepressants).

    c. A convenience sample of 200 patient cases pre- and post-PGx-CDSS implementation.
4. Intervention: Implementation of a PGx-CDSS integrated into the hospital's electronic health record (EHR) system, providing real-time, personalized dosing recommendations based on genetic and clinical data.
5. Data Collection / Measurement:
    a. Medication Safety Metrics: Comparison of medication error rates before and after PGx-CDSS implementation.
    b. Patient Outcomes: Evaluation of adverse drug events (ADEs), therapeutic efficacy, and length of hospital stay.
    c. Usability and Adoption: Surveys and semi-structured interviews with clinicians to assess user satisfaction and workflow integration.
6. Data Analysis and Validation:
    a. Quantitative Analysis: Statistical comparison of pre- and post-intervention data using t-tests and chi-square analysis.
    b. Qualitative Analysis: Thematic analysis of clinician feedback to identify barriers and facilitators to adoption.
    c. Validation: Triangulation of data from multiple sources to ensure robustness of findings.

This study will provide insights into the effectiveness, usability, and integration of PGx-CDSS in real-world clinical settings, informing future improvements and broader implementation strategies.

Evaluation Methods:

1. Medication Safety Metrics:
    o Compare medication error rates before and after PGx-CDSS implementation.
    o Analyze reductions in adverse drug events (ADEs) and medication-related complications.
2. Patient Outcomes:
    o Assess changes in therapeutic efficacy, measuring whether prescribed medications achieve desired effects with fewer side effects.
    o Evaluate differences in length of hospital stays as an indicator of improved treatment management.
3. Usability and Clinician Adoption:
    o Conduct surveys and semi-structured interviews with physicians, pharmacists, and nurses to assess:
        ▪ Ease of system use
        ▪ Perceived effectiveness in clinical decision-making
        ▪ Workflow integration and alert fatigue
4. Statistical Analysis & Validation:
    o Quantitative analysis: Use statistical methods such as t-tests and chi-square analyses to compare pre- and post-intervention data.
    o Qualitative analysis: Perform thematic analysis on clinician feedback to identify common barriers and facilitators for system adoption.
    o Triangulation: Validate findings by combining data from multiple sources, ensuring robust conclusions.

These methods will provide a comprehensive evaluation of the PGx-CDSS system's effectiveness, usability, and clinical impact, informing potential future improvements and broader implementation strategies.

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