INPLASY

Implementation of therapeutic drug monitoring and pharmacogenomics in older adults as a model of care: a scoping review protocol

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ADMINISTRATIVE INFORMATION

Support - n/a.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - Yang Qing Hu, Cindy Woodland, and Tony Antoniou are affiliated with the University of Toronto.Yang Qing Hu, Joanne Ho, Kassandra Lemmon are affiliated with GeriMedRisk. Joanne Ho is additionally affiliated with McMaster University. Kassandra Lemmon and Joanne Ho are additionally affiliated with the Schlegel-UW Research Institute for Aging.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 November 2024 and was last updated on 7 November 2024.

INTRODUCTION

Review question / Objective The objective of this scoping review is to answer the following questions:
• In older patients, what is the impact of implementing therapeutic drug monitoring (TDM) and/or pharmacogenomics (PGx) into clinical care?
• In older patients, what are facilitators or barriers to implementing TDM and PGx in routine clinical care?

Background Adverse drug events (ADEs) in older adults result in greater morbidity, mortality, and health care costs.1 This increases the financial burden on healthcare systems, with ADE treatment costing billions of dollars annually worldwide.2 The risk of adverse drug events (ADEs) increases with age, with older adults aged ≥65 years being approximately seven times more likely to experience ADEs compared to younger adults.1,3 Age-related physiological changes, polypharmacy causing drug-drug interactions and comorbidities may alter the pharmacokinetics of medications resulting in elevated levels, prolonged half-lives and the risk of toxicity.4 In addition, inter-individual variability arising from pharmacogenomic differences may affect the effectiveness and safety of select pharmacotherapy.
ADEs may be mitigated with modified dosing among older adults, with up to 50% of these ADE-related hospitalizations being avoidable.5 Preventable ADEs may be due to prescribing errors due to inadequately monitoring patients when they begin a new drug, and/or not responding to symptoms of drug toxicity.6 There is opportunity for improvement in this area, which could

drastically increase older patients' quality of life and decrease healthcare costs.
There is, however, a lack of data in this population as they are often excluded from clinical drug trials.7.

Rationale Therapeutic drug monitoring (TDM), the measurement of drug concentrations in blood and other bodily fluids, and pharmacogenomics (PGx), how variations in an individual's genome may impact their response to medications, may help reduce ADEs in not only older patients, but other vulnerable populations. Use of TDM and PGx have been established in patients on medications with narrow therapeutic indices such as those with mental health disorders on psychotropics, autoimmune disease on immunosuppressants, and seizure disorder on anticonvulsants.8–12 But TDM and PGx are not yet part of routine care for older adults.13 Potential barriers to implementation, such as increased costs associated with laboratory testing, insufficient clinical expertise to interpret laboratory results, increased time lag between diagnosis and treatment, and lack of site resources and conversely facilitators in implementation, are unclear in the older adult population.14,15 This scoping review therefore aims to understand the existing literature to determine the overall impact, facilitators, and barriers of TDM and PGx implementation in the care of older adults.

METHODS

Strategy of data synthesis A comprehensive literature search will be conducted in Medline, Embase, the Cochrane Library, Web of Science, CINAHL, PsychINFO, and Ageline. The electronic search strategy will be developed by a reviewer with the aid of a librarian with expertise in review methodology in pharmacology. Grey literature, such as government or CADTH documents, conference proceedings, or theses, will also be utilized. The grey literature catalogue Overton was searched to identify policy documents.

Search Strategy (Medline Ovid)
1. Pharmacogenetics/ or Precision Medicine/
2. (pharmacogenetic* or pgx or pharmacogenomic* or personalized medicine or precision medicine or individual* medicine).tw,kf.
3. Drug Monitoring/
4. tdm.tw,kf.
5. (drug adj2 monitor*).tw,kf.
6. 1 or 2 or 3 or 4 or 5
7. Aged/
8. Geriatrics/
9. (older* or elder* or geriatric*).tw,kf.
10. (age adj3 "65").tw,kf.
11. 7 or 8 or 9 or 10
12. Delivery of Health Care/
13. (implement* or interven* or facilitat* or barrier* or attitude* or perception* or perceive*).tw,kf.
14. (care adj2 model*).tw,kf.
15. ("health care" adj3 delivery).tw,kf.
16. 12 or 13 or 14 or 15
17. 6 and 11 and 16.

Eligibility criteria Patient Population
We will include studies that include older patients aged 60 years or older.

Intervention
All studies need to include evaluation of implementation of TDM and/or PGx in patient care. Studies that focus on quantifying differences in pharmacokinetics, pharmacodynamics, or drug response without addressing the practical implementation in clinical settings will be excluded.

Comparison
The comparison for this scoping review will be usual care, without use of TDM and/or PGx.

Outcomes
A wide range of outcomes will be considered in this study, including but not limited to patient-related outcomes, clinician-related, health system-related, and feasibility. Feasibility-related outcomes will include cost, burden on personnel/participants, privacy, virtual vs hybrid vs in-person, scope, staff training, site resources, consent, staff required for implementation, and other facilitators or barriers. Pharmacokinetic or pharmacodynamic outcomes will be excluded.

Study Type
All types of papers will be considered. There will be no restrictions on language, year of publication, or publication status.

Source of evidence screening and selection
Reviewers consulted with a pharmacology librarian to develop the search strategy. Relevant keywords, synonyms, descriptors, and Medical Subject Headings were conceptualized or identified via a preliminary search in various databases. The identified search terms were combined with Boolean operators (AND and OR). Notably, this search was focused on evaluating implementation of TDM and/or PGx. The scope was narrowed by only identifying papers that specifically included keywords such as implementation, feasibility, barriers, models of care, and related synonyms. While this may impact the search from including some papers which discuss implementation but do not use our predefined key words, it would focus

our search and decreases the number of unrelated papers thereby enhancing feasibility. A pilot test will be performed with 5 selected studies to determine whether the developed search strategy is sufficient to capture all relevant evidence sources. The database search was conducted on August 15, 2024, and the grey literature search was conducted on August 24, 2024, identifying 10 341 relevant articles.

Identified studies will be grouped in Covidence software. Duplicates will be removed automatically by Covidence, followed by a manual process using Mendeley by QYH. Covidence will be used for both the title and abstract screening, and the subsequent full-text screening. The selection process will be carried out by two independent reviewers, who will assess whether the studies meet eligibility criteria and include the relevant participants, interventions, and outcomes. Any disagreements that arise between the reviewers will be resolved through discussion with a third reviewer to reach a consensus. Any reasons for excluding studies will be recorded and reported in the final review via the PRISMA-ScR flow diagram, generated via Covidence. If further information on a study is required, the authors of the publication will be contacted if possible.

Data management Identified studies will be captured using the Covidence Systematic Review Tool and Mendeley Reference Management Software. Covidence will be used for title and abstract screening, full-text screening, data charting, and extraction. Mendeley will be used to store the studies for future use and to upload full text into Covidence.

Covidence will also be used to perform data charting and extraction. Charting will be performed by two independent reviewers, using a data extraction form adapted from the JBI template.16 This form will be pilot tested with 5 studies to check whether it was sufficiently comprehensive to answer the research question, and to ensure the reviewers are performing data extraction using a consistent methodology. The data extraction form will be adapted and refined as necessary, and any changes will be reported. Any disagreements that arise between the reviews will be resolved through discussion with a third party to reach a consensus.

Reporting results / Analysis of the evidence A descriptive summary of the results will be done. Data will be stratified by study design (RCT vs not) or review type (followed review protocol vs not). Absolute frequencies and percentages will be reported and presented with diagrams for all patient populations, interventions, comparators, outcomes, and conclusions.

Presentation of the results The screening and data extraction process will be presented via PRISMA-ScR flow diagram. A descriptive summary, including absolute frequencies and percentages, will be reported and presented with diagrams for all patient populations, interventions, comparators, outcomes, and conclusions.

Language restriction None.

Country(ies) involved Canada.

Keywords Geriatrics, Therapeutic Drug Monitoring, Pharmacogenomics, Pharmacogenetics, Older Adults, Implementation, Precision Medicine, Personalized Medicine.

Dissemination plans The results of the scoping review will be shared at a research and implementation collaborative meeting attended by patient advocates, members of organizations involved in advocating for the care of older adults or drug safety, decision makers, geriatric psychiatrists, geriatricians, pharmacists, clinical pharmacologists, and biochemists with experience in TDM, pharmacokinetics and toxicological testing from across Ontario, Canada. We will be presenting the results at a meeting with health care professionals from across the province of Ontario.

Contributions of each author

Author 1 - Yang Qing Hu - Author 1 performed the scoping review design, and wrote the protocol and manuscript, and will also perform screening, data extraction, and data analysis.
Email: yangqing.hu@mail.utoronto.ca
Author 2 - Kassandra Lemmon - Author 2 contributed to scoping review design, protocol and will be involved with screening, data extraction, data analysis, and manuscript preparation.
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Author 3 - Cindy Woodland - Author 3 contributed to scoping review design, protocol, and manuscript prescription and will also provide expertise in clinical pharmacology, toxicology, and drug safety.
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Author 4 - Tony Antoniou - Author 4 participated in scoping review design, protocol, screening and will perform data extraction, data analysis, and manuscript preparation. Author 4 also provided expertise in pharmacy, drug safety, systematic and scoping review methodology, thematic analysis, and pharmacoepidemiology.
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Author 5 - Joanne Ho - Author 5 reviewed and edited the scoping review design, protocol, and manuscript and will also performed screening, data extraction, data analysis, and provided expertise in clinical pharmacology and geriatric medicine, drug safety, virtual care, and interdisciplinary geriatric models of care.

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