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Medication Use Quality and Safety in Older Adults: 2022 Update

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Abstract

Improving the quality of medication use and medication safety are important priorities for healthcare providers who care for older adults. The objective of this article was to identify four exemplary articles with this focus in 2022. We selected high-quality studies from an OVID search and hand searching of major high impact journals that advanced the field of research forward. The chosen articles cover domains related to deprescribing, medication safety, and optimizing medication use. The MedSafer study, a cluster randomized clinical trial in Canada, evaluated whether patient specific deprescribing reports generated by electronic decision support software resulted in reduced adverse drug events in the 30 days post hospital discharge in older adults (domain: deprescribing). The second study, a retrospective cohort study using data from Premier Healthcare Database, examined in-hospital adverse clinical events associated with perioperative gabapentin use among older adults undergoing major surgery (domain: medication safety). The third study used an open-label parallel controlled trial in 39 Australian aged-care facilities to examine the effectiveness of a pharmacist-led intervention to reduce medication-induced deterioration and adverse reactions (domain: optimizing medication use). Lastly, the fourth study engaged experts in a Delphi method process to develop a consensus list of clinically important prescribing cascades that adversely affect older persons' health to aid clinicians to identify, prevent, and manage prescribing cascades (domain: optimizing medication use). Collectively, this

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review succinctly highlights pertinent topics related to promoting safe use of medications and promotes awareness of optimizing older adults' medication regimens.

Keywords

medication-related problems; aged; 80 years and over; deprescribing; polypharmacy; inappropriate prescribing

INTRODUCTION

Medication use quality and safety is a global public health issue and an important national health priority in many countries. The key areas for medication safety as outlined in the third World Health Organization (WHO) Global Patient Safety Challenge: Medication Without Harm include: high-risk situations, polypharmacy, and transitions of care.[1] Optimal medication use can improve health outcomes in older adults and reduce healthcare costs. Unfortunately, older adults are underrepresented in premarketing medication trials leaving gaps in the knowledge and prescribing guidance needed by clinicians.[2] Coupled with age-related changes in physiology, altered pharmacokinetics and pharmacodynamics, polypharmacy, and multiple comorbidities, medication use is often suboptimal (i.e., over-, inappropriate-, and under-use) and can lead to often preventable adverse drug events.

It is often challenging to identify relevant literature related to the quality use of medications and medication safety among older adults because of the lack of consistent search terms in electronic databases. Therefore, in this special article, we identify exemplary articles published in 2022 related to medication use quality and medication safety. We highlight four articles, by providing a study summary, critique, and implications.

METHODS

Data sources and search strategy

We performed a manual search for relevant articles from 14 select high-impact journals in general medicine, aging/geriatrics, and clinical pharmacology (Supplementary File S1). We also supplemented this with a PubMed database search with MESH terms "drug related side effects" or "adverse reactions" and restricted the search to English language articles published (in print) in 2022 and including older adults (mean age ≥ 65 years).

Eligibility criteria and study selection

We included articles related to medication use quality and medication safety with innovative objectives and those that utilized rigorous observational or experimental designs with reliable and valid measures. We excluded review articles (except systematic reviews with a meta-analysis), cross-sectional studies, case-series, case reports and small single-center epidemiological studies.

Three authors (SLG, NB, JTH) reviewed articles from the selected journals which yielded 38 relevant articles. The PubMed search yielded 179 titles, of which six additional studies were identified. Of the 44 selected articles, we individually rated the top four articles based on

study methods, innovation, clinical relevance, and likelihood of advancing the field forward (vs. replication studies). Through consensus we selected the four articles to feature in this review.[3–6] For each chosen article, we provided a study summary, strengths and limitations, and interpretation and implications to the care of older adults. We categorized all articles under major domains in Supplementary File S2.

SUMMARY OF SELECTED STUDIES

The MedSafer Study—Electronic Decision Support for Deprescribing in Hospitalized Older Adults: A Cluster Randomized Clinical Trial (Domain: Deprescribing)

Study summary—Many deprescribing trials have demonstrated the effectiveness of interventions to reduce medication use and potentially inappropriate medications (PIMs).[7,8] However, trials are often not large enough to measure downstream outcomes such as ADEs. The assessment of ADEs and adverse drug withdrawal events (ADWEs), are critical outcomes to assess in deprescribing trials to understand the potential harm and whether interventions vary according to these harms.[9] The potential for ADWEs, including physiological withdrawal symptoms and return of original symptoms, is a substantial barrier for clinicians to deprescribe medications in older adults.[10] Thus, the MedSafer Study, a cluster randomized trial designed to reduce ADEs within the first 30 days after hospital discharge in older participants, addresses this important gap.[5] The study was conducted in Canada at 11 acute care hospitals between August 22, 2017 to January 13, 2020. Secondary outcomes included PIMs and ADWEs. The intervention consisted of personalized deprescribing reports given to the treating team generated from electronic decision support software. They also sent the reports to community pharmacies and patient's primary care physician at hospital discharge.

Of 6633 eligible participants, a total of 5698 participants were included in analyses (median [range] age, 78 [72–85] years; 50.2% female; race and ethnicity data were not collected) with nearly 90% (n=4989) completing telephone interviews to collect ADE information one month after discharge. There was no significant difference in ADEs between control (138 events [5%]) and intervention participants (111 events [4.9%)], with an adjusted risk difference of −0.8% (95% CI, −2.9% to 1.4%) or ADWEs. Deprescribing of one of more PIMS at hospital discharge occurred more frequently in the intervention participants compared with controls (1249 (55.4%) vs. 795 [29.8%]; aRD=22.2%; 95% CI 16.9% to 27.4%).

Strengths and limitations—This study has several strengths including the study design, the large sample size, low risk of bias, and the use of a standardized Likert scale to evaluate ADEs by a pair of blinded physicians with discrepancies resolved by a third person. It is also notable that the authors measured ADWEs. A few limitations should be noted. First, the sample included those receiving palliative care for which deprescribing may be more common given the limited life expectancy. Second, there is some concern that the rate of ADEs (approximately 5% in both groups) was low compared to previously reported trials. This may be due in part to the short follow up period and measuring PIMs that have a low risk of causing an ADE. Moreover, they did not subtract ADWEs from the ADE rates to

calculate adverse drug reactions (ADRs) or measure severe ADRs (e.g., rehospitalization). The terms ADEs and ADRs are often used interchangeably in the literature but they are distinct concepts. ADRs, a noxious or unintended consequences of a drug given at its normal dose, are a subset of ADEs, with the later term also including ADWEs and therapeutic failures.

Interpretation and implications—This cluster randomized controlled study demonstrated that electronic medical records can be used to screen and reduce the rate of PIMs. It also suggests that technology interventions alone are not sufficient to reduce ADEs as has been reported previously.[11,12] In contrast, a pharmacist-led study that was supported by CDSS to identify potential drug-related problems did lead to a significant reduction in ADRs.[13] Future work should examine a combined intervention of electronic decision support software and pharmacist support and determine whether it is cost-effective or not.

Perioperative Gabapentin Use and In-Hospital Adverse Clinical Events Among Older Adults After Major Surgery (Domain: Medication Safety)

Study Summary—Gabapentin may be employed to reduce pain and opioid use in perioperative pain management programs but the safety of this practice among older patients needs to be better understood. This study used a retrospective cohort design to examine in-hospital adverse clinical events associated with perioperative gabapentin use among patients aged 65 years and older undergoing major surgery (i.e. cardiac, gastrointestinal, genitourinary, orthopedic, neurological, thoracic and vascular surgery) within 7 days of hospital admission.[4] Patients were excluded if they used gabapentin the day prior to surgery or had indications for gabapentin use (e.g., alcohol use disorder, alcohol withdrawal, fibromyalgia, neuropathic pain, postherpetic neuralgia, restless legs syndrome, seizure, and social anxiety disorder). Recruitment occurred between January 1, 2009, to March 31, 2018. The data source was the Premier Healthcare Database. The exposure was gabapentin use within 2 days after surgery. Gabapentin use was measured by charge codes. The primary outcome was delirium and secondary outcomes were new antipsychotic use, pneumonia, and in-hospital death between postoperative day 3 and hospital discharge. Delirium was identified via validated claims-based algorithm. The authors performed 1:1 propensity score matching and estimated risk ratios (RRs) and risk differences (RDs) with 95% confidence intervals (CIs).

Among the 967,547 older patients who underwent major surgery, 119,087 (12.3%) used perioperative gabapentin (before propensity score matching). After propensity score matching, 237,872 (118,936 pairs) gabapentin users and nonusers were identified (mean [SD] age, 74.5 [6.7] years; 62.7% female; 17.2% non-White; 2.4% uninsured or had Medicaid). For the primary outcome, compared with nonusers, gabapentin users had increased risk of delirium (4040 [3.4%] vs 3148 [2.6%]; RR,1.28 [95%CI, 1.23–1.34]; RD, 0.75 [95%CI, 0.75 [0.61–0.89] per 100 persons). For secondary outcomes, compared with nonusers, gabapentin users had increased new antipsychotic use (944 [0.8%] vs 805 [0.7%]; RR, 1.17 [95% CI, 1.07–1.29]; RD, 0.12 [95% CI, 0.05–0.19] per 100 persons), and pneumonia (1521 [1.3%] vs 1368 [1.2%]; RR, 1.11 [95%CI,1.03–1.20]; RD, 0.13 [95%

CI, 0.04–0.22] per 100 persons). There was no difference in in-hospital death (362 [0.3%] vs 354 [0.2%]; RR, 1.02 [95% CI, 0.88–1.18]; RD, 0.00 [95% CI, −0.04 to 0.05] per 100 persons).

Strengths and Limitations—The strengths of the study include the use of a database containing more than 900 hospitals that covers approximately 25% of annual inpatient admissions in the US; inclusion of multiple types of major surgery (as defined by the Agency for Healthcare Research and Quality procedure classification); appropriate eligibility criteria; a large sample size; the use of a validated claims-based algorithm to measure delirium and propensity score matching to reduce bias from confounding. The limitations include a non-randomized design, measurement bias for delirium by using diagnosis codes (the algorithm has a positive predictive value of 80% against the Confusion Assessment Method), potential residual confounding inherent in observational retrospective cohort studies (especially confounding by pain severity), and a mostly white population.

Interpretation and Implication—The Food and Drug Administration (FDA) authorizes gabapentin for only two indications: management of postherpetic neuralgia in adults and adjunctive therapy in the treatment of partial onset seizures in adults and pediatric patients 3 years and older with epilepsy. Promotion of off-label prescribing of gabapentin by the manufacturer for conditions other than the above indications led to some of the largest clinical and criminal penalties in the industry.[14] The potential adverse effects of gabapentin in older adults are well described and a reason that gabapentin is listed as a potentially inappropriate medication when used with other medications with effects on the central nervous system (e.g., benzodiazepines and opioids) in the American Geriatrics Society Beers Criteria®.[15] This study found perioperative gabapentin use was associated with increased risk of delirium, new antipsychotic use, and pneumonia among older patients after major surgery. These results add to the studies that do not support the routine use of gabapentin for the management of postoperative pain in older adult patients.[16,17]

Effect of an ongoing pharmacist service to reduce medicine-induced deterioration and adverse reactions in aged-care facilities (nursing homes): a multicentre, randomised controlled trial (the ReMInDAR trial, domain: optimizing medication use)

Study summary—Older patients residing in nursing homes commonly have polypharmacy which puts them at risk for ADEs. The objective of the ReMInDAR trial was to assess the effectiveness of a 12 month pharmacist-led intervention using validated tools to reduce medicine-induced deterioration (e.g., falls, fractures, bleeding or bruising) and adverse reactions.[6] This was a multicenter, open-label parallel randomized controlled trial involving 39 Australian aged-care facilities. Eligible residents included those ≥4 medicines or ≥ 1 anticholinergic or sedative medicine. In the intervention arm, pharmacists reviewed the care records every 8 weeks to identify medication changes and new illnesses or conditions present since the last assessment, including evidence or any adverse events. Further, the pharmacist met with the resident and care staff to discuss and identify concerns and to assess activity and cognition using standardized measures. Usual care consisted of yearly or biyearly residential medication management review provided by accredited pharmacists. Recommendations were provided to the residents' physicians in the case that

medicine-induced deterioration was considered clinically significant. The primary outcome was change in Frailty Index at 12 months. Secondary outcomes included changes in cognition as per the Montreal Cognitive Assessment (MoCA), 24-hour movement behavior by accelerometry, grip strength, weight, quality of life, and ADRs as per a three-person expert panel using the Naranjo causality algorithm.

A total of 248 participants (median age 87 years; 68% female) of 282 enrolled completed the study; 120 in the intervention and 128 in control arms. In total, 575 pharmacist sessions were undertaken in the intervention arm. Pharmacists made recommendations to reduce medication use for 61% of the participants and increase use for 29%. There was no statistically significant difference for change in frailty between groups (mean difference: −0.009, 95% CI, −0.028 to 0.009, p = 0.320). A significant difference for cognition was observed, with a mean difference of 1.36-point change at 12 months (95% CI: 0.01, 2.72, P=0.048). A two- point change is thought to be clinically significant. However, there were no statistical changes in any other secondary outcome. The authors noted that the point estimates favored the intervention arm at 12 months for frailty, 24-hour movement behavior and grip strength.

Strengths and limitations—The strengths of this study include the rigorous trial design, inclusion of 39 facilities, use of validated outcome measures and the on-going pharmacist assessment throughout the study period. Additionally, a novel aspect was the objective measurement of 24-hour movement behavior via an accelerometer as a method to measure sedative effects of medications in the aged-care setting. A few limitations should be noted. The study was open-label and therefore bias could have been introduced, however, the research assistants performing the outcome measures were blinded to treatment assignment. The study did not meet target sample size of 354, therefore was underpowered for the primary outcome. The study focused on those who were less frail, representing about 8% of residents in aged care, thus the results are not generalizable to most individual living in these settings. Finally, AWDEs were not measured to determine the risks of deprescribing.

Interpretation and implications—Medications may cause adverse effects that are associated with cognitive and physical decline.[18–20] Older adults with multimorbidity and frailty may be especially vulnerable to these effects, and clinicians may overlook that changes may be related to medication use. The authors noted that at least 60% of participants had a problem at each 8-week review session suggesting that in older adults with mild frailty, an ongoing intervention may be needed to reduce medication-related changes in function. Future research is needed in larger samples to determine whether this intervention is effective and whether it is cost-effective.

ThinkCascades: A Tool for Identifying Clinically Important Prescribing Cascades Affecting Older People (domain: optimizing medication use)

Study Summary—Prescribing cascades can be defined as a situation in which one drug's side effect are misinterpreted as a new medical condition that leads to a new prescription to treat this medical condition. Of concern is that prescribing cascades can adversely affect older patients' outcomes such as functional status decline. Moreover, their identification

by clinicians can be difficult, especially given the multitude of medications available to prescribe with their numerous side effects. Thus, McCarthy et al conducted a modified three round Delphi survey using an international, multidisciplinary (i.e., geriatricians, primary care physicians, pharmacists, nurses) expert panel of 40 clinicians (cis-gender, 58% female) to compile a list of clinically important prescribing cascades that represent potentially inappropriate prescribing.[3] None of the authors of this article were panelists. The study started with a comprehensive literature review that identified 139 prescribing cascades. Panelists were then asked to rate the clinical importance of each prescribing cascades on a 5-point Likert scale (1 = 'definitely not important'; 5 = 'definitely important') with an option to indicate when they were 'not sure'. Cascades highly rated (4 or 5 rating) by ≥ 70% of panelists were included in subsequent rounds. After three rounds, 13 cascades received a high rating. Then the study team reviewed the 13 retained prescribing cascades to determine the final list of clinically important cascades consistent with potentially inappropriate prescribing. They settled upon a short list of nine clinically important prescribing cascades affecting older adults focused on the following domains: cardiovascular system (n=2); central nervous system (n=4); musculoskeletal system (n=1) and urogenital system (n=2). See infographic showing the 9 individual cascades. Both over the counter and prescription medications were included.

Strengths and Limitations—The authors used a rigorous multiphase process originating from an evidence-based literature review. The modified Delphi method employed international as well as interprofessional perspectives across care settings. The study team focused on prescribing cascades that represented inappropriate prescribing, rather than those that are intentional and represent rational prescribing (i.e., use of proton pump inhibitor if long-term NSAID therapy is needed). The panel included geriatricians, primary care physicians, pharmacists, and nurses from six countries with extensive clinical practice experience. The response rates were nearly 90% in all three rounds yet some panelists were unable to complete round three. There are potential limitations that merit discussion. The specific search terms used in the literature review were not provided, making future replication difficult. There were few nurses that were members of the expert panel. The threshold of 70% to define a high rating is arbitrary as was the paring of 13 to 9 final cascades by the authors. An additional limitation was that response order bias influenced the process for round 3.

Interpretation and implications.

The findings from this work not only provide a useful tool but identified areas for additional research. There were certain professions that had more agreement among rating the prescribing cascades namely pharmacists and geriatricians compared to general practitioners and nurses. The implications are that decision-making processes for determining the clinical relevance are multifactorial which make it hard to operationalize in clinical practice. This explicit list of cascades will help to overcome this hurdle. This tool could be used as "flags/alerts" in electronic health care records so that the healthcare team can reassess the medication combination and justify if truly clinically indicated in older patients regardless of setting.

DISCUSSION

In this review, we identified and provided a summary for four studies published in 2022 that highlight important topics relating to medication use quality and safety. While the search strategy was thorough, it was relatively limited (English language, only Pubmed, etc.) and therefore may not have found all relevant articles. Nonetheless, the first article, the MedSafer study, showed that an electronic deprescribing clinical decision support during acute hospitalizations did not reduce ADEs, but did reduce PIMs. The second article concluded that peri-operative gabapentin use increased risk for delirium, new antipsychotic use and pneumonia during the hospitalization. The third article, the ReMInDAR trial, found a multiple session pharmacist-led intervention over 12 months did not change the frailty index from baseline, although the study did not meet recruitment targets. The fourth article highlights an expert consensus report on nine clinically relevant prescribing cascades in older adults. Together, these studies along with articles included in Supplementary File S2 highlight challenges related to medication quality and safety in older adults as well as highlight further research opportunities. While the studies summarized in this paper serve as exemplary research on optimizing medication use in older adults, research using robust methods and quality data remain critical to answering clinically important questions. By improving appropriate prescribing in clinical practice and better understanding how to achieve this through research, we stand to improve older adults' health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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None.

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Key points

- Medication optimization in older adults presents many challenges.
- We identified major studies published in 2022 on medication use quality and safety in older adults to help guide care.

Why does this paper matter?

This review features new research that adds to the evidence base to promote optimal medication use in older adults.

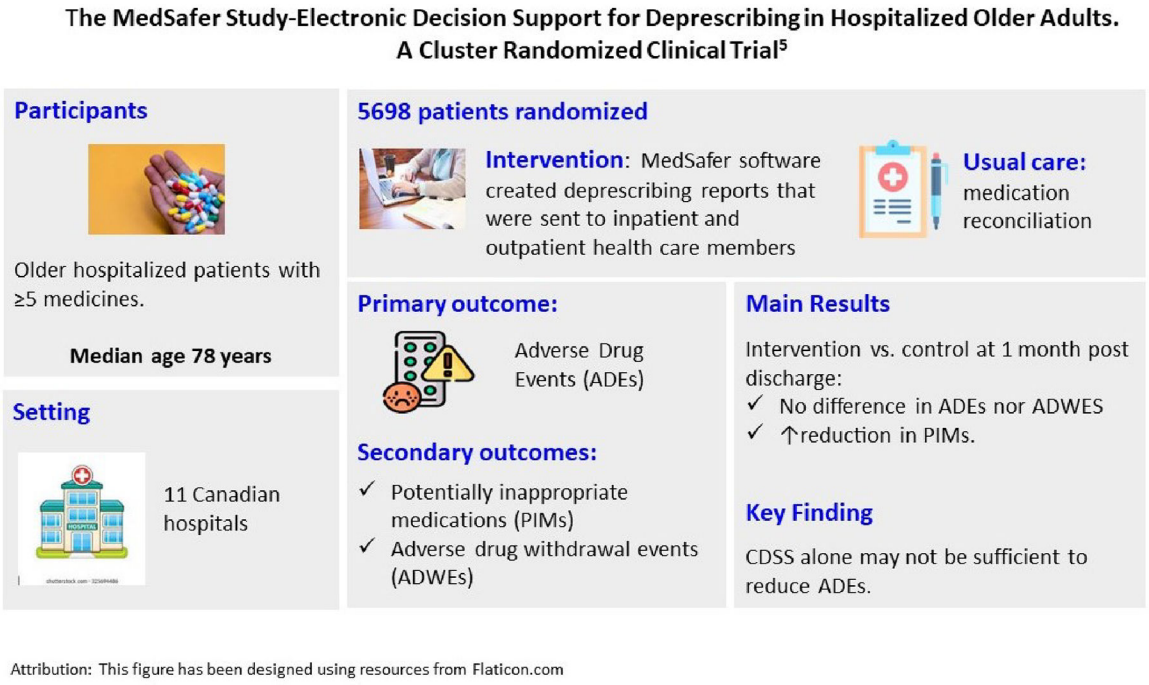

Figure 1:

The MedSafer Study-Electronic Decision Support for Deprescribing in Hospitalized Older Adults. A Cluster Randomized Clinical Trial

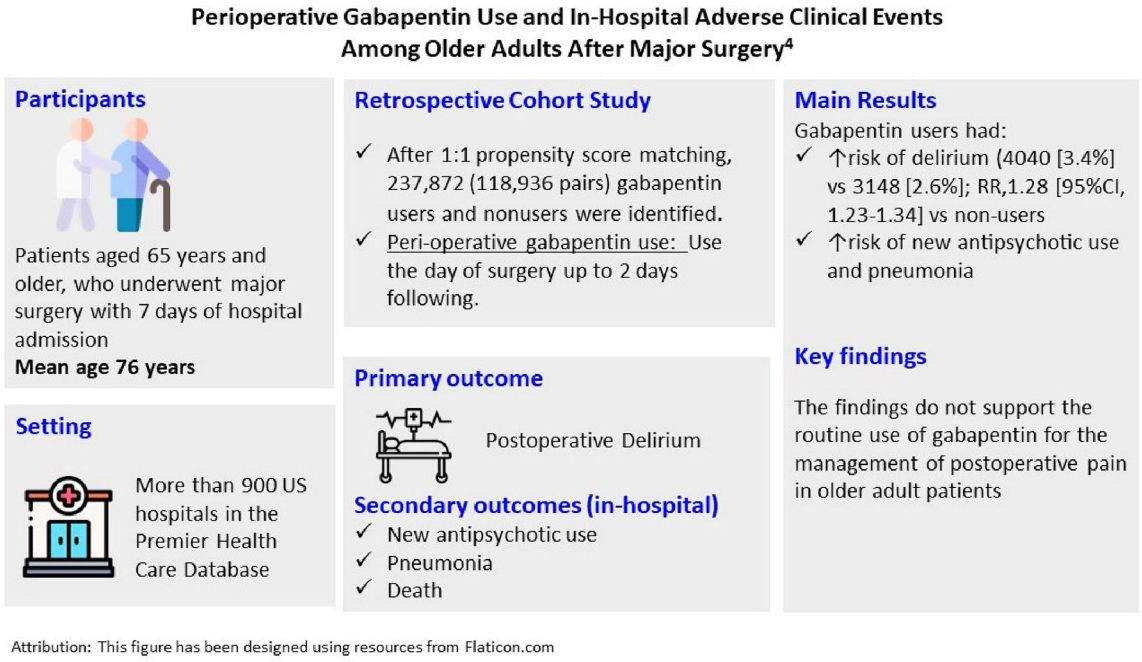

Figure 2:

Perioperative Gabapentin Use and In-Hospital Adverse Clinical Events Among Older Adults After Major Surgery

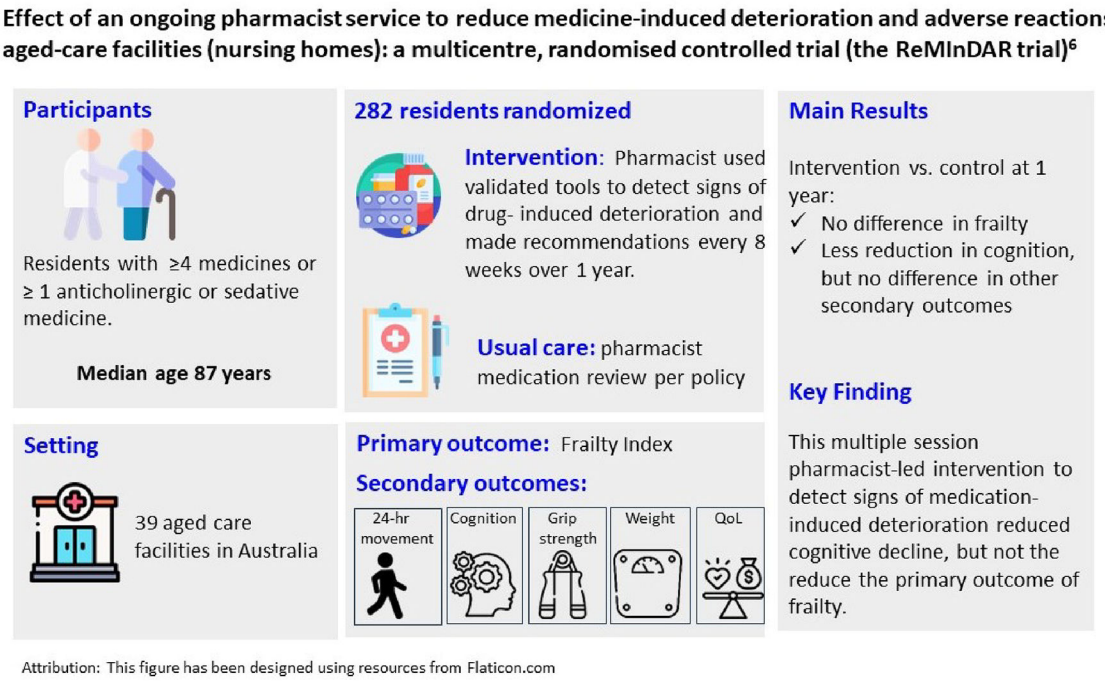

Figure 3:

Effect of an ongoing pharmacist service to reduce medicine-induced deterioration and adverse reactions in aged-care facilities (nursing homes): a multicentre, randomised controlled trial (the ReMInDAR trial, domain: optimizing medication use)

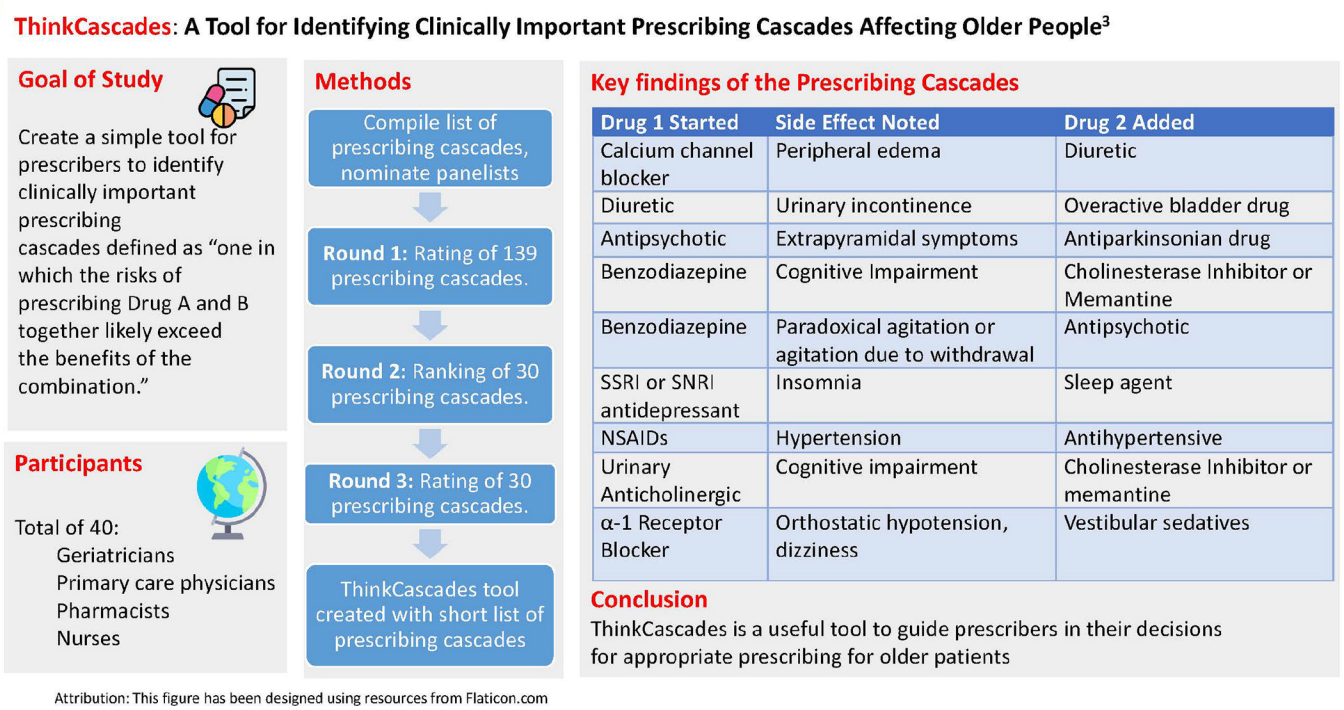

Figure 4:

ThinkCascades: A Tool for Identifying Clinically Important Prescribing Cascades Affecting Older People