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REVIEW ARTICLE

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Interventions to deprescribe potentially inappropriate medications in the elderly: *Lost in translation*?

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Abstract

What is known and objective: Use of potentially inappropriate medications (PIMs) remains common in older adults, despite the easy availability of screening tools such as the Beers and Screening Tool of Older Person's Prescriptions (STOPP) criteria. Multiple published studies have implemented these screening tools to encourage deprescribing of PIMs, with mixed results. Little is known about the reasons behind the success or failure of these interventions, or what could be done to improve their impact. Implementation science (IS) provides a set of theories, models and frameworks to address these questions. The goal of this study was to conduct a focused narrative review of the deprescribing literature through an IS lens—to determine the extent to which implementation factors were identified and the intermediate steps in the intervention were measured. A better understanding of the existing literature, including its gaps, may provide a roadmap for future research.

Methods: PubMed search from 2000-2019 using appropriate MeSH headings. Inclusion criteria: controlled trials or prospective cohort studies intended to reduce PIMs in the elderly that used hospitalizations and/or emergency department visits as outcome measures. Studies were reviewed to identify potential implementation factors (known as determinants), using the Consolidated Framework for Implementation Research (CFIR) as a guide. In addition, intermediate outcomes were extracted.

Results and discussion: Of the 548 reviewed abstracts, 14 studies met the inclusion criteria and underwent detailed analysis. Of the 14 studies, 10 acknowledged potential implementation determinants that could be mapped onto CFIR. The most commonly identified determinant was the degree of pharmacist integration into the medical team (seven of 14 studies), which mapped onto the CFIR construct of 'networks and communication'. Several important CFIR constructs were absent in the reviewed literature. Intermediate measures were captured by 12 of the 14 reviewed papers, but the choice of measures was inconsistent across studies.

What is new and conclusion: In recent high-quality studies of deprescribing interventions, we found limited acknowledgement of factors known to be important to successful implementation and inconsistent reporting of intermediate outcomes. These findings indicate missed opportunities to understand the factors underlying study outcomes. As a result, we run the risk of rejecting worthwhile interventions

due to negative results, when the correct interpretation might be that they failed in implementation. In other words, they were 'lost in translation'. Studies that rigorously examine and report on the implementation process are needed to tease apart this important distinction.

KEYWORDS

adverse event, appropriateness, beers criteria, clinical pharmacy, consolidated framework for implementation research, deprescribing, elderly, guideline adherence, implementation science, pharmacy practice, physician, polypharmacy, potentially inappropriate medications, prescribing practices

1 | WHAT IS KNOWN AND OBJECTIVE

Striking the critical balance between benefit and harm from medication use in older adults continues to be a challenge. In recent studies, anywhere from 16% to 40.8% of elderly patients are on potentially inappropriate medications.[1-9] The term potentially inappropriate medication (PIM) implies that risks will usually outweigh benefits and is operationalized using criteria that are based partly on evidence and partly on expert opinion. The Beers Criteria and the Screening Tool of Older Person's Prescriptions (STOPP) are the most well known of these.[10,11] Although they are not perfect, these criteria are well defined and there is broad consensus as to their value as screening tools. Various interventions to deploy these kinds of tools in clinical practice have been designed and tested with the goal of deprescribing potentially inappropriate medications in older adults, reducing their exposure to unwarranted risks and ultimately reducing harm.[12-14] Pharmacist-led medication reviews and clinical decision support are among the common approaches used in these studies.

However, a 2018 Cochrane review based on 32 studies found that although such interventions can reduce polypharmacy, it is unclear whether they result in reductions in drug-related problems, quality of life or hospitalizations.[15] These findings raise the question of whether the interventions (eg deployment of a pharmacist using a screening tool such as Beers or STOPP, or use of clinical decision support) need to be redesigned or whether other factors are at play.

It is well known that the success of a clinical intervention in practice depends not only on the details of the intervention itself but also on the way that it is implemented into clinical settings.[16] Successful implementation of deprescribing is a complex process that starts with identifying a medication that should be stopped (eg using Beers or STOPP tools) but must be followed by communication of the recommendation to the prescriber and patient/caregiver and engagement with them in the decision. Additional steps may also be needed, including dose titration, identifying and initiating alternative therapies and communicating the plan to other providers. In other words, deprescribing is an individualized process that can be time-intensive and may involve multiple team members and workflow changes. The field of implementation science (IS) provides a set of theories, models and frameworks that can be deployed to better understand and evaluate the implementation process and its effects on outcomes. Implementation science is rich and diverse but one of the key insights that transcends much of IS in that failure of an intervention may result either from flaws in the intervention itself (intervention failure) or from inadequate deployment (implementation failure) in which the intervention is 'lost in translation'.[17] It follows that understanding the reasons for failure (or for that matter, success) requires looking beyond clinical (end point) outcomes to understand the implementation context and process.

Multiple contextual and process factors may influence success of deprescribing interventions. These could include the provider's perception of the strength of evidence, whether providers are open to incorporation of a pharmacist in the clinical team, the skill level of the pharmacist or the usability of a clinical decision support tool, as applicable. Understanding of these types of factors, sometimes called implementation determinants, can shed light on why an intervention does or does not work in real-world settings. Capturing and reporting on these issues would therefore be important to allow the end users of research, including practitioners and other researchers, to correctly interpret study findings. One of the most well-established frameworks in implementation science is the Consolidated Framework for implementation research.[18] It was developed to support the systematic study of implementation of known practices into real-world settings by providing a common language by which implementation can be described and studied. CFIR provides, among other things, a structure for identifying and reporting on implementation determinants. Table 1 shows the CFIR Domains and constructs under each domain. It has been used to study and/or guide the implementation of interventions in diverse areas of healthcare such as health promotion, mental health, obesity and chronic disease management, but has not been applied to the deprescribing literature to our knowledge.

In addition to examining determinants in the implementation process, describing and evaluating the steps in the process can be very valuable. This can be accomplished through measurement and reporting of intermediate outcomes that characterize the steps in terms such as time and resources expended, types of recommendations made and their acceptance rate. This can shed light on its success or failure of the intervention and guide future intervention efforts.[17,19]

TABLE 1 Overview of the consolidated framework for implementation research

Domain	Constructs
Intervention characteristics	Intervention source
	Evidence strength and quality
	Relative advantage
	Adaptability
	Trialability
	Complexity
	Design quality and packaging
	Cost
Outer setting	Patient needs and resources
	Cosmopolitanism
	Peer pressure
	External policy and incentives
Inner setting	Structural characteristics
	Networks and communication
	Culture
	Implementation climate
	Readiness for implementation
Characteristics of individuals	Knowledge and beliefs about the intervention
	Self-efficacy
	Individual stage of change
	Individual identification with organization
	Other personal attributes
Process	Planning
	Engaging
	Executing
	Reflecting and evaluating

Note: Damschroder et al.[18]

This narrative literature review examines published deprescribing interventions through the lens of implementation science. The goal was to critically evaluate selected deprescribing studies with an IS lens to determine the extent to which implementation determinants and important intermediate outcomes are captured. This would aid the interpretation of their findings as well as potentially guide the design of future deprescribing studies. With these goals in mind, we undertook a narrowly focused review, limited to high-quality studies that examined the most significant clinical outcomes.

2 | METHODS

To identify high-quality studies of deprescribing interventions with older adults that measured direct medication harm, we searched PubMed for relevant abstracts dated between 2000 and 2019 using search term, 'Drug-related side effects AND Adverse Reactions AND Aged AND Intervention'.

Abstracts were evaluated for study inclusion using the following criteria:

1. A deprescribing intervention
2. Targeted patients 65 years or older
3. Utilized a controlled clinical trial, cluster trial or prospective cohort design
4. Included emergency department (ED) visits and/or hospitalizations in their measured outcomes
5. Completed research.

Of 548 unique abstracts that were identified and screened, 42 warranted full paper review. After review of the full text of each article by two of the authors, 14 articles remained eligible for inclusion in this review.

The included studies were first characterized by intervention type using a classification system by Onder et al[20] for appropriate description and comparison. Table 2 provides a summary of the included studies and their outcomes.

The next step included an in-depth review of the selected articles, which included identification of any determinant factors described, as defined by the CFIR.[18] Two reviewers independently identified any implementation factors discussed in the paper (regardless of whether the paper's authors identified them as such), and mapped each onto a construct according to the CFIR framework (see Table 1). Descriptions and explanations of each CFIR construct were utilized to help classify each factor. Intermediate outcome measures reported in each paper were also recorded and classified. Discrepancies between the reviewers were resolved with in-person discussion.

3 | RESULTS AND DISCUSSION

As shown in Table 2, eight of the studies took place in the hospital setting,[21-25] four were in the outpatient setting,[26-28] and two took place in skilled nursing facilities.[29,30] Eleven of the interventions involved a manual medication review,[21,23-28] whereas other intervention types included clinical decision support, provider education or comprehensive pharmaceutical care.

Only one study showed a statistically significant improvement in medication-related hospital admissions in the primary analysis,[31] whereas 3 showed improvement after post hoc analysis.[26,32,33]

We were able to identify the discussion of implementation factors in 10 of the included papers, with a range of 1-4 factors discussed in each paper, as detailed in Table 3.[21-23,26-28] Each of the implementation factors could be categorized within the CFIR. The most commonly occurring CFIR domain was the inner setting. Within this domain, the most commonly occurring construct was Networks and Communication (seven papers).[22,23,26,27,31-33] Networks and Communication included topics such as the relationship between the pharmacist and the rest of the care team, which was the single

TABLE 2 Overview of the studies included in the literature review

Author	Setting (type, country)	Study design	Targeting method	Intervention method	Duration of intervention	Number of patients	Duration of follow-up for outcome	Outcome (effect on ED visits or hospitalizations
Mannheimer	Hospital, Sweden	Randomized controlled trial	Patients taking two or more drugs	Medication review	9 mo	300	6 mo	NS
Surgery and Pharmacy in Liasion	Hospital, Netherlands	Cluster-randomized controlled trial	Patients admitted to an elective surgery ward, with an expected hospital stay longer than 48 h	Medication review	18 mo	1094	3 mo	NS
Marusic	Hospital, Croatia	Randomized controlled trial	Patients aged ≥65 y admitted to the clinic during the study period	Medication review	3 mo	160	30 d	NS
Kjeldsen	Hospitals, Denmark	Non-randomized controlled trial	Inpatients using at least one of five high-risk medication classes: anticoagulants, digoxin, methotrexate, NSAIDS and opioids	Medication review	4 wk	1782	6 mo	NS
Lapane	Skilled Nursing Facility, USA	Cluster-randomized controlled trial	Residents living in nursing homes in the study period	Clinical decision support with medication review	2 y	6523	12 mo	NS
Lenander	Outpatient, Sweden	Randomized controlled trial	Patients aged ≥65 y with five or more different medications	Medication review	15 mo	209	12 mo	NS
Leenderstse	Outpatient, Netherlands	Non-randomized controlled trial	Patients ≥65, on five or more medications, with a refill rate of <80% as a measure of non-adherence, and where dispensed one or more drugs from the anatomical therapeutic chemical class A or class B	Medication review	12 mo	674	20 mo	HR 0.28, 95% CI 0.056-0.73 (hospitalizations, post hoc analysis)
Touchette	Outpatient, USA	Randomized controlled trial	Aged 65 y or older with three or more chronic illnesses and six or more prescription medications, and at risk for a DRP	Medication review	3 y	637	3 and 6 mo	NS
Donovan	Skilled Nursing Facility, USA	Prospective cohort	Patients aged 65 and older, discharged from SNF to home	Clinical decision support	1 y	313	Rehospitalization within 30 d, adverse drug events within 45 d	NS
Farris	Hospital, USA	Randomized controlled trial	Patients with cardiovascular-related conditions and/or asthma or chronic obstructive pulmonary disease discharged from study wards	Other 'Faxed medication care plan to their community physician and pharmacy and telephone call 2-5 d post-discharge'	5 y	945	90 d post-discharge	NS

(Continues)

TABLE 2 (Continued)

Author	Setting (type, country)	Study design	Targeting method	Intervention method	Duration of intervention	Number of patients	Duration of follow-up for outcome	Outcome (effect on ED visits or hospitalizations
Bos	Hospital, Netherlands	Prospective Cohort	Patients admitted to surgical, urologic or orthopaedic units	Prescriber education and pharmacist medication review	6 mo	11 651	30 d	RR 0.72, 95% CI 0.53-0.97 (hospitalizations)
Campins	Outpatient, Spain	Randomized controlled trial	Patients 70 or older with eight or more medications with a participating primary care physician	Pharmacist medication review	4 mo	503	1 y	NS
Lenssen	Hospital, Germany	Randomized controlled trial	Patients 65 or older, who were home cared or nursing home residents in ambulatory care, with admission to a cooperating ward and a minimum hospital stay of 3 d	Pharmacist medication review	2 y	60	1 y	HR 0.86, 95% CI 0.76-0.97 (Hospitalizations, post hoc analysis)
Gustafsson	Hospital, Sweden	Randomized controlled trials	Patients 65 or older with dementia or cognitive impairment	Pharmacist medication review	2 y	473	180 d	HR 0.49, 95% CI 0.27-0.90 (Hospitalizations, post hoc analysis)

most commonly identified implementation determinant identified in the papers that were reviewed.

Table 4 summarizes findings related to intermediate outcome measures. Twelve of the 14 papers utilized such measures as part of their analysis, ranging from 1-4 measures.[21,22,24-28,30-34] The most commonly reported intermediate outcomes were number or rate of drug-related problems (six papers),[24,26,27,32-34] types of recommendations made (six papers)[21,24,26,31,33,34] and rate of prescriber acceptance of the recommendations (six papers).[21,22,28,32-34]

In our review of high-quality studies that focused on deprescribing PIMs in older adults, we found minimal evidence of reduced medication-related ED or hospital admissions, and little explicit acknowledgement of implementation determinants. The only explicit reference was by Bos et al who mentioned that the 'implementation process was relatively straightforward', because the intervention was performed by providers already within the hospital system. By using the CFIR, we were able to identify implementation determinants even if they were not explicitly described as such. Presentation of intermediate measures was also very limited. These limitations in the literature represent missed opportunities to understand the reasons for the apparent failure of these studies.

The most commonly discussed implementation determinant was the relationship between the pharmacist and the rest of the medical team. Kjeldsen et al[23] described that 'the majority of [their] clinical pharmacists felt that their professional work was accepted by the physicians'. Conversely, Farris et al[22] indicated that their pharmacists were not part of the inpatient team and that this had a negative effect on the physician-pharmacist dynamic. These examples fall under the CFIR construct 'networks and communication' which is defined as 'the nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organization'.[18] For the interventions depending on a pharmacist, it makes intuitive sense that said pharmacist's formal and informal relationships with their colleagues would influence a provider's decision to accept their recommendation. Seven of 14 studies acknowledged this issue and its potential impact on their findings.[22,23,26,27,31,33,34]

It addition to identifying and categorizing some of the implementation factors that were acknowledged in the literature, CFIR can also help elucidate parts of the implementation process that may have been overlooked. For example, the knowledge or training level of the professionals taking part in the intervention was given little attention. Only two authors referenced the clinical competencies and post-graduate degrees of the pharmacists involved with their study.[32,33] This falls under the 'characteristics of individuals' domain. Knowing what sort of training the care team needs in order to accomplish the intervention and whether the staff felt their training was sufficient for the intervention are critical questions that may dramatically impact the ability of other groups to replicate and optimize the intervention in the clinical setting.

TABLE 3 Overview of implementation factors and associated CFIR domain and construct identified in the review

Author	Implementation factor	CFIR domain → Construct
Mannheimer	N/A	
Surgery and Pharmacy in Liaison Study Group	ADE rate in surgical patients and in patients on this particular surgical ward prior to the intervention	Outer setting → patient needs and resources
	Logistical strain on the pharmacist	Inner setting → available resources
Kjeldsen	Pharmacist integration into the medical team	Inner setting → networks and Communication
	Intervention was limited to 5 high-risk meds	Intervention → evidence strengths and quality
Marusic	N/A	
Lenander	Pharmacist integration into the healthcare centre	Inner setting → networks and communication
Lapane	N/A	
Leenderste	Pharmacists utilized were community pharmacists with access to a pharmacotherapy help desk staged by a hospital clinical pharmacist	Characteristics of individuals → other personal attributes
	Pharmacist spent about 4 h per patient for the intervention, which was perceived as adequate to meet the documentation needs	Inner setting → available resources
	Pharmacist involved already know the patient and had a relationship with them	Inner setting → networks and communication
	Integrated care setting in which the GP and pharmacist discussed the case together after the patient meeting with the pharmacist	Inner settings → network and communication
Touchette	N/A	
Donovan	Many of the rehospitalizations took place immediately after SNF discharge, implying that the intervention needed to begin during the SNF stay or even before discharge from the hospital to be effective	Process → reflecting and evaluating
Farris	Broad inclusion criteria: 18 y or older with a qualifying diagnosis,	Process → reflecting and evaluating
	Patient's pre-intervention medication management ability and self-reported medication adherence	Outer setting → patient needs and resources
	Pharmacists were not part of the inpatient medical teams	Inner setting → networks and communications
	Community physician involvement was poor	Inner setting → networks and communication
Lenssen	Clinical pharmacists involved had 1-3 y of experience in clinical pharmacy	Characteristics of individuals → other personal attributes
	Pre-intervention, a detailed medication review was only preformed on explicit request of a physician	Inner setting → networks and communication
Bos	Patient selection was limited to high-risk individuals in order to reduce the workload of the hospital pharmacist	Inner setting → readiness for implementation
	Estimated proportion of preventable, clinically relevant DRPs to be 0.7%	Outer setting → patient needs and resources
	'Implementation was relatively straightforward', because the intervention was performed by providers already active in the hospital system	Intervention characteristics → networks and communication
	Intended to identify specific predictive factors for patients at risks of clinically relevant preventable medication-related adverse events	Outer setting → patient needs and resources
Campins	Most common comorbidities were hypertension, osteoarthritis, dyslipidaemia, heart disease, diabetes and depression	Outer setting → patient needs and resources
	The translation of potential drug appropriateness into a reduction in hospital visits and admissions may require a more sustained intervention over time…since the incidence of DRPs that require hospitalization is relatively small	Process → reflecting and evaluating
Gustafsson	Clinical pharmacists had post-graduate degrees in clinical pharmacy and experience preforming medication reviews	Characteristics of individuals → other personal attributes
	Pharmacists were already part of the ward teams for up to 8 y at the time when the study started	Inner setting → networks and communication

Abbreviations: ADE, adverse drug event; CFIR, consolidated framework for implementation research; GP, general practitioner; SNF, skilled nursing facility.

TABLE 4 Intermediate outcomes, also known as process measures, utilized by reviewed articles

Author	Process measures/ intermediate outcomes					
	Pt characteristics associated with DRPs	Number or rate of DRPs	Types of recommendations made	Time spent by pharmacist	Rate of prescriber acceptance of recommendations	Costs
Mannheimer	X	X	X			
SPLG			X	X	X	
Kjeldsen						
Marusic				X		
Lapane	X					
Lenander		X		X		
Leenderstse		X	X			
Touchette					X	
Donovan						
Farris				X	X	
Bos			X	X		X
Campins		X	X		X	X
Lenssen		X			X	
Gustafsson		X	X	X	X	

Abbreviations: DRP, drug-related problems; SPLG, Surgery and Pharmacy in Liaison Group.

Another overlooked CFIR construct was 'relative advantage' which emphasizes the importance of the perceived advantage of the intervention by key stakeholders.[18] We found no discussion of perceptions of the benefits or risks of deprescribing by key stakeholders, such as physicians, nursing staff or patients in the reviewed studies. Without buy-in, an intervention may fail to have the deep impact required for a medication to be deprescribed and for it to stay deprescribed. Without being investigated further, this remains as a possible explanation for limited effectiveness.

Further, closely examining intermediate outcomes, such as the rate and type of problems identified, the time spent by various team members and prescriber response to recommendations are also critical to understanding how an intervention worked (or didn't) and can be used to evaluate fidelity and inform feasibility considerations. Although intermediate outcome measures were addressed in several studies, it was very inconsistent and multiple opportunities to study the implementation process were missed such as reporting on types of drugs associated with DRPs. Intermediate outcomes have been used as a surrogate for clinical outcome measures in other studies.[14] However, they provide the most information when used in conjunction with, as opposed to in place of, clinical outcome measures, to shed further light on the mechanisms behind the outcomes.

A limitation of this study is that our assessment of implementation factors and intermediate measures was limited by what authors chose to report in their published studies. We do not know whether implementation was informed by any of these considerations, or whether additional process measures were tracked. In addition, the authors may have published information relevant to implementation of their interventions in sibling papers that we did not review. Another limitation of this study is the subjective component of categorizing implementation factors. We attempted to minimize this effect by having two authors separately categorize implementation factors. We believe that these limitations do not detract from our main finding that most current studies are overlooking an important set of issues.

4 | WHAT IS NEW AND CONCLUSION

Our findings suggest that the conclusions of recent systematic reviews that current deprescribing interventions are ineffective might need to be re-evaluated.[15] The correct conclusion might be that, although the tools and approaches have potential, their implementation was poor. In other words, the interventions were 'lost in translation'. Studies that rigorously examine and report on the implementation process are needed to tease apart this important distinction.

The CFIR was intended to be used for systematic analysis of the implementation process for a given intervention.[18] Although it has been use prospectively in other fields to guide pragmatic and effective study design, it has yet to be used to guide a deprescribing intervention. We found the framework to be relevant and applicable to deprescribing interventions and identified significant gaps in descriptions of the implementation process in published studies.

In addition to systematically evaluating and reporting on implementation determinants (including barriers and facilitators) and reporting on intermediate outcomes, the field of implementation offers multiple other approaches that can be brought to bear on the challenge of deprescribing.[35] We suggest that future studies of

deprescribing interventions use a variety of implementation science approaches including: (a) identifying factors that are most important to the success of an intervention; (b) considering these factors in the explicit design of implementation strategies; and (c) developing approaches that permit adaptation to the unique characteristics of individual settings. Such studies would have a high potential to move the field of deprescribing forward ultimately leading to improved medication safety for older adults.

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CONFLICT OF INTEREST

No conflicts of interest have been declared.

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