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Recommendations for Outcome Measurement for Deprescribing Intervention Studies

Running title: Deprescribing intervention outcomes

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Abstract

Background. Interpreting results from deprescribing interventions to generate actionable evidence is challenging owing to inconsistent and heterogeneous outcome definitions between studies. We sought to characterize deprescribing intervention outcomes and recommend approaches to measuring outcomes for future studies.

Design. A scoping literature review focused on deprescribing interventions for polypharmacy and informed a series of expert panel discussions and recommendations.

Setting and Participants. Twelve experts in deprescribing research, policy, and clinical practice interventions participated in the Measures Workgroup of the U.S. Deprescribing Research Network.

Results. The scoping review identified 125 papers reflecting 107 deprescribing studies. Common outcomes included medication discontinuation, medication appropriateness, and a broad range of clinical outcomes potentially resulting from medication reduction. Panel recommendations included clearly defining clinically meaningful medication outcomes (e.g., number of chronic medications, dose reductions), ensuring adequate sample size and follow-up time to capture clinical outcomes resulting from medication discontinuation (e.g., quality of life [QOL]), and selecting appropriate and feasible data sources. A new conceptual model illustrates how downstream clinical outcomes (e.g., reduction in falls) should be interpreted in the context of initial changes in medication measures (e.g., reduction in mean total medications). Areas needing further development include implementation outcomes specific to deprescribing interventions and measures of adverse drug withdrawal events.

Conclusions. Generating evidence to guide deprescribing is essential to address patient, caregiver and clinician concerns about the benefits and harms of medication

discontinuation. This article provides recommendations and an initial conceptual framework for selecting and applying appropriate intervention outcomes to support deprescribing research.

Key Words: Deprescription, Polypharmacy, Outcome assessment.

Key points

- Thus far, deprescribing studies have used inconsistent outcome definitions making it difficult to synthesize results and generate clinical evidence.
- Key outcome domains that have been commonly measured, include medication discontinuation, dose reduction, and patient-centered outcomes reflecting personal well-being.
- Clinical outcomes should be interpreted in the context of initial medication reduction.

Why does this matter?

More consistent outcome definitions and effective applications of those outcomes in study designs will make it easier to synthesize results across studies to generate actionable clinical evidence for deprescribing.

Introduction

Deprescribing is defined as discontinuing or reducing the dose of medications that are no longer needed, for which risks outweigh benefits, or are inconsistent with goals of care.[1] Deprescribing is particularly relevant for older adults who are more likely to experience polypharmacy, changes in clinical conditions, or revised goals of care.[2-4] Although medication reconciliation is a longstanding best practice, it focuses on reducing medication discrepancies and has had variable effects on patient outcomes.[5] Evidence-based deprescribing has the potential to improve clinical outcomes for older adults.[1]

Although the potential to improve clinical outcomes through deprescribing is substantial (as reflected by a marked increase in deprescribing studies published during the past 12 years), the evidence base to support medication discontinuation or reduction is not yet well established. Systematic reviews assessing the relationships between deprescribing interventions and clinical outcomes have drawn limited conclusions due to inconsistent and heterogeneous outcome definitions between studies.[6-9] This methodological barrier has limited high quality evidence generation and subsequent translation of evidence-based interventions into practice and policy. [10, 11]

Efforts to generate evidence about the clinical impact of deprescribing would benefit from clarifying meaningful outcomes, standard definitions for outcome measures, and recommended approaches for implementing these definitions.[12-14] More consistent definitions and approaches would be especially helpful for designing pragmatic trials and quasi-experimental studies that rely on clinically derived data to identify eligible

participants and measure outcomes.[15, 16] Consistent outcome definitions are particularly important for interventions targeting polypharmacy (the use of more medications than medically necessary) because interventions targeting single drugs may be able to rely on recurring signs and symptoms as primary outcomes.

As part of the U.S. Deprescribing Research Network (USDeN) mission to catalyze high quality, clinically impactful research about deprescribing, the network includes a Measures Workgroup tasked with 1) identifying measures and outcome definitions commonly used in deprescribing studies with an emphasis on interventions targeting polypharmacy, 2) prioritizing constructs most likely to be valuable for future deprescribing evidence generation, and 3) informing operational definitions and applications for these measures.[17] The overarching goal of the discussions was to make recommendations that could inform deprescribing evidence generation by facilitating evidence syntheses.

Methods

To achieve goals of identifying, prioritizing, and recommending applications for measuring deprescribing study outcomes, we gathered and synthesized input from two sources: 1) A scoping literature review of deprescribing research focusing on randomized trials and rigorous observational studies; and 2) an expert panel that identified gaps in evidence and recommended approaches to outcome measurement. Experts represented a range of settings and backgrounds and contributed information through a survey and group discussions. We used an iterative approach in which

literature precedent informed expert input and expert input prompted further literature queries to inform discussions (see Figure 1). The Kaiser Permanente Colorado (KPCO) Institutional Review Board determined that the tasks of the Measures Workgroup did not constitute Human Subjects' research.

Scoping literature review

Scoping reviews of the literature are most relevant for clarifying key concepts and definitions, examining how research is conducted in a field, and identifying knowledge gaps—an approach well suited to understanding existing precedent for outcome definitions and measures and informing further studies.[18] This scoping review of the deprescribing literature was conducted by the project team at KPCO to address the first workgroup goal of identifying measures and outcome definitions commonly used in deprescribing studies with an emphasis on interventions targeting polypharmacy.

Search strategy. We initially searched articles published between 2005 and 2020, but ultimately focused on 2011-2020as the interval with most contemporary deprescribing research. Abstracts were obtained from PubMed and Ovid indices and contained MeSH terms or text words related to deprescribing. We also examined systematic reviews to identify additional articles. See Supplementary File S1 for the full search strategy.

Abstract screening and article review. Abstracts were screened and selected for full manuscript review if they had a) clearly defined, generalizable, outcomes relevant to multiple medication classes; and b) well-described target populations. We excluded interventions targeting single drug classes with only outcomes that were drug- or class-specific (such as recurrent signs or symptoms resulting from treatment discontinuation).

Four abstractors collected the following information: Study design, setting, and characteristics of target population; intervention description; target drug classes; definition of deprescribing; primary and secondary outcomes with associated definitions and data sources; and measurement intervals. Questions and discrepancies were resolved through KPCO team discussions. Since the goal of the scoping review was to identify common outcomes used in deprescribing studies (not determine the validity of the studies) , we did not categorize each article on strength of evidence but retained articles with clear descriptions of how outcomes were assessed and applied. Supplementary Figure 1 describes criteria for retaining articles.

Expert panel engagement

The expert panel comprised 12 members (see Authors) who met virtually nine times between November 2019 and December 2020. All panel members had expertise in deprescribing research in addition to geriatric and internal medicine (n=9), clinical pharmacology (n=5), family medicine (n=2), and implementation science (n=2). First the panel grouped outcomes by category (e.g., medication counts, quality of life [QOL], utilization), using an iterative process of reviewing outcomes from the scoping review and revising categories based on discussion. Next, outcome categories were incorporated into a survey completed by panel members to prioritize categories for deprescribing evidence generation (the second work group goal). The survey asked experts to evaluate a) each category's importance as an outcome for deprescribing interventions, and b) whether measures in that category were mature (needing no further refinement), in need of standardized definition or application, or in need of

development. (See Supplementary File S2 for survey.) Third, in a series of small and large group discussions, panel members formulated recommendations for defining and operationalizing outcomes.

RESULTS

Literature overview

Of 1321 papers identified, 238 were selected for full review. From these, 113 were excluded due to low relevance, insufficient information, or lack of clarity, leaving 125 articles reflecting 107 studies. (Supplementary Tables S2 and S3). Most studies (86) focused on more than one drug class. Thirty-two were observational studies with the remainder being controlled trial designs. Table 1 summarizes study characteristics.

Expert input: Conceptual framework

Through iterative discussions about outcomes identified through the literature search, the panel proposed a conceptual framework (Figure 2) to describe relationships between outcomes. In this framework, *medication outcomes* directly reflect the deprescribing intervention—quantifying changes in metrics such as total medications, medication appropriateness, and medication doses. *Clinical outcomes* reflect the downstream effects of medication reduction on patients (e.g., changes in cognitive or physical function or adverse drug withdrawal events [ADWE]). *System outcomes* (such as utilization) capture further downstream effects at the population level. Essential to evaluating strategies for implementing evidence-based interventions at scale are outcomes reflecting *implementation* such as adoption by providers and reach within and

across populations. All outcomes draw on multiple data sources, are relevant for varied populations, and are potentially informative for diverse stakeholders. The proposed theoretical framework can inform project designs by, for example, illustrating differences in sample size needed for more distal outcomes, or selecting primary versus secondary outcomes. It could be further developed to incorporate additional outcomes and relationships between them.

Expert input: Outcome categorization

Through the above processes, the expert panel identified outcome categories that, a) were likely to accurately reflect the impact of deprescribing and guide designs of future intervention trials, and b) could benefit from panel recommendations on applying the measures in research studies. High priority topics were: 1) outcomes quantifying medication changes which could benefit from more standard definitions, 2) established measures of clinical outcomes which would benefit from guidance for deprescribing applications; and 3) constructs deemed essential for assessing deprescribing interventions but for which measures were not yet well defined for that purpose. Due to time constraints, the panel chose not to discuss certain outcomes with relatively well-established measurement approaches including healthcare utilization, mortality, cost of care, medication adherence, and new prescriptions; or outcomes that could be incorporated into broader evaluation constructs, including patient satisfaction, knowledge, and attitudes about care. Table 2 lists the outcome categories considered with example measures for each category and notes on panel decisions, and

Supplementary Table S1 summarizes survey responses including example comments from panel members.

Expert input: Outcome measurement recommendations

Based on the scoping review, survey process, and iterative discussions, the panel developed recommendations to inform operational definitions and applications of common outcome categories for deprescribing evidence generation (the third workgroup goal).

Medication outcome measures

Panel members considered measures quantifying medication change to be key indicators of successful deprescribing. Most deprescribing interventions in reviewed articles focused either on decreasing the number of medications (e.g., number of chronic medications) or decreasing potentially inappropriate medications (PIMs). Medication appropriateness was usually assessed by counting PIMs or using a medication appropriateness index.

Definitions for long-term medications were inconsistent across studies due in part to differences in data sources and prescribing patterns by setting. For example, interventions in inpatient facilities might assess active medications on the medication list or patient/caregiver interviews to compare drug regimens pre- and post-intervention.[19, 20] Pragmatic interventions or quasi-experimental studies might quantify medications using prescribing data from the electronic health record, pharmacy dispensing data, or billing claims.

Panel members concluded that the range of possible deprescribing intervention study designs, settings and resources precluded a uniform definition for quantifying medications. Instead, they emphasized defining medication outcomes in the context of the study design, articulating the rationale for those definitions, and—if needed—validating medication-related measures as part the study. To improve comparability across studies, they recommended the following approaches to selecting medication outcomes:

- Select clinically meaningful medication outcomes. When targeting polypharmacy, assess appropriateness in addition to medication count. If dose reduction is an intervention goal, consider calculating dose over a specified period (such as using total daily dose or dose-equivalents per day).[21] Clinically meaningful dose reductions may differ by medication.
- Clearly define medication outcomes and provide a rationale for the definition. To be comparable across studies, definitions should incorporate: duration of use (e.g. at least 30 days' supply dispensed), standardized doses, indication for use, source (e.g. prescribed vs. over the counter), and any specific criteria to assess appropriateness (e.g. Beers list).[22] Non-standardized definitions (e.g., combining medical record review with patient report) may limit the ability to compare between studies.[23]
- When feasible, select continuous rather than categorical outcome measures. A continuous scale will improve the ability to detect statistically significant

intervention effects that may otherwise be missed with grouped or dichotomous measures (e.g., measuring number of long-term medications rather than achieving a polypharmacy threshold).[24, 25] Like dichotomous event measures, continuous outcome measures can be reported in terms of absolute effect sizes and number needed to treat, i.e., per unit change in the continuous outcome. Depending on the target population and medication, even small effect sizes may be clinically meaningful on a population level. Continuous scales measuring cumulative drug effect (e.g., anticholinergic burden or drug burden) may also capture incremental but meaningful change.[26, 27]

- Understand the feasibility, limitations, and reliability of data sources. Accuracy, measurement timing, burden associated with data collection, amount and characteristics of missing data, and ability to determine dose changes are among factors that need to be considered when choosing data sources.
- Measure medication changes temporally aligned with the intervention. For individuals with complex care needs, medication lists may be dynamic with frequent adjustments. Outcome measurement should allow time for enough patient-provider communication about deprescribing, but not be so long that goals of care change substantially. The timeframe for deprescribing may differ across medications, and long-term medications or those likely to promote withdrawal symptoms may take longer to deprescribe. The setting (e.g., institutional vs. community) may influence discontinuation timeframe.

Clinical outcome measures

Panel members considered clinical outcomes (downstream of medication outcomes in Figure 2) reflecting benefits and harms of reducing medications to be the primary outcomes of interest in deprescribing trials. Outcomes capturing QOL, comprehensive functional assessments, and adverse drug events (ADE) were considered highly relevant. This was reflected in the literature review, where studies frequently used established measures (e.g., EQ-5D, Mini Mental State Exam, Vulnerable Elders Survey, and others) for QOL or functional constructs.[28-30] However, established measures were often applied to insufficient sample sizes, or measured too soon or too late to detect potential clinical effects of medication discontinuation. Sometimes instruments validated only for screening were used to assess change over time. Inappropriate applications of established measures risked wasting study resources on time- or labor-intensive assessments. A wide range of ADEs were assessed through medical or pharmacy record review, and by interviews with patients, family members, providers, and pharmacists. Although important for deprescribing, developing recommendations for measuring ADEs were considered beyond the scope of the panel.

To enhance evidence generation using existing measures to assess clinical outcomes, panel members proposed the following guidelines:

- Select measures sensitive to change over time. Measures should be applied over an interval in which a change is likely to be attributed to the deprescribing intervention and should measure a clinically plausible change. For example, cognitive function may decline more slowly (rather than improve) because of

medication discontinuation and an improved trajectory of cognitive decline may require months to become clinically (or statistically) detectable.

- Consider the clinical relevance of the instrument for the targeted medication(s). For example, when studying an intervention to reduce psychoactive medications, a QOL subscale of emotional well-being (such as from the SF-36®) may be more relevant than a broad QOL measure.
- Design the study so it is powered to detect a clinically meaningful effect size for clinical outcomes in addition to medication outcomes. Not all medication discontinuations will cause changes in clinical outcomes, and many clinical outcomes (e.g., physical function) are multifactorial. An appropriate analytic plan should consider whether outcomes are measured as intention to treat (among all who received the intervention) or per protocol (only among those who actually discontinued). Therefore, sample size estimates for clinical outcomes should consider the effects of the intervention on medication discontinuation plus medication discontinuation as a mediator of more downstream clinical outcomes.
- Ensure that required data are accurate and readily available for the deprescribing study population. This is particularly important for investigations that rely heavily on clinically derived data such as observational studies or pragmatic trials. Individuals targeted for deprescribing may have healthcare utilization patterns that affect data consistency. Data should be accessible, feasibly collected, and not likely to be disproportionately missing within the study population. For example, some electronic health record (EHR) variables may depend on regular contact with the healthcare system—resulting in missing data for patients who

have fewer visits; or rehospitalization may be difficult to identify without access to the original inpatient admission. If pharmacy dispensing data are used to capture medication discontinuation, the dispensing pharmacy should have data on all fills or be supplemented with complete pharmacy claims data. Approaches to reduce bias due to differential loss-to-follow-up should also be considered in the study design.

- Consider respondent burden when using self-report instruments. If self- or proxy-report is needed, ensure that the research question, study design, staffing, budget, and sample size support and justify the burden of self-reported data collection. This is particularly important for study populations with functional or cognitive limitations. Consider pragmatic study designs that use routine clinical data to minimize respondent burden.
- Choose outcome measures relevant for target medication class(es). Unlike interventions to reduce polypharmacy, interventions that focus on single medications or medication classes may yield different effect sizes and may focus on specific biologic parameters (e.g., blood pressure) or symptoms (e.g., insomnia).
- Where possible use outcome measures that have been validated in deprescribing trials—recognizing that this will not always be possible. When not possible, otherwise well validated instruments that can be feasibly applied in the study population are acceptable.

Outcomes needing further development

Panelists identified several high priority outcome domains for which measures need further development. These domains were considered important for patients and providers but current measures either did not exist, were not practical (e.g., could not be applied at scale) or were not sufficiently validated for deprescribing applications. Panelists highlighted ADWEs, treatment burden, and implementation evaluation as domains that would benefit from further measure development for deprescribing studies.

Adverse drug withdrawal events reflecting deprescribing safety were highlighted as an essential domain for outcome development. Potential effects of medication discontinuation include recurrent symptoms requiring represcribing the medication (or a similar one), physiologic symptoms of medication withdrawal, and specific adverse outcomes such as myocardial infarction or stroke. Clinicians (and patients) are concerned about possible ADWEs; however, for many medications little is known about the frequency and severity of ADWEs.[31-33] In reviewed studies, potential effects of medication discontinuation were collected through patient or provider interviews or medical record reviews. Panelists recommended considering ADWE measurement separately for single drug vs. polypharmacy studies. For interventions focused on single drug classes, ADWEs could be quantified through signs and symptoms of the treated condition (e.g., blood pressure values) and/or asking patients about specific symptoms. Identifying and measuring potential ADWEs in interventions targeting multiple drug classes is more complex and was considered an area for measure development—either through standardized patient queries or through sophisticated approaches using EHR data (e.g., natural language processing coupled with medication orders and/or specific

diagnoses). Direct patient queries about ADWE in studies targeting multiple medications might require an open-ended approach assessing, for example, new symptoms arising (or previous symptoms returning) within a time window following medication discontinuation.

Treatment burden was identified as another key outcome in need of development. Treatment burden is a subjective construct that reflects the work of being a patient, such as managing self-care tasks, taking medication, and attending medical visits.[34-37] It is associated with multimorbidity and polypharmacy, and has the potential to decrease with deprescribing.[35] Existing measures of medication burden such as the Medication Regimen Complexity or Anticholinergic Burden Indices reflect characteristics of the medications rather than the patient's subjective experience of managing care.[38, 39] Of available treatment burden measures, our panelists preferred the self-report Multimorbidity Treatment Burden Questionnaire for deprescribing intervention populations.[40] Developing and/or further validating a treatment burden measure for deprescribing would capture an important clinical outcome. If feasible, a proxy measure using EHR data could expand treatment burden assessment to pragmatic and observational study designs.

*Implementation assessment*s traditionally use established frameworks and process evaluations to understand the feasibility and effectiveness of strategies for implementing evidence-based interventions.[41-43] However, traditional implementation frameworks have not yet been adapted to evaluate deprescribing interventions. Outcome measures

reflecting implementation strategies could, for example, identify contextual factors supporting communication between prescribers and pharmacists and patients about risks of ADWE, or types of computerized decision support likely to improve medication appropriateness. Incorporated into study designs, such outcomes could be assessed alongside clinical effectiveness outcomes to accelerate evidence generation on integrating deprescribing into clinical practice. Deprescribing evaluations might also be informed by *de-implementation* frameworks (which help evaluate discontinuing low value care) to understand the unique challenges associated with changing processes to stop rather than start and continue medications.[44-47]

Summary

Rigorous deprescribing studies require appropriate outcome measures to produce valid and actionable results. Investigators designing those studies need information on how to best define these measures, which data are required, which outcomes are most important to key stakeholders and which are likely to be comparable across studies.[48-50]

Through a scoping review, we identified common outcome measures, and engaged content experts to prioritize outcome constructs for future evidence generation and develop recommendations for using common outcome measures. Their recommendations add to previous calls for measures to understand deprescribing success and acceptability.[14] Outcomes should reflect the process and potential causal pathways of deprescribing as conceptualized above (Figure 2). Medication outcomes reflecting discontinuations or dose reductions should be coupled with clinical outcomes

indicating the effects of medication changes for individuals. System level outcomes can capture subsequent effects, such as changes in healthcare utilization or quality metrics reflecting under- or over-treatment. For all outcomes, it is essential to consider clinical relevance, sample sizes, meaningful effect sizes, and the time required for an intervention to lead to a given outcome. Also essential are outcomes assessing implementation at scale such as—adoption by providers and reach within and across populations.

There were limitations to our process. Our scoping review of 107 studies identified outcomes commonly used in deprescribing interventions and informed expert panel discussions by illustrating outcome domains, definitions, and applications. It was not intended to rigorously synthesize the literature as in a systematic review.[18] Owing to the variety of data sources available for outcome measurement (e.g., EHR data, insurance claims, self-report), panelists did not recommend definitions for specific outcome variables (e.g., what constitutes a long-term medication). Rather they emphasized articulating clear rationales for variable definitions and measure selection within individual studies to facilitate future evidence syntheses. Some clinical and system outcomes not considered by the panel such as cost of care and patient satisfaction deserve further study in the context of deprescribing.

Conclusion

Generating evidence to guide deprescribing is essential for addressing patient, family and clinician concerns about the risks and benefits of medication discontinuation. These

recommendations and framework for selecting and applying appropriate intervention outcomes can help guide the design of studies to build this evidence base.

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Figure Titles and Legends

Figure 1.

Title: Iterative approach to information synthesis

Figure 2.

Title: Conceptual Framework with Example Deprescribing Intervention Outcomes

Legend: Medication, clinical, and system outcomes reflect the effectiveness of the deprescribing intervention. Implementation outcomes would be applied to an effective intervention and assess implementation strategies and other relevant influences and factors.

Supplemental Materials

Supplementary File S1

Title: Library search strategies and literature search schematic

Supplementary Figure S1

Title: Literature Search Schematic

Legend. Since the goal of the scoping review was to characterize identify common outcomes, we did not categorize each article on strength of evidence but retained articles with clear descriptions of how outcomes were assessed and applied in the target study populations. Articles were removed from consideration if they focused primarily on single diseases or single drugs, did not provide definitions for deprescribing

or for outcome measures, did not describe the intervention or analytic methods, or described small exploratory or feasibility pilot studies.

Supplementary File S2

Title: Survey instrument for expert panel

Supplementary Table S1: Summary of workgroup survey responses for ranking deprescribing outcome domains

Supplementary Table S2

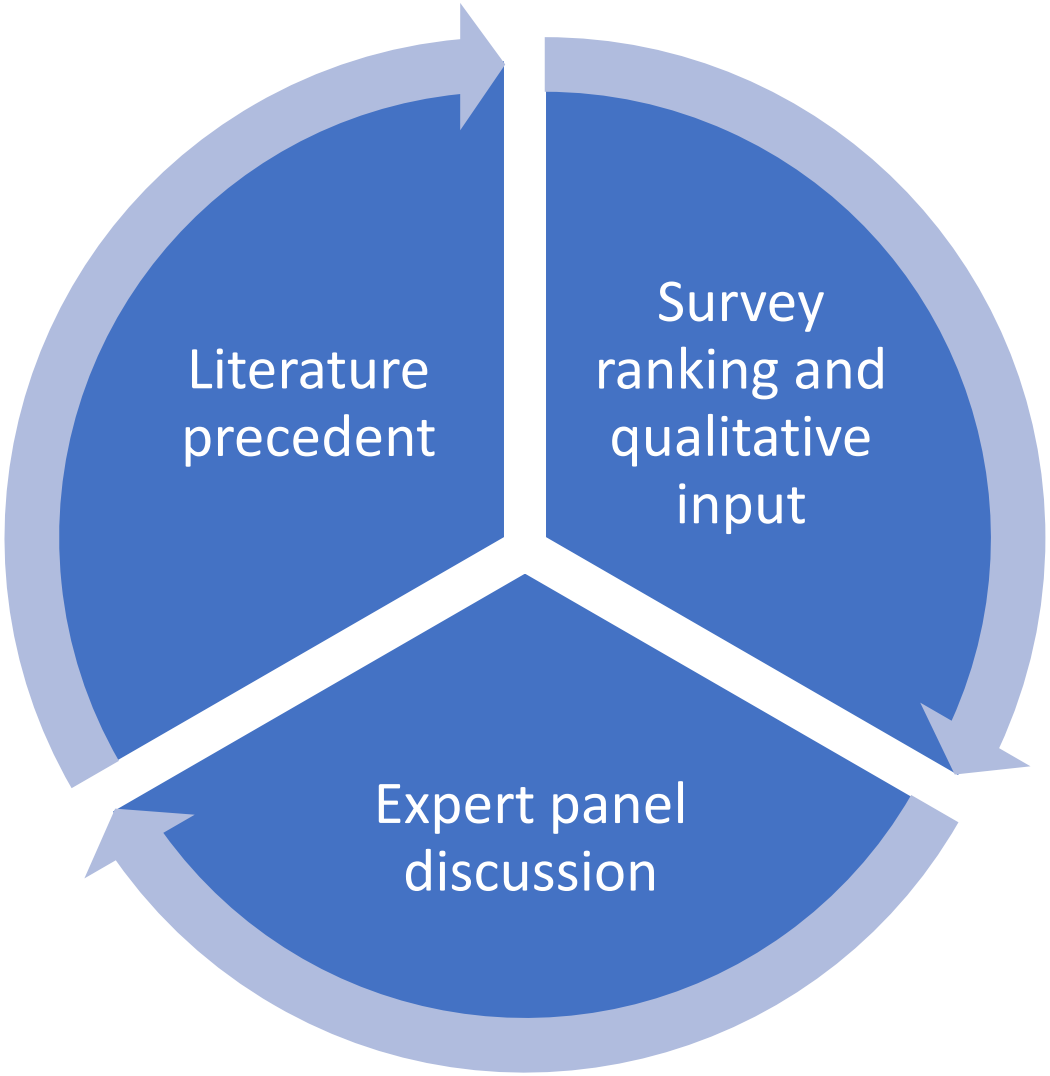
Title: Studies identified in literature review targeting polypharmacy

Supplementary Table S3

Title: Studies identified in literature review targeting single drug classes

Supplementary References S1

Title: References for Supplementary Tables S2 and S3



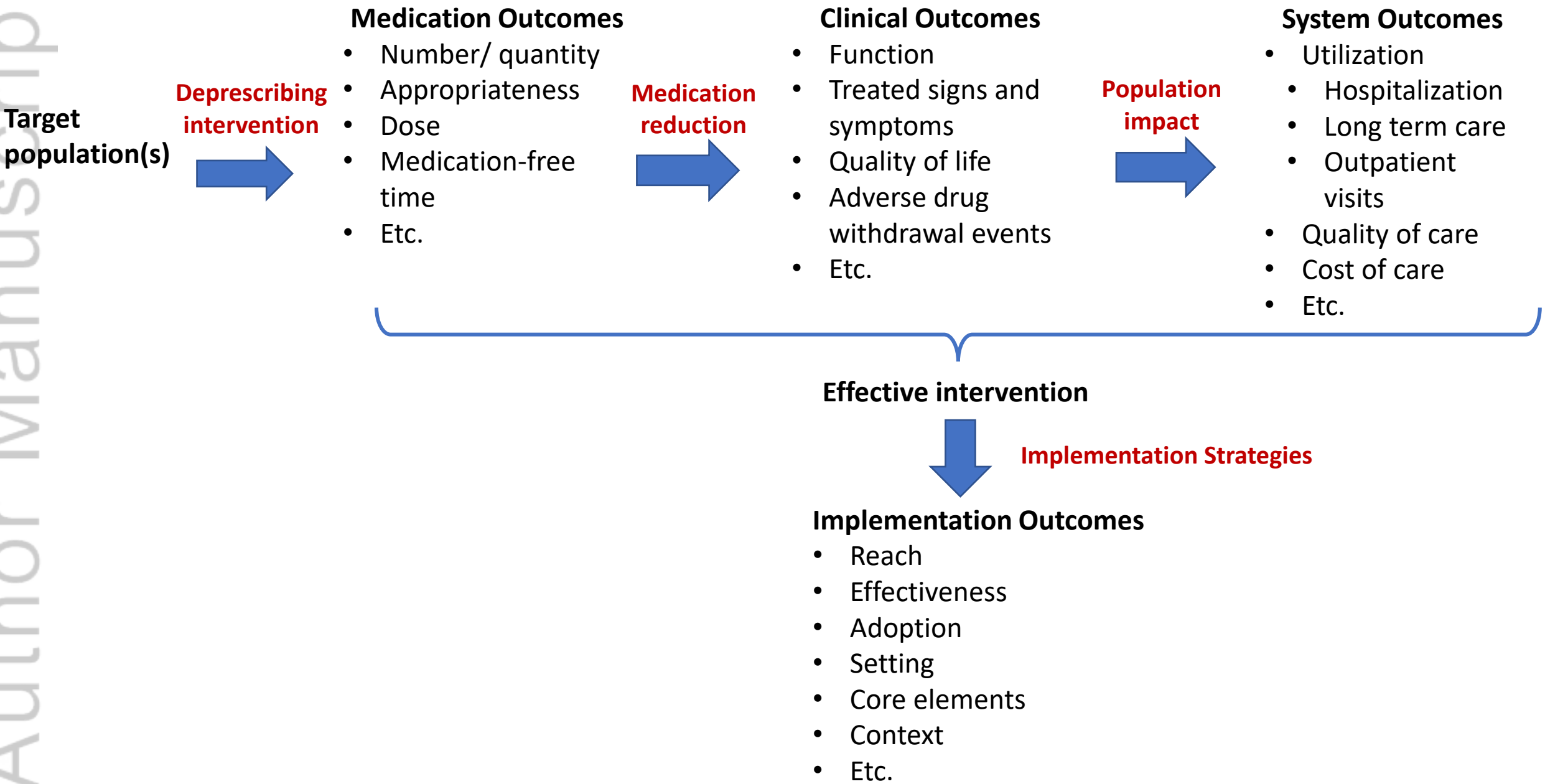


Table 1. Characteristics of Reviewed Studies

TOTAL		N=107 (%)
Study Design	Observational	32 (30%)
	Individual level randomized controlled trial	42 (39%)
	Cluster randomized controlled trial	33 (31%)
Target Medication(s)	More than one drug class	86 (80%)
	Single drug class	21 (20%)
Setting	Outpatient	54 (50%)
	Assisted living	3 (2%)
	Hospice	1 (1%)
	Inpatient	23 (22%)
	Post-acute and long-term nursing facility	21 (20%)
	Combination of the above	5 (5%)
Participants per study	<100	13 (12%)
	100-<500	54 (50%)
	500-<1000	22 (21%)
	1000+	18 (17%)
Duration of Follow up	1 month	3 (2%)
	3 months	1 (1%)
	6 months	38 (35%)
	12 months	40 (38%)
	24 months	12 (12%)
	>24 months	3 (2%)
	At hospital discharge	9 (9%)
	Not stated	1 (1%)

Table 2. Summary of Expert Panel Outcome Categorization and Discussion Focus

Outcome category	Example measures (number of studies*)	Panel assessment	Decision on panel discussion focus
Medication use	Number of medications (37), discontinuations (24), substitutions (15), dose decrease (13) Appropriateness (59)	Important measure affecting downstream outcomes.	Definitions would benefit from recommendations for standardization.
Quality of life (QOL)	QOL (46)	Improving QOL is a primary goal of deprescribing. Many valid existing measures.	Would benefit from recommendations for applying existing measures in the context of deprescribing.
Functional status	Cognitive function (18) Physical function (13)	Change in function is an important outcome in deprescribing trials. Many valid existing measures.	
Treatment Burden	Drug burden (12) Treatment burden (0)	Treatment burden is important for deprescribing and measures are not well developed.	Area for further measure development for deprescribing implementation.
System implementation	Acceptability to patients or providers (8) Feasibility (9)	Implementation outcomes are important to understand feasibility and acceptability. Not yet well developed for deprescribing.	
Adverse drug withdrawal event (ADWE)	ADWE- nonspecific (12) Recurrent symptoms (10)	Important to generate evidence on ADWE to inform deprescribing practice. Currently, this area is poorly defined and inconsistently measured.	Area for foundational measure development.

Healthcare utilization	Hospitalization (31) Length of stay (7) Cost of care (18)	Important for patients and systems. Well defined measures exist.	Low priority for panel discussion.
Adverse drug event (ADE)	Falls/ Fractures (23)	Important measure for deprescribing. Many existing measures exist. Some may be drug specific. Beyond scope of panel discussion.	
Mortality	All cause (1)	Multifactorial outcome, likely to require large sample.	Low priority for panel discussion

* Out of 107 studies described in 125 articles