


Tools for Deprescribing in Frail Older Persons and Those with Limited Life Expectancy: A Systematic Review

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OBJECTIVES: To summarize available tools that can assist clinicians in identifying and reducing or stopping (deprescribing) potentially inappropriate medications and that specifically consider frailty or limited life expectancy.

DESIGN: Systematic review and narrative synthesis.

SETTING: We searched MEDLINE (via Ovid SP), EMBASE (via Ovid SP), and CINAHL from inception to December 2017, along with grey literature. We included articles that described a tool to guide deprescribing of medications.

PARTICIPANTS: Frail older persons and older persons with limited life expectancy.

MEASUREMENTS: Narrative description of tools.

RESULTS: We identified 15 tools and organized them into three main categories: tools (n = 2) that described a model or framework for approaching deprescribing, tools (n = 9) that outlined a deprescribing approach for the entire medication list, and tools (n = 4) that provided medication-specific advice. The complexity of the tools ranged from simple lists to detailed, step-wise protocols. The development methodology varied widely, and the methods used to synthesize the tools were generally not well described. Most tools were based on expert opinion. Only four of the 15 tools have been tested in clinical practice (in very low-quality studies).

CONCLUSION: Tools exist to help clinicians deprescribe in frail older persons and those with limited life expectancy. These tools may assist clinicians at various stages in the deprescribing process. However, it remains to be investigated whether use of such tools in practice is likely to improve clinical outcomes or reduce inappropriate medication use. *J Am Geriatr Soc* 00:1–9, 2018.

Key words: deprescribing; end of life; frail

Older persons often take many medications¹ and are more susceptible to the adverse effects of medications compared to younger persons.^{2,3} Polypharmacy has been defined as concomitant use of multiple medications (often arbitrarily defined as use of ≥ 5 or ≥ 10 medications), use of medications that are not indicated, or use of medications for which harms outweigh benefits.^{4,5} Regardless of the definition, the prevalence of polypharmacy is increasing in older persons,⁶ and it is associated with an increased risk of adverse health outcomes such as falls, adverse drug events, and hospitalizations, even after accounting for comorbidities.^{4,7} In frail older persons and those with limited life expectancy, there is also a lack of evidence of benefit from some common treatments⁸ (e.g., statins or intensive blood glucose control in type 2 diabetes mellitus). However, these individuals sometimes continue on such treatments⁹ without reassessment when the potential for harm may outweigh the potential for benefit. Older persons may also be started on medications for which the known time to benefit exceeds life expectancy.^{10,11} Finally, goals of drug treatment may shift from reducing risk of disease and prolonging life to maintaining quality of life and reducing treatment burden.⁸

When medications are potentially inappropriate for the reasons outlined above, patients and prescribers may be interested in reducing or stopping them. Deprescribing is the planned, supervised dose reduction or stopping of a medication.¹² Prescribers sometimes view deprescribing as

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challenging because of lack of time and resources as well as low self-efficacy^{13,14}, but some resources are available to help clinicians with deprescribing decisions. These include resources focusing on screening for potentially inappropriate medications (e.g., Beers criteria, Screening Tool of Older People's Prescriptions (STOPP) criteria), providing a general framework for the deprescribing process, and giving medication-specific guidance.¹⁵

The range of tools available to support deprescribing was summarized in 2012¹⁵ and 2017 (search conducted December 2015)¹⁶, but neither review focused specifically on frail older persons or those with limited life expectancy. Although deprescribing is important to consider at all stages of medical care, it is particularly important in frail older adults and those with limited life expectancy for the reasons outlined above. Thus, it will be helpful for clinicians to be aware of and use the deprescribing tools that are most applicable to this population.

With this systematic review, we aimed to identify and describe tools focused on deprescribing medications in frail older persons and those with limited life expectancy. We wanted to provide an overview of tools that clinicians can use to manage polypharmacy in this population and identify what is needed from future studies within the field.

METHODS

We conducted a systematic review with narrative synthesis, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.¹⁷

Population

The population of interest was frail older persons and those with limited life expectancy. Therefore, we were interested only in tools aimed at this population. There were no specific criteria for frailty or limited life expectancy, but studies had to state explicitly that the tool was designed for this population or include specific considerations relevant to this population. We excluded tools that were aimed exclusively at individuals with cancer in the palliative care setting.

Tools

Tools could be algorithms, guidelines, websites, scientific publications, or any other resource that provides guidance on deprescribing of medications in our population of interest (for an overall medication list or medication-specific advice). Tools used as interventions in clinical studies were also eligible.

Search Strategy

We searched the following databases from inception to December 2017: MEDLINE (via Ovid SP), EMBASE (via Ovid SP), and CINAHL. The search terms can be found in Supplementary Appendix S1. We also searched the bibliographies of eligible studies and known major works in the field of deprescribing to identify tools. Finally, we conducted a grey literature search using Google, Google Scholar, UpToDate, the TRIP database, clinicaltrials.gov,

and the World Health Organization register for clinical trials. We included only articles in English.

Screening

Two authors (CL, TG) screened titles and abstracts retrieved from databases and grey literature using the eligibility criteria described above. If articles or resources were possibly relevant, the full text was retrieved. Two authors (CL, WT) screened the full-text articles and grey literature for eligible publications or resources. Covidence software was used as a screening tool (Cochrane Collaborative, Melbourne, Australia). Disagreements were resolved by all authors. The full author group discussed the final study selection, and all authors agreed on the final decision for inclusion.

Data Extraction and Synthesis

One author (WT) went through eligible articles and resources and extracted the following information: tool name, publication year, who developed the tool, development methodology, and whether the tool has been tested or evaluated. We summarized the extracted information narratively to provide a brief, structured overview of the tools.

RESULTS

Our search produced 2,149 titles and abstracts after removing duplicates. We reviewed 144 full-text articles and resources, from which 15 tools were eligible for inclusion (Figure 1). Four studies addressed individuals with limited life expectancy, four addressed frail older persons, and seven studies addressed both. The characteristics of the tools are briefly summarized in Table 1, and further details are available in the Supplementary Table S1.

We identified three main categories of tools. Two tools described a model or framework for approaching deprescribing,^{18,19} nine tools outlined a deprescribing approach for the individual's entire medication list,²⁰⁻²⁸ and four tools provided guidance on deprescribing of individual medications.³²⁻³⁵ A summary of the features of each of these categories is outlined in Figure 2.

Three tools were developed using Delphi methodology,²¹⁻²³ two using a systematic review and GRADEing of evidence (explicit and systematic method for rating quality of evidence and synthesizing recommendations),^{32,33} one from a literature review,²⁶ and one from an expert panel reviewing literature;³⁵ eight tools did not describe the development methodology in detail.^{18-20,24,25,27,28,34} Formally organized panels of experts developed six tools,^{21-23,32,33,35} and study authors (experts in the field) developed eight.^{18-20,24,26-28,34} The person(s) responsible for developing one of the tools was not described.²⁵ Four tools have been implemented and evaluated in prospective studies (see Supplementary Table S1 for further details).^{19,20,24,25} A reliability study has been conducted for one of the tools.³⁶

Tools used different approaches to identify frailty or limited life expectancy. Specific scales or indices used included life tables,¹⁸ Necesidades Paliativas (NECPAL) Centro Colaborador de la OMS para Programas Públicos de Cuidados Paliativos (NECPAL CCOMS-ICO),^{19,37} Clinical Frailty Scale,^{24,32,35,38} Mortality Score,^{24,39} PROFUND index,^{22,40}

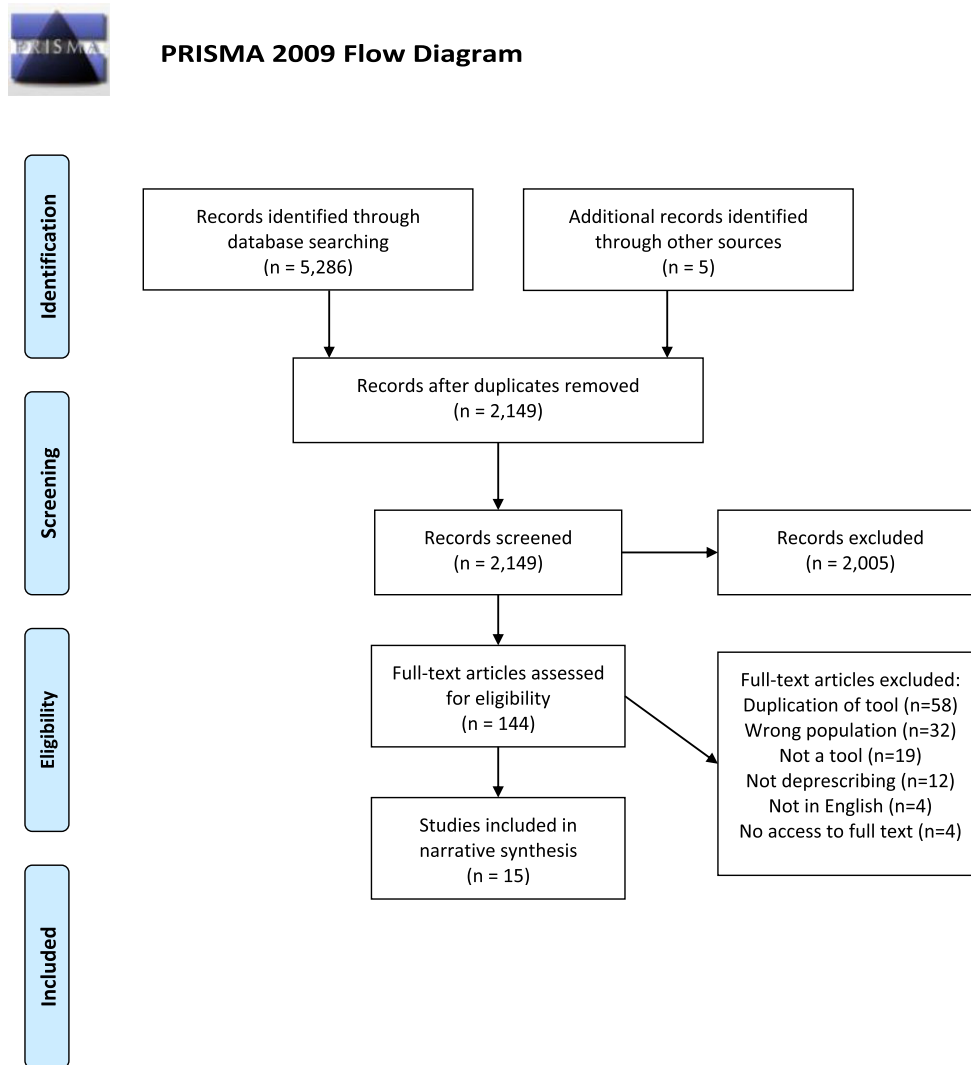


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Pfeiffer questionnaire,^{22,41} Barthel Index,^{22,42} and the Functional Assessment Stages (FAST) score.^{23,43} The STOPPFrail tool used the following criteria: end-stage irreversible pathology, aged 65 and older, poor 1-year survival prognosis, severe functional or cognitive impairment, and goal of symptom control versus prevention of disease progression.²¹ The Geriatric-Palliative algorithm did not use specific criteria, but was designed for use in nursing home patients.²⁰ Similarly, an algorithm used in another study did not provide specific criteria for frailty or limited life expectancy, but it was noted that this tool was intended for frail individuals.²⁶ One tool was designed for nursing home residents with a comfort-focused treatment plan.²⁵ The tools developed in two other papers did not mention specific criteria, but a core component of these tools was assessing life expectancy and functional limitations.^{27,28} The tools from Primary Health Tasmania did not describe measures to assess life expectancy or frailty.³⁴ The authors of the algorithm for deprescribing of cholinesterase inhibitors and memantine suggested that the tool could be used in individuals with advanced dementia characterized by dependence in most activities of daily living and inability to respond to their environment.³³ Finally, the algorithm for deprescribing of antihyperglycemics did not

endorse a specific measure for life expectancy or frailty but discussed use of the Clinical Frailty Scale, hypoglycemia unawareness, comorbidities, and functional limitations.³²

DISCUSSION

We have identified tools that specifically address deprescribing in frail older persons and those with limited life expectancy. This will allow clinicians to use the most applicable tools when considering deprescribing in this population. General deprescribing tools may be useful in frail older persons and those with limited life expectancy, but it is likely that the tools that we have identified are particularly useful because they incorporate additional considerations such as time to benefit and goals of care. As outlined in Figure 2, we could categorize tools based on where they would be used during the deprescribing process. We saw the deprescribing process as a continuum on which a clinician would first need high-level instruction on how to approach deprescribing (a deprescribing mindset), would then need to evaluate the entire medication list, and lastly would require guidance on how to deprescribe one or more specific medications.

Table 1. Eligible Studies

Tool	Population of Interest	Brief Description
Models or frameworks		
Holmes et al. ^{18 a}	Individuals with limited life expectancy (based on life tables), particularly older adults	Model to guide discontinuing medications in individuals with limited life expectancy
Molist Brunet et al. ^{19 a}	Individuals with limited life expectancy (based on NECPAL CCOMS-ICO), particularly older adults	Model for assessing pharmacotherapy, including considerations for discontinuing medications
Entire medication list		
Geriatric-Palliative algorithm ^{20 a}	Frail older persons (nursing home residents with incurable disease)	Algorithm aimed at identifying whether a drug can be deprescribed based on indication, safety, alternative therapies
Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) ^{21 a}	Frail older persons (e.g., end-stage irreversible pathology, poor 1-year survival prognosis, severe functional impairment, goal of symptom control)	List of criteria for specific medications and health conditions for which deprescribing can be considered; provides suggested monitoring parameters
List of Evidence-Based Deprescribing for Chronic Patients (LESS-CHRON) ^{22 a}	Older persons with multiple comorbidities, specifically frail older persons (criteria are medication specific)	List of medications and conditions for which deprescribing can be considered; provides monitoring and follow-up guidance
Holmes et al. ^{23 a}	Individuals with advanced dementia (Functional Assessment Stages score 6E, 7A, 7B, 7C)	List of medications to guide deprescribing; medications considered never appropriate, rarely appropriate, sometimes appropriate, always appropriate in advanced dementia
McKean et al. ^{24 a}	Older persons with polypharmacy, specifically frail individuals with limited life expectancy (based on CFS, mortality score)	Decision support tool based on 5-step deprescribing protocol
Pruskowski and Handler ^{25 a}	Individuals with limited life expectancy (with comfort-focused treatment plan), particularly older nursing home residents	List of medications to consider deprescribing
Frank and Weir ^{26 a}	Older persons, specific discussion of frail individuals and those with limited life expectancy (no specific criteria described)	Algorithm to guide deprescribing process for entire medication list
Scott et al. ^{27 a}		Ten-step framework to approach deprescribing process for entire medication list
Scott et al. ^{28 a}		Five-step approach and algorithm to guide deprescribing process for entire medication list
Medication specific		
Palliative and Therapeutic Harmonization Program (PATH) Clinic guidelines ^{29–31,35} https://pathclinic.ca/education/clinical-practice-guidelines/	Frail older persons (based on CFS)	Condition-specific guidelines (hypertension, cardiovascular disease, diabetes) providing advice and guidance for when medications can be deprescribed
Deprescribing antihyperglycemic agents ³² https://deprescribing.org/wp-content/uploads/2017/11/AHG-deprescribing-algorithms-2017-English.pdf	Older persons in general, but frail older persons and those with limited life expectancy discussed (e.g. based on CFS)	Criteria and guidance for deprescribing diabetes medications
Deprescribing cholinesterase inhibitors and memantine ³³ http://sydney.edu.au/medicine/cdpc/resources/deprescribing-algorithm.php	Older persons with dementia in general but those with limited life expectancy (advanced dementia, e.g., dependent on most activities of daily living) discussed	Criteria and guidance for deprescribing dementia medications
Guide to deprescribing ³⁴ https://www.primaryhealthtas.com.au/resources/deprescribing	Older persons in general but frail older persons and those with limited life expectancy discussed (no specific criteria described)	Multiple medication-specific guides (e.g., statins, bisphosphonates) providing deprescribing rationale, instructions

See Supplementary Table S1 for More Detail

^aTool only available in publication.

CFS = Clinical Frailty Scale; NECPAL CCOMS-ICO = Necesidades Paliativas Centro Colaborador de la OMS para Programas Públicos de Cuidados Paliativos.

Models or Frameworks

The first category of tools highlights a high-level model or framework for making medication decisions in older persons with limited life expectancy. These tools outline a way of thinking about or approaching medication use in the population of interest. For example, in one model,¹⁸ it is

proposed that medication use in individuals with limited life expectancy should take into consideration time to benefit of a medication, life expectancy, goals of care, and whether a medication is likely to achieve goals or targets. Similarly, another group¹⁹ outlined a multiple-step person-centered approach for making medication decisions in older persons

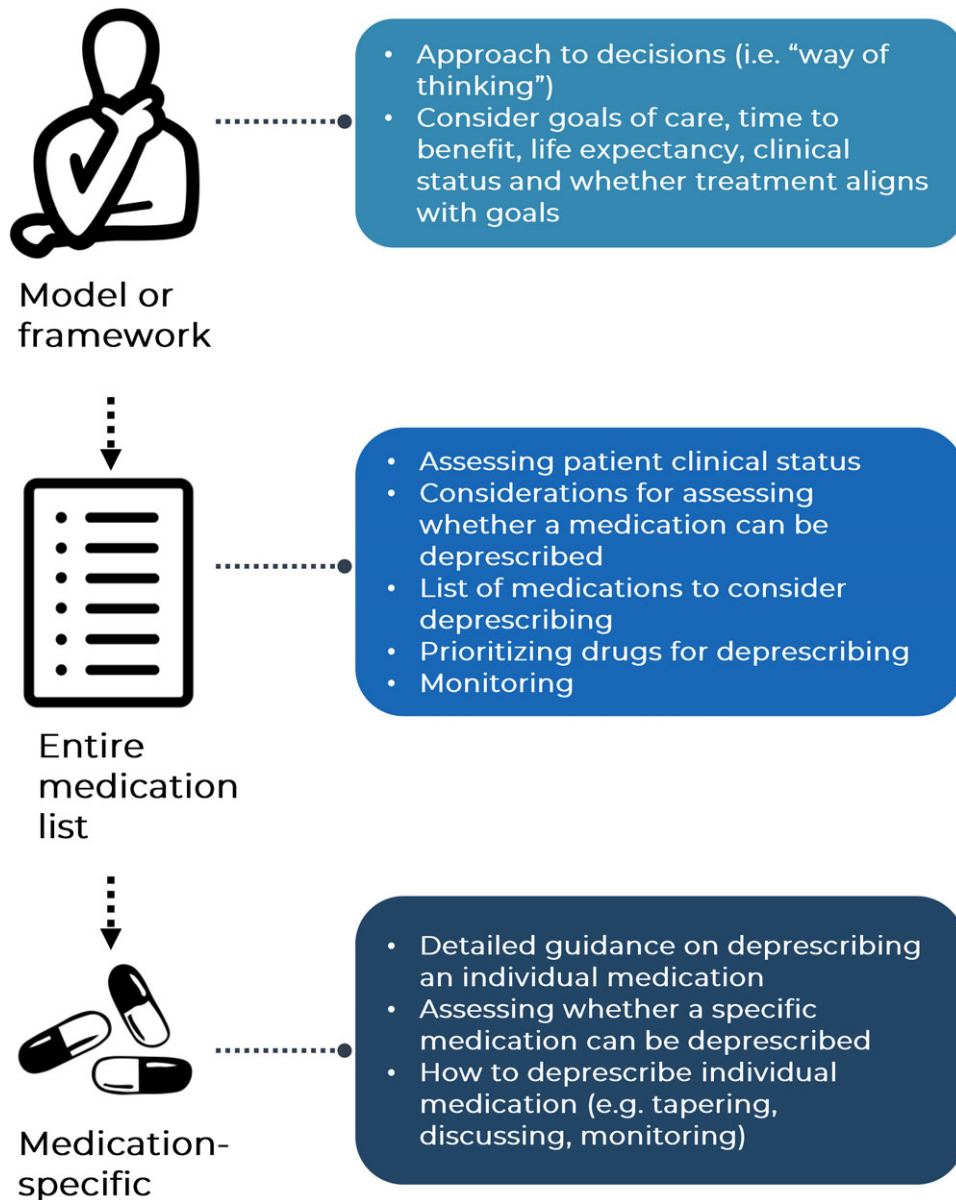


Figure 2. Categories of deprescribing tools. Thinking man icon by Takao Umehara, List icon by Nice and Serious, Pill icon by Sketch2SVG, all from thenounproject.com.

with limited life expectancy. This involved a comprehensive assessment of the individual’s clinical status, diagnosis-specific status, and medications, with goals of care and shared decision-making incorporated at every step.

Clinicians may require guidance on estimating life expectancy to aid medication decisions. Various methods have been proposed, although many are unvalidated and with unknown accuracy.⁴⁴ As such, these measures can be considered mainly as rough guides that may be helpful to inform approximate estimation of life expectancy. A detailed discussion of this topic is beyond the scope of this review, although we will highlight some methods that have been proposed. It has been suggested that life tables (which account for persons who may be more or less healthy than average, based on the presence of multiple co-morbidities and/or functional impairment, for example) can be used for insight into life expectancy.^{18,45} One study in our review

categorized persons as having limited life expectancy based on the NECPAL CCOMS-ICO tool.¹⁹ Mortality indices and online calculators have also been suggested as ways to estimate life expectancy in the context of medication decisions.^{45,46} Finally, the “surprise question” (Would you be surprised if this patient died in the next 12 months?) has been used to predict mortality in individuals with advanced illness, although its performance is poor in noncancer illness.^{47,48}

Approaching the Entire Medication List

The second category features tools that outline approaches to identify and prioritize drugs for deprescribing. These tools include general principles to use when evaluating the whole medication list. For example, weighing the benefits and harms of the medications, considering whether a

medication is likely to help an individual achieve goals of care, and considering burden of treatment. The tools in this level differ considerably in terms of comprehensiveness. Some of the tools provide a stepwise approach or algorithm with which to evaluate an individual's medication list. These tools provide general instructions or considerations at each step and provide some examples for specific medications.^{20,24,26-28} Other tools in this category provide a list of medications, with deprescribing considerations or criteria for each medication or medication class,^{21,22} for example, providing a drug class and identifying conditions under which deprescribing may be considered.²² Some of the tools also contain considerations for monitoring and follow-up, although they do not provide great detail.^{22,27,28} For example, one study discusses general principles such as educating patients on what to monitor for and tapering medications likely to cause adverse withdrawal effects.²⁸ Another study offers brief suggestions regarding follow-up after deprescribing for specific medication classes.²² Finally, some tools in this category are simply a list of medications that could be considered for deprescribing with no specific details or considerations.^{23,25} Tools that contain lists of medications may be useful in screening for potential candidates for deprescribing from an entire medication list. Once a potential medication is identified, a clinician could use the more detailed approaches from the step-wise tools or algorithms. Although more detailed tools^{22,27,28} provide useful advice for deprescribing, it may still be challenging to describe individual medications in practice. Clinicians may want detailed information on tapering, monitoring, or weighing benefits and harms for specific drugs. Thus, clinicians could also consult tools that provide detailed guidance on deprescribing of individual medications.

Medication-Specific Tools

Although the tools from the second category are useful in identifying which drugs can be deprescribed, the tools in this category have more detail on how to approach deprescribing for individual drugs. Some of the tools in the second category take into consideration the development of deprescribing plans, although the advice provided in those tools is general. The tools in the third category therefore build on the second category in giving detailed monitoring and tapering advice, as well as benefits and harms of specific medications. Tools in the third category also differ in terms of comprehensiveness and scope. Some focus primarily on weighing the benefits and harms of an individual medication (how to decide whether to continue or deprescribe that individual medication).³⁵ For example, the Palliative and Therapeutic Harmonization clinic guidelines primarily outline and analyze the clinical evidence (or lack thereof) and considerations for using various preventive medications in frail older persons.²⁹⁻³¹ Other tools provide guidance on both how to approach deprescribing decisions and how to deprescribe the medication.^{32,33} For example, the tools and guidelines from two papers^{32,33} outline specific details about frequency of monitoring and tapering rates for specific medications and medication classes. They also include detailed considerations for assessing whether an individual medication can be deprescribed (e.g., weighing benefits and harms of continued use, considering patient values and preferences regarding a

specific medication or class). Thus, they may be particularly helpful in providing targeted guidance for a specific medication or class.

Development Methods for the Tools

Eight tools provided little description of development and appeared to be based on the expert opinions of the authors. One study described a nonsystematic literature review used to inform tool development, but the approach for synthesizing the tool from the literature was not described.²⁶ Another group described use of an expert committee to develop recommendations based on available literature, although the methods for synthesizing recommendations was not provided.³⁵ Although evidence may inform some steps, considerations, and recommendations provided in these tools, this is not explicitly described. Therefore, it is difficult to gauge which areas are informed by evidence and which by expert opinion or clinical judgement. Although there is generally limited evidence on pharmacotherapy in frail older persons,^{8,49} it would be helpful to understand how steps or recommendations were arrived at (especially considering that expert opinion is acknowledged as the lowest level on the evidence-based medicine pyramid).⁵⁰

Three tools were developed using Delphi methodology.²¹⁻²³ In these tools, the methodology for arriving at recommendations is explicit and well described, although the recommendations in such tools were also based on expert opinion. Although some of the recommendations may be informed by evidence, it is difficult to evaluate the extent to which the criteria are evidence-based.

Finally, two tools were based on evidence from systematic reviews and an explicit approach for developing recommendations from evidence.^{32,33} These tools were developed using more rigorous methods, although given scant evidence on the topics some of the content was based primarily on expert opinion.

The fact that much of the content of the tools is based on expert opinion is not surprising given the paucity of evidence in this field, although the tools also varied considerably in how well the development methodology was described. This ranged from an explicit, well-described approach to no description of development methodology.

Implementation of Tools

Four tools have been tested in prospective studies.^{19,20,24,25} Three of the studies used an uncontrolled before-after design.^{19,24,25} They measured the number of changes made to medication regimens and the rate of discontinuation of medications after the intervention. One study tested the tool using a controlled before-after study.²⁰ This study measured the discontinuation rate in the intervention group and compared mortality and acute care referrals in the intervention group with those in the control group. This study was not randomized, and the developer was the only clinician implementing the tool. While these studies would be considered to be of very low-quality evidence because of their nonrandomized design and small sample sizes,⁵¹ they suggest that these tools may be useful in reducing the number of medications people are taking. However, they

provide little insight into the potential clinical effects of using the deprescribing tools. The algorithm section of one tool²⁸ was part of a medication review-based intervention tested in a randomized controlled trial.⁵² The deprescribing intervention led to a greater reduction in medication than in a control group, with no effect on mortality or quality of life.

The interreliability of the STOPPFrail tool was evaluated in general practitioners, geriatricians, and palliative care physicians.³⁶ There was good reliability between physicians and a criterion standard assessment (mean kappa 0.76 ± 0.06) and no differences between specialists.

Eleven of the tools developed have not been tested in clinical practice. Therefore, it is unclear whether using these tools is likely to result in a meaningful reduction in inappropriate medication use and improve outcomes, or even cause harm.⁵³ A previous review also noted this limitation.¹⁶ Lack of clinical outcome data and inconsistency in outcome measurement have also been highlighted as limitations in deprescribing studies.^{54,55} A 2018 systematic review evaluating deprescribing interventions in older persons found that few studies measured clinical outcomes and that none were adequately powered to detect differences in clinical outcomes between intervention and control groups.⁵⁶ A number of deprescribing tools have been developed in recent years, but they remain largely untested.¹⁶ Researchers and clinicians should focus on developing quality tools using systematic and explicit methods. Such tools should be tested in well-designed clinical trials that are powered to measure meaningful clinical outcomes (e.g., quality of life, mortality, patient function).⁵⁴ Trials should clearly describe their implementation approach to allow for reproducibility of the intervention.

Tools in Clinical Practice

Lack of resources and time as well as poor self-efficacy have been cited as barriers to deprescribing in practice.¹³ Although deprescribing is often time consuming by nature, tools may improve self-efficacy.⁵⁷

Clinicians may be interested in which tools are most useful clinically. There is limited evidence to guide this choice, although useful tools would be those developed using rigorous methods and those that have been tested in clinical practice. One tool is likely to be useful as an overall resource to guide deprescribing.²⁴ It contains a detailed section dedicated to patient assessment and includes a step-wise approach and algorithm, but it does not contain specific advice on tapering or monitoring. Part of that tool was based on a five-step framework.²⁸ The List of Evidence-Based Deprescribing for Chronic Patients (LESS-CHRON) criteria²² and STOPPFrail²¹ tools, along with the criteria from another study,²³ would be helpful in assessing whether medications are candidates for deprescribing. Finally, the algorithms for deprescribing antihyperglycemics and cholinesterase inhibitors are likely to be useful for guidance on those individual medication classes.^{32,33} A challenge for some tools is that they are available only in published manuscripts, and may therefore not be easily accessible to all (Table 1).

Strengths and Limitations

We used a systematic search to identify tools, with two authors screening and all authors approving final study selection. The systematic, up-to-date search allowed us to identify tools not summarized in previous reviews, and thus there was little overlap.^{15,16} By focusing our review on tools applicable to frail older persons and individuals with limited life expectancy, we provide insight into the tools most applicable to this population. Our search was limited by excluding non-English language reports. We were unable to access four full-text articles (two of these records were likely duplicates).⁵⁸⁻⁶⁰

CONCLUSION

We identified 15 tools that could be used during the deprescribing process in frail older persons and individuals with limited life expectancy. It is likely that individual tools are useful to clinicians at different stages of deprescribing. Tools could be used as models or frameworks for pharmacotherapy in persons with limited life expectancy (a way of thinking), to approach the entire medication list (a global approach), and to guide deprescribing of a specific medication or medication class (medication-specific guidance). Much of the content of the tools was based on expert opinion or clinical experience. Development methodology was poorly described for most tools. Finally, only four of 15 tools have been tested in clinical practice (and these were considered to be very low-quality studies). It is unclear whether existing tools are likely to improve the quality of prescribing and improve clinical outcomes or even cause harm. Future work should focus on developing tools according to explicit and rigorous methods and testing developed tools in well-designed clinical trials that measure clinically important outcomes.

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Author Contributions: AP, JR, JS, and DSN conceived the study. All authors designed the study. TG, CL, and WT completed the screening process with input from AP, JR, JS, and DSN. WT extracted data, and all authors provided input on synthesis and analysis. WT drafted the manuscript. All authors provided critical feedback and revisions on the manuscript. All authors approved the final version for submission.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Supplementary Appendix S1. Search strategy.

Supplementary Table S1. Detailed characteristics of eligible studies.