

# Recommendations for Outcome Measurement for Deprescribing Intervention Studies

## Supplemental Material

### Supplementary File S1: Library search strategies and literature search schematic

We initially identified articles published from 2005 to 2020; subsequently refining the publication time frame to 2011-2020 as more relevant to contemporary deprescribing research. Abstracts were obtained from PubMed and Ovid indices using the terms and strategy described below.

#### 1. MeSH terms search strategy in PubMed:

((("Polypharmacy"[Mesh] AND Clinical Trial[ptyp] AND English[lang] AND "adult"[MeSH Terms]) OR (((("Observational Studies as Topic"[Mesh] OR "Interrupted Time Series Analysis"[Mesh]) OR "Evaluation Studies as Topic"[Mesh]) AND "Polypharmacy"[Mesh]) AND English[lang] AND "adult"[MeSH Terms])) AND English[lang] AND "adult"[MeSH Terms]) OR (((("Observational Studies as Topic"[Mesh] OR "Interrupted Time Series Analysis"[Mesh]) OR "Evaluation Studies as Topic"[Mesh]) AND "Polypharmacy"[Mesh]) AND English[lang] AND "adult"[MeSH Terms]) AND (("Inappropriate Prescribing"[Mesh] OR "Potentially Inappropriate Medication List"[Mesh]) AND English[lang] AND "adult"[MeSH Terms])) AND English[lang] AND "adult"[MeSH Terms]) OR (("Inappropriate Prescribing"[Mesh] OR "Potentially Inappropriate Medication List"[Mesh]) AND Clinical Trial[ptyp] AND English[lang] AND "adult"[MeSH Terms]) AND (English[lang] AND "adult"[MeSH Terms])

#### 2. Textword search strategy in OVID:

1. (deprescribe\* or medication cessation or medication discontin\* or inappropriate prescrib\* or inappropriate medication\* or unnecessary prescription\* or polypharm\* or medication overload).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

2. (clinical trial or RCT).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3. (intervention\* or observation\* or cohort).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4. 2 or 3

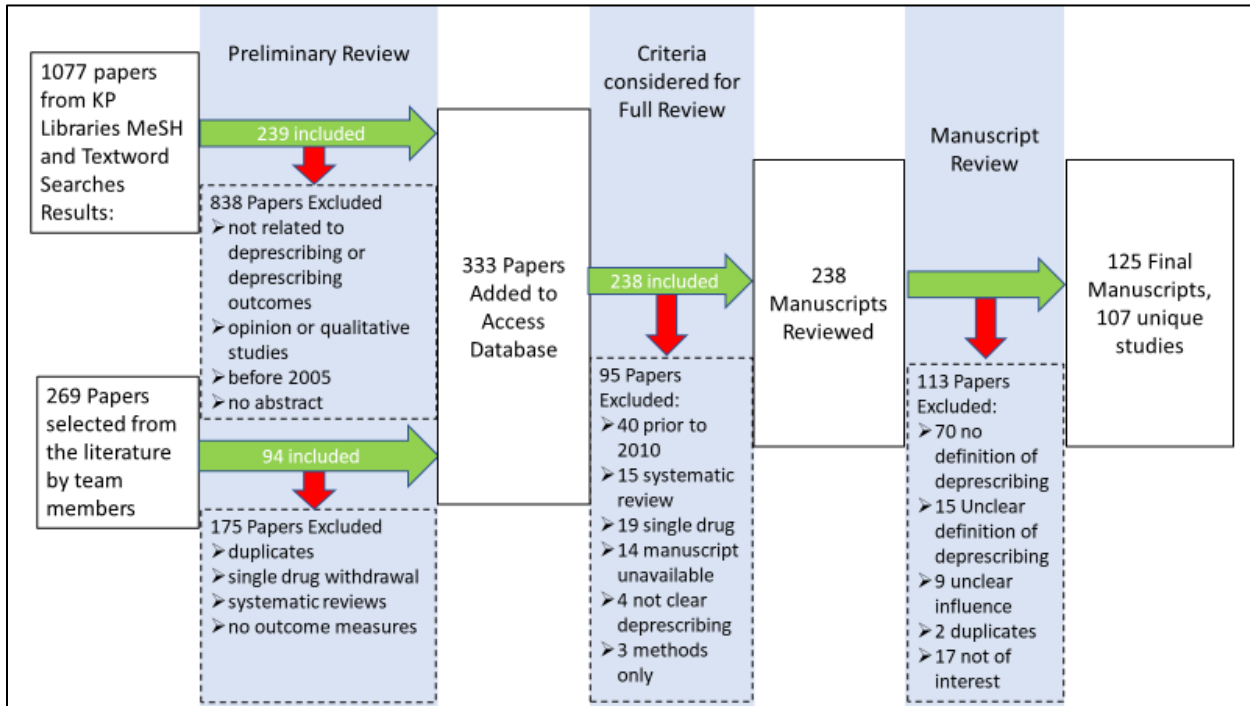
5. 1 and 4

6. (Outcome or measure).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

7. 5 and 6

8. limit 7 to English language

## Supplementary Figure S1. Literature search schematic



**Figure 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: Survey instrument for expert panel

For each of the outcome domains for deprescribing interventions listed in the table, please answer the questions below the table.

### Outcome Domains for Deprescribing Interventions

Measure category	Examples
Adverse drug event	Fall, drug-drug interaction
Adverse drug withdrawal event	Physiologic withdrawal, recurrent symptoms
Functional status	Physical function, cognitive function
Deprescribing implementation	Acceptability to patient, adoption by staff
Medication use	Quantity, appropriateness, dose change
Mortality	All cause, disease specific
Patient-reported outcomes	Patient experience, quality of life
Utilization	Readmissions, cost of care

1) How important is this measurement category as an outcome for deprescribing interventions?

2) Which of the following approaches should the workgroup consider?

- **Mature:** This measure category is well established and needs little further development therefore the workgroup should not spend time on it. (Examples might include hospitalization or length of stay.)
- **Needs standardization:** This measure category could benefit from recommendations for standard definitions or associated data sources and it should be a focus of the workgroup. (Examples might include number of chronic medications.)
- **Needs development:** This measure category is not well defined and development should be part of a research agenda articulated by the workgroup. (Examples might include adverse drug withdrawal events.)
- **Out of scope:** This measure category is beyond the scope of the workgroup for any reason.

3) Why do you consider the category to be important for deprescribing studies?

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

Domain	Example categories	Importance	Approach	Example comments
Adverse Drug Event (ADE)	Any ADE	Very important	Needs standardization; beyond scope of current group	<p>It seems like [reducing ADE] might be the primary benefit of deprescribing.</p> <p>It would be good for us to learn how to measure better.</p> <p>Evidence is needed that shows deprescribing reduces the number of ADEs.</p> <p>No measures of ADEs are perfect but it will be hard for this group to do better, as plenty of other people have tried...</p>
	Fall/Fracture			
Adverse Drug Withdrawal Event	Physiological Effects	Very important	Needs standardization	<p>I think this is a category that people often use as an argument against deprescribing. It will be important to measure how often people suffer immediate symptoms because of stopping a medication.</p> <p>Important to consider the potential adverse impact of deprescribing.</p> <p>ADWE are poorly defined and difficult to identify in electronic data.</p> <p>ADWEs are really important; not a whole lot of literature on the topic but I think a high priority.</p>
	Recurrent Symptoms			
Functional Status	Cognitive	Very important	Needs standardization	<p>Many meds are taken to improve quality of life at a cost of function and cognition.</p> <p>Cognition measurement needs to be standardized.</p> <p>Cognitive status is important to readily detect improvements with stopping medications.</p> <p>We have observed associations of reduced functional status with the use of certain medication classes but need to determine if this can be reversed with deprescribing.</p>
	Physical			

Implementation	Acceptability to Patient	Very important	Needs development	<p>Understanding how an implementation works in one setting is vital to the successful scale and spread of evidence-based interventions.</p> <p>To be effective and change practice, an implementation has to be feasible and acceptable to patients, clinicians, systems and payers.</p> <p>It would be a useful contribution to have a 'tool kit' list of implementation measures specific to deprescribing interventions</p> <p>Ultimately, describing things doesn't make a difference in the real world without successful implementation.</p>
	Acceptability to Physician			
	Adoption/Uptake by Users			
	Clinician Experience with Intervention			
	Feasibility			
	Patient Experience with Intervention			
Medication Use	Adherence	Moderately important	Needs standardization	<p>I consider most important the measures that intuitively seem likely to be tightly linked to deprescribing, that is, very likely to change if an intervention succeeds...We can't expect to see clinical outcomes improve if we don't see these kinds of process outcomes improve.</p> <p>Medication use is a more proximal outcome. Without changes in medication measures it would be impossible to relate these to more distal and patient-centered outcomes including functional status.</p> <p>Very common primary outcome. Would be helpful to have definitions of 'chronic med.'</p> <p>Treatment burden is most important.</p>
	Appropriateness			
	Burden			
	Quantity-Chronic Meds			
	Dose changes			
	Substitutions			
New prescriptions				
Mortality	All Cause	Moderately important	Mature, well established	<p>Mortality important but already well defined.</p> <p>Mortality is important to monitor but not as a primary outcome.</p> <p>Disease specific mortality is more valuable, especially in situations where meds are tightly linked to the outcome.</p> <p>Mortality is extremely important, however, outside of large interventions, we are unlikely to obtain statistical significance.</p>
	Disease Specific			

Patient-Centered Outcomes	Attitude-Patient	Very important	Needs standardization	<p>Quality of life is the most important measure in this domain.</p> <p>Quality of life is the primary reason for deprescribing and might drive buy-in.</p> <p>Attitudes and knowledge are very important are to the extent to which they are focused on deprescribing, could be worthwhile to explore... other outcomes such as symptoms, satisfaction are also important.</p>
	Attitude-Provider			
	Knowledge			
	Quality of Life			
	Satisfaction			
Utilization	Ambulatory	Moderately important	Mature, well established	<p>A stronger argument would be made for prescribing interventions if there were offsets in health care utilization/cost measures.</p> <p>The link between deprescribing and overall costs may be quite weak because so many other factors cause high costs.</p> <p>Medication costs are important but there are too many factors affecting the other outcomes in this category to expect deprescribing to have a significant impact.</p>
	Cost			
	ED/ER			
	Hospitalization			
	Length of Stay			
	Readmissions			
	SNF/NH			

**Supplementary Table S2. Studies identified in literature review targeting polypharmacy**

<b>First Author (Year)</b>	<b>Study design</b>	<b>Setting</b>	<b>Intervention</b>	<b>N</b>	<b>Follow-up</b>	<b>Outcomes</b>
Abdelaziz et al. (2019) <sup>1</sup>	Observational	Amb	Medication reconciliation	78	6 months	Adherence; Adverse Drug Withdrawal; Recurrent Symptoms
Alosaimy et al. (2019) <sup>2</sup>	Observational	Hosp	Pharmacist review	82	Hosp Discharge	Number of Chronic Medications; Appropriateness (# of PIMs)
Altiner et al. (2012) <sup>3</sup>	Cluster RCT	Amb	Physician education	362	24 months	Number of Chronic Medications; Quality of Life
Alves et al. (2019) <sup>4</sup>	Observational	SNF	Pharmacist quality review	10405	>24 months	Number of Chronic Medications; Feasibility; Costs
Ammerman et al. (2019) <sup>5</sup>	Observational	Amb	Interdisciplinary team with pharmacist	568	Not Stated	Number of Chronic Medications; Dose Reductions; Appropriateness (PIMs discontinuations)
Anderson et al. (2020) <sup>6</sup>	Observational	Amb	Multicomponent care model	153	6 months	Number of Chronic Medications; Discontinuations; Dose Reductions; Appropriateness; Adverse Drug Withdrawal: Physiological Change; Adverse Drug Withdrawal: Recurrent Symptoms; Implementation-Adoption; Feasibility; Patient's Attitude; Quality of Life; Hospital Utilization
Andrew et al. (2018) <sup>7</sup>	Observational	SNF	Multicomponent care model	529	6 months	Number of Chronic Medications; Appropriateness (PIMs rates); Burden
Anrys et al. (2016) <sup>8</sup>	Cluster RCT	SNF	Multicomponent care model	2205	24 months	Number of Chronic Medications; Appropriateness (proportion of PIMS reduction, new PIM prescription); Implementation; Costs



Basger et al. (2015) <sup>9</sup>	RCT/Experimental	Hosp	Discharge medication counselling and pharmacist recommendations to PCP	183	6 months	Appropriateness; Drug Related Problems; Implementation-Adoption; Quality of Life
Bayliss et al. (2020) <sup>10</sup>	Cluster RCT	Amb	Patient/family and provider education	3012	6 months	Number of chronic medications, appropriateness, physical and cognitive function, falls
Bryant et al. (2011) <sup>11</sup>	RCT/Experimental	Amb	Community pharmacist review and recommendations to PCP	498	12 months	Substitutions; Appropriateness (MAI Index); Other Implementation Outcome; Quality of Life
Campins et al. (2016) <sup>12</sup>	RCT/Experimental	Amb	pharmacist review (algorithm)	503	12 months	Number of Chronic Medications; Substitutions; Treatment Restart Ratio; Adherence; Implementation-Adoption; All Causes of Death; Emergency Room; Hospital Utilization; Quality of Life;
Cardwell et al. (2020) <sup>13</sup>	Observational	Amb	pharmacist medication reviews	786	12 months	Substitutions; Practice-Level medication changes Appropriateness (pharmacist recommendations); Patient's Attitude; Quality of Life; Costs; Other Utilization Outcome
Chen et al. (2016) <sup>14</sup>	Observational	Amb	pharmacist decision support tool	152	6 months	Adherence (self-reported); Patient's Attitude; Patient Knowledge
Clyne et al. (2013), Clyne et al. (2015), Clyne et al. (2016) <sup>15-17</sup>	Pragmatic cluster randomized trial	Amb	Pharmacist medication review, PCP education, patient education	220	6 months	Number of Chronic Medications; Appropriateness (proportion with PIMs, mean # of PIMs per patient); Burden; Drug-specific Outcomes; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Other Adverse Drug Effects; Implementation-Acceptability; Implementation-Adoption; Feasibility;

						Physician Experience; Patient Experience; Other Implementation Outcome; Patient's Attitude; Physician's Attitude; Quality of Life; Ambulatory; Costs; Hospital Utilization; Hospital Length-of-Stay; SNF Utilization
Cool et al. (2018) <sup>18</sup>	RCT/Experimental	SNF	Clinician education	629	24 months	Appropriateness (proportion with PIMs)
Corbi et al. (2015) <sup>19</sup>	Observational	SNF	Clinician education	790	12 months	Appropriateness (# of PIMs per patient); SNF Rehab Length-of-Stay
Coronado-Vazquez et al. (2019) <sup>20</sup>	Observational	Amb	Decision support tool	137	12 months	Substitutions; Discontinuations; Appropriateness (proportion with PIMs change)
Cossette et al. (2017) <sup>21</sup>	Observational	Hosp	Decision support process	231	12 months	Discontinuations; Dose Reductions; Appropriateness (PIMs discontinuations)
Curtin et al. (2020) <sup>22</sup>	RCT/Experimental	Hosp/SNF	Research physician record review and recommendation	130	6 months	Number of Chronic Medications; Discontinuations; Appropriateness; Changes in Specific Medications; Adverse Drug Related Cognitive Change; Fall/Fractures due to Adverse Drug Effects; All Causes of Death; Quality of Life; Costs; Hospital Utilization
Dalleur et al. (2014) <sup>23</sup>	RCT/Experimental	Amb/Hosp	Geriatric consult team medication review	146	12 months	Appropriateness (Reduction in PIMs)
Dalton et al. (2019) <sup>24</sup>	RCT/Experimental	Hosp	Physician vs. pharmacist recommendations	1440	Hosp Discharge	Adverse Drug Reactions; Implementation-Adoption
Dauphinot et al. (2017) <sup>25</sup>	RCT/Experimental	Amb	Pharmacist and geriatric medication review	302	24 months	Appropriateness; Drug-Related Problems; Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Pain and

						Mood changes; ADL and IADL Scales; Quality of Life; Emergency Room; Hospital Utilization
Edey et al. (2018) <sup>26</sup>	RCT/Experimental	Hosp	Pharmacist review and recommendation	358	Hosp Discharge	Discontinuations (proportion discontinued); Emergency Room; Hospital Utilization; Readmission
Fog et al. (2017) <sup>27</sup>	Observational	SNF	Multidisciplinary team med review	2465	>24 months	Number of Chronic Medications; Substitutions; Dose Reductions; Drug-Related Problems; Other Implementation Outcome
Frankenthal et al. (2014) <sup>28</sup>	RCT/Experimental	SNF	Pharmacist review and recommendation	359	12 months	Fall/Fractures due to Adverse Drug Effects; Physical Function; Quality of Life; Costs; Hospital Utilization
Fried et al. (2017) <sup>29</sup>	RCT/Experimental	Amb	Decision support tool with feedback	128	6 months	Number of Chronic Medications; Substitutions; Other Patient-Centered Outcome; Shared decision-making
Gallagher et al. (2011) <sup>30</sup>	RCT/Experimental	Hosp	Medication review	400	6 months	Appropriateness; Implementation-Acceptability
García-Gollarte et al. (2014) <sup>31</sup>	RCT/Experimental	SNF	Physician education	716	6 months	Number of Chronic Medications; Appropriateness (# of PIMs); Fall/Fractures due to Adverse Drug Effects; Ambulatory; Emergency Room; Hospital Utilization; Hospital Length-of-Stay; SNF Utilization
Geurts et al. (2016) <sup>32</sup>	RCT/Experimental	Amb	Pharmacist review and care plan	512	12 months	Drug-Related Problems
Gibert et al. (2018) <sup>33</sup>	Observational	Amb	Physician education	172	6 months	Number of Chronic Medications; Appropriateness (# of PIMs)
Gillespie et al. (2013) <sup>34</sup>	RCT/Experimental	Amb/Assist	Pharmacist review and recommendation	368	Hosp Discharge	Appropriateness; Drug-Related Problems; Emergency Room; Hospital Utilization; Readmission
Gillespie et al. (2017) <sup>35</sup>	RCT/Experimental	Amb	Pharmacist medication review, PCP education, patient education	220	12 months	Costs

Greiver et al. (2019) <sup>36</sup>	Pragmatic Cluster RCT	Amb	Multi component QI approach	NA	12 months	Appropriateness (# of PIMs); Implementation; Physician Experience; Patient Experience; Quality of Life
Grischott et al. (2018) <sup>37</sup>	RCT/Experimental	Hosp	Clinician education and medication review	2100	6 months	Number of Chronic Medications; Appropriateness (proportion of PIMs); Implementation-Adoption; Quality of Life; Ambulatory; Emergency Room; Readmission
Hannou et al. (2017) <sup>38</sup>	Observational	Hosp	Clinical pharmacist on team	102	12 months	Implementation-Acceptability
Hasler et al. (2015) <sup>39</sup>	RCT/Experimental	Amb	Decision tool and clinician education	429	12 months	Number of Chronic Medications; Time and Reason for change in medications; Substitutions; New prescriptions; Adverse Drug Withdrawl Effects; Implementation-Adoption; Quality of Life; Shared decision-making
Jager et al. (2017), Jager et al. (2017) <sup>40, 41</sup>	Cluster RCT	Amb	Clinician and patient education; implementation action plan	273	12 months	Implementation-Program Adoption; Patient Knowledge
Johansen et al. (2018) <sup>42</sup>	RCT/Experimental	Hosp	Medication reconciliation, patient education, discharge follow up	500	12 months	Substitutions; Appropriateness; Fall/Fractures due to Adverse Drug Effects; Cardiovascular events; All Causes of Death; Quality of Life; Emergency Room; Hospital Length-of-Stay; Readmission
Komagamine et al. (2018) <sup>43</sup>	RCT/Experimental	Hosp	pharmacist review and recommendation, patient education	220	12 months	Appropriateness; Fall/Fractures due to Adverse Drug Effects; Adverse Drug Withdrawal: Recurrent Symptoms; All Causes of Death; Patient Knowledge; Emergency Room; Readmission

Kua et al. (2017), Kua et al. (2020) <sup>44, 45</sup>	Cluster RCT	SNF	multidisciplinary team med review	288	12 months	Number of Chronic Medications; Discontinuations; Appropriateness; Burden; Drug-Related Problems; Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Implementation-Acceptability; Implementation-Adoption; Feasibility; Other Implementation Outcome; Costs; All Causes of Death; Physician's Attitude; Hospital Utilization
Lenander et al. (2014) <sup>46</sup>	RCT/Experimental	Amb	pharmacist medication review	209	12 months	Number of Chronic Medications; Drug-Related Problems; Patient Knowledge; Quality of Life; Other Utilization Outcome
Lin et al. (2018) <sup>47</sup>	RCT/Experimental	Amb	pharmacist-physician medication management program	178	24 months	Costs
Löffler et al. (2014) <sup>48</sup>	Cluster RCT	Hosp	pharmacist medication review	1626	12 months	Number of Chronic Medications; Appropriateness; Fall/Fractures due to Adverse Drug Effects; All Causes of Death; Quality of Life; Patient Satisfaction; Readmission
Malet-Larrea et al. (2016) <sup>49</sup>	Cluster RCT	Amb	Community pharmacist review	1403	6 months	Costs; Hospital Utilization
Martin et al. (2015), Martin et al. (2018) <sup>50, 51</sup>	Cluster RCT	Amb	Community pharmacist review and recommendation to pcip	450	12 months	Other Specific Drug Outcome; Discontinuations (rate); Appropriateness (rate of PIMs discontinued); Implementation-Acceptability; Implementation-Adoption; Quality of Life

McCarthy et al. (2017) <sup>52</sup>	Cluster RCT	Amb	Decision support tool; PCP medication review; patient goals of care	450	6 months	Number of Chronic Medications; Substitutions; Appropriateness; Burden; Adverse Drug Withdrawal: Physiological Change; Adverse Drug Withdrawal: Recurrent Symptoms; Patient's Attitude; Quality of Life
McDonald et al. (2019) <sup>53</sup>	Observational	Hosp	Computerized clinical decision support tool	1066	1 month	Discontinuations; Appropriateness (proportion with PIM described); Adverse Drug Reactions
Milos et al. (2013) <sup>54</sup>	RCT/Experimental	Amb/SNF	pharmacist medication review	369	6 months	Appropriateness (proportion with PIMs); Dose Changes; Proportion with 10+ medications; Drug-Related Problems
Muth et al. (2016) <sup>55</sup>	Cluster RCT	Amb	Assistant conducted checklist interview; GP used computerized decision support	100	6 months	Adherence; Appropriateness (MAI); Physical Function; Feasibility; Quality of Life
Muth et al. (2018) <sup>56</sup>	Cluster RCT	Amb	Assistant conducted checklist interview; GP used computerized decision support	505	12 months	Adherence; Appropriateness (MAI); Physical Function; Quality of Life
Nachtigall et al. (2019) <sup>57</sup>	RCT/Experimental	Hosp	Prioritized pharmacist recommendation on admission	411	Hosp Discharge	Number of Chronic Medications; Appropriateness (MAI); Drug-Related Problems; Other Adverse Drug Withdrawal Effects; Implementation-Adoption; All Causes of Death
O'Connor et al. (2016) <sup>58</sup>	RCT/Experimental	Hosp	Researcher medication review and recommendation	732	24 months	Adverse Drug Reactions; Costs; Hospital Length-of-Stay
O'Donnell et al. (2020) <sup>59</sup>	Cluster RCT	Amb	Computerized clinical decision support tool	500	6 months	Discontinuations; Dose Reductions; Adherence; Burden (Drug Burden Index); Fall/Fractures due to Adverse Drug Effects; Cognitive Function;

						Physical Function; Other Implementation Outcome; All Causes of Death; Hospital Utilization
O'Sullivan et al. (2016) <sup>60</sup>	RCT/Experimental	Hosp	Computerized clinical decision support tool	737	Hosp Discharge	Adverse Drug Reactions; All Causes of Death; Hospital Length-of-Stay
Vasilevskis et al. (2019), <sup>61</sup> Petersen et al. (2018) <sup>62</sup>	RCT/Experimental	Hosp/SNF	Multidisciplinary team, patient-centered med review and recommendation with follow-up	576	6 months	Quantity; Discontinuations; Dose Reductions; Adherence; Appropriateness; Burden; Adverse Drug Reactions; Cognitive Function; Physical Function; Feasibility; Patient's Attitude; Emergency Room; Hospital Utilization
Piau et al. (2017) <sup>63</sup>	Observational	Hosp	physician med review on admission	216	6 months	Number of Chronic Medications; Discontinuations; Substitutions
Pitkälä et al. (2014), <sup>64</sup> Juola et al. (2015) <sup>65</sup>	Cluster RCT	SNF	Educate nursing staff	227	12 months	Appropriateness (# of PIMs); Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Physical Function; Quality of Life; Hospital Length-of-Stay
Potter et al. (2016) <sup>66</sup>	RCT/Experimental	Assist	Researcher medication review and recommendation	95	12 months	Number of Chronic Medications; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Physical Function; All Causes of Death; Quality of Life; Utilization
Potter et al. (2019) <sup>67</sup>	Observational	Hosp	pharmacist med review and recommendations	129	6 months	Discontinuations
Prados-Torres et al. (2017) <sup>68</sup>	Cluster RCT	Amb	Physician training plus physician-patient interview	286	12 months	Quantity; Adherence; Appropriateness (MAI score); Quality of Life; Other Patient-Centered Outcome; Other Utilization Outcome
Quintana-Barcena et al. (2018) <sup>69</sup>	Cluster RCT	Amb	Computerized clinical decision support tool and	1732	12 months	Drug-Related Problems Adverse Drug Reactions

			pharmacist to patient support			
Riecker et al. (2020), <sup>70</sup> Sonnichsen et al. (2016) <sup>71</sup>	Cluster RCT	Amb	computerized decision support tool	3904	24 months	Number of Chronic Medications; Discontinuations; Number and Type of recommendations; Adverse Drug Reactions--Recurrent Symptoms; Fall/Fractures due to Adverse Drug Effects; All Causes of Death; Quality of Life; Hospital Utilization
Rognstad et al. (2013), Rognstad et al. (2018) <sup>72, 73</sup>	Cluster RCT	Amb	Clinician education	80000	12 months	Appropriateness (# of new and ongoing PIMs); characteristics of GPs with prescribing changes
Romskaug et al. (2017), Romskaug et al. (2020) <sup>74, 75</sup>	Cluster RCT	Amb	Geriatric consult and PCP recommendations	200	6 months	Substitutions; Discontinuations; Dose Reductions; Appropriateness (MAI); Burden; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Physical Function; All Causes of Death; Quality of Life; Hospital Utilization; SNF Utilization
Rose et al. (2015) <sup>76</sup>	Cluster RCT	Amb	pharmacist medication review and recommendation plus case management	165	24 months	Adherence; Appropriateness (MAI); Burden; Drug-Related Problems; Physical Function; Quality of Life; Costs
Roth et al. (2013) <sup>77</sup>	Observational	Amb	pharmacist medication review and recommendation	64	6 months	Drug-Related Problems; Implementation-Acceptability; Emergency Room; Hospital Utilization
Schafer et al. (2018) <sup>78</sup>	Cluster RCT	Amb	Clinician education plus goal oriented patient consultations	604	12 months	Discontinuations; Quality of Life



Schmidt-Mende et al. (2017) <sup>79</sup>	Cluster RCT	Amb	Clinician education	119910	12 months	Appropriateness (# of PIMs); Implementation-Adoption; Emergency Room; Hospital Utilization
Simoes et al. (2018) <sup>80</sup>	Cluster RCT	Amb	PCP education to do patient-centered medication discontinuation	564	6 months	Other Implementation Outcome; Patient's Attitude; Patient Knowledge; Quality of Life
Sluggett et al. (2018) <sup>81</sup>	Cluster RCT	SNF		194	>24 months	Number of Chronic Medications; Burden; Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Patient Experience; All Causes of Death; Quality of Life; Patient Satisfaction; Hospital Utilization
Soerensen et al. (2018) <sup>82</sup>	RCT/Experimental	Hosp	nurse vs. physician review of medications	396	12 months	Appropriateness (# of PIMs); Implementation-Adoption
Steinman et al. (2018) <sup>83</sup>	Observational	Amb	longitudinal nurse intervention based on Guided Dare	1218	12 months	Substitutions; Discontinuations; Dose Reductions; Other Patient-Centered Outcome; Hospital Utilization
Twigg et al. (2015) <sup>84</sup>	Observational	Amb	Community pharmacist consultation	441	6 months	Adherence; Appropriateness (# of PIM-related recommendations); Drug-Related Problems; Fall/Fractures due to Adverse Drug Effects; Hospital Utilization
Urfer et al. (2016) <sup>85</sup>	RCT/Experimental	Hosp	clinical decision support tool	900	Hosp Discharge	Quantity; Appropriateness (proportion with PIMs)
van der Linden et al. (2017) <sup>86</sup>	Observational	Hosp	Pharmacist medication review	172	3 months	Discontinuations; Dose Reductions; Appropriateness (Proportion with PIMs discontinued); Quality of Life; Emergency Room
van der Linden et al. (2018) <sup>87</sup>	RCT/Experimental	Hosp	Pharmacist medication review	59	Hosp Discharge	Quantity; Appropriateness; Implementation-Acceptability; Other Implementation Outcome

van der Meer et al. (2015), van der Meer et al. (2018) <sup>88, 89</sup>	RCT/Experimental	Amb	pharmacist medication review and recommendation to pcp	160	6 months	Number of Chronic Medications; Burden (proportion with reduced Drug Burden Index); Drug-Related Problems; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Physical Function; All Causes of Death; Quality of Life; Hospital Utilization
van Summeren et al. (2017) <sup>90</sup>	Observational	Amb	Medication review guided by goals of care	59	12 months	Number of Chronic Medications; Discontinuations; Substitutions
Verdoorn et al. (2019) <sup>91</sup>	RCT/Experimental	Amb	Pharmacist medication review guided by goals of care	629	6 months	Quality of Life
Willeboordse et al. (2017) <sup>92</sup>	Cluster RCT	Amb	multidisciplinary medication review and recommendation	518	6 months	Quality of Life
Wouters et al. (2014), Wouters et al. (2017) <sup>93, 94</sup>	Cluster RCT	SNF	multidisciplinary medication review and recommendation	426	6 months	Discontinuations; Dose Reductions; Appropriateness (PIMs proportion and changes); Other Specific Drug Outcome; Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Quality of Life; Ambulatory; Costs; Emergency Room; Hospital Utilization
Wuyts et al. (2018) <sup>95</sup>	Observational	Amb	Pharmacist medication review	900	12 months	Adherence; Burden; Drug-Related Problems (# and type); Adverse Drug Reactions; Fall/Fractures due to Adverse Drug Effects; Quality of Life; Patient Satisfaction; Emergency Room
Young et al. (2016) <sup>96</sup>	RCT/Experimental	Amb	computerized decision support tool	367	6 months	Substitutions; Adherence; All Causes of Death; Quality of Life; Emergency Room; Hospital Utilization

Zechman et al. (2020) <sup>97</sup>	Cluster RCT	Amb	clinician education, shared decision making support tool	334	12 months	Quantity; Other Adverse Drug Effects; Quality of Life
Zintchouk et al. (2019) <sup>98</sup>	RCT/Experimental	SNF	geriatric care with medication review	368	6 months	Number of Chronic Medications; Appropriateness; Cognitive Function

SNF: Skilled nursing or post-acute care facility; Amb: Ambulatory care; Hosp: Hospital; Assist: Assisted living residence

**Supplementary Table S3. Studies identified in literature review targeting single drug classes**

<b>First Author (Year)</b>	<b>Study design</b>	<b>Setting</b>	<b>Intervention</b>	<b>Target Study Population</b>	<b>N Participants</b>	<b>Follow-up</b>	<b>Outcomes</b>
Ailabouni et al. (2017), Ailabouni et al. (2019) <sup>99, 100</sup>	Observational	Assist	Pharmacist review and recommendation (per guideline)	Anticholinergics and Sedatives	46	12 months	Drug Burden Index; QOL; cognition; ADE; falls; depression; pain; behavior; deprescribing recommendation uptake; Adverse Drug Withdrawal: Recurrent Symptoms; Cognitive Function; Physical Function; Implementation-Adoption
Azermai et al. (2013) <sup>101</sup>	Observational	Hosp	Discontinue med without taper	Antipsychotics	40	1 month	Adverse Drug Withdrawal: Physiological Change; Cognitive Function
Bergh et al. (2012) <sup>102</sup>	RCT/Experimental	SNF	Antidepressant taper and discontinuation	Antidepressants	128	12 months	Other Adverse Drug Withdrawal Effects; Cognitive Function; Physical Function; Quality of Life; Other Patient-Centered Outcome
Bourgeois et al. (2014) <sup>103</sup>	Observational	SNF	pt-physician agreement of taper medication	Benzodiazepines, Z Drugs	38	12 months	Adverse Drug Withdrawal: Physiological Change; Quality of Life; Other Patient-Centered Outcome
Brodaty et al. (2018), <sup>104</sup> Jessop et al. (2017) <sup>105</sup>	Observational	SNF	deprescribing protocol plus clinician education	Antipsychotics	139*	24 months	Adverse Drug Related Cognitive Change; Fall/Fractures due to

							Adverse Drug Effects; Hospital Utilization
Desveaux et al. (2015), Desveaux et al. (2017) <sup>106, 107</sup>	Cluster RCT	SNF	Clinician education, audit and feedback	Antipsychotics	60*	6 months	Rates of Antipsychotic Dispensing; Other Specific Drug Outcome; Implementation-Acceptability; Physician Experience; Other Implementation Outcome; Quality of Life; Other Utilization Outcome;
Eveleigh et al. (2014) <sup>108</sup>	RCT/Experimental	Amb	Physician education based on med review	Antidepressants	146	12 months	Quality adjusted life years (QALY); Costs
Kormelinck et al. (2019) <sup>109</sup>	Cluster RCT	SNF	Clinician education and process improvement	Psychotropics	607	24 months	Appropriateness; Other Specific Drug Outcome; Cognitive Function; Implementation-Adoption; Other Implementation Outcome; Quality of Life
Krause et al. (2019) <sup>110</sup>	Cluster RCT	SNF	pharmacist med review plus clinician education and decision support	Antipsychotics	760	6 months	Appropriateness (proportion with PIM); Fall/Fractures due to Adverse Drug Effects; Cognitive Function; Quality of Life; Costs; Emergency Room; Hospital Utilization

Kuntz et al. (2019) <sup>111</sup>	RCT/Experimental	Amb	pharmacist consultation plus pt education	Nonbenzodiazepine Sedative Hypnotics	150	6 months	Discontinuations; Ambulatory; Emergency Room; Hospital Utilization; Other Utilization Outcome
Kutner et al. (2015) <sup>112</sup>	RCT/Experimental	Hospice care	Discontinue statin medication	Statins	381	12 months	Mortality, CV Events; QOL; CV Symptoms, Total medications; Costs
Lopez-Peig et al. (2012) <sup>113</sup>	Observational	Amb	Medication taper among willing patients	Benzodiazepines	51	12 months	Number of Chronic Medications; Duration of Discontinuation; Other Specific Drug Outcome; Patient Knowledge; Quality of Life
Luymes et al. (2018) <sup>114</sup>	Cluster RCT	Amb	Physician education, defined deprescribing guideline	Statins and Anti-Hypertensive medications	1067	24 months	10-year CV risk; Costs
Martin et al. (2013), <sup>115</sup> Tannenbaum et al. (2014), <sup>116</sup> Martin et al. (2017) <sup>117</sup>	Cluster RCT	Amb	community pharmacy patient education	Benzodiazepines	303	12 months	Number of Chronic Medications; Discontinuations; Dose Reductions; Other Specific Drug Outcome; Appropriateness; Implementation-Adoption; Patient's Attitude; Patient Knowledge
Moga et al. (2017) <sup>118</sup>	RCT/Experimental	Amb	patient-centered, pharmacist-physician intervention	Anticholinergics	50	6 months	Appropriateness

Pellicano et al. (2018) <sup>119</sup>	Observational	Hosp	multidisciplinary team med review	Psychotropics	125	Hosp Discharge	Discontinuations; Feasibility
Reeve et al. (2015) <sup>120</sup>	Observational	Amb	pharmacist med review, recommendations, and support	Proton Pump Inhibitors	57	6 months	Appropriateness (number PPIs); Patient Experience; Feasibility
Sheppard et al. (2018) <sup>121</sup>	RCT/Experimental	Amb	Clinician education and DP of one antihypertensive	Antihypertensives	540	6 months	Duration of Discontinuation; Other Specific Drug Outcome; Adverse Drug Reactions; Other Adverse Drug Effects; Adverse Drug Withdrawal: Recurrent Symptoms; Physical Function; Feasibility; Quality of Life; Costs
van der Spek et al. (2018) <sup>122</sup>	RCT/Experimental	SNF	Biannual medication reviews	Psychotropics	380	24 months	Appropriateness (APID index score)
Westbury et al. (2018) <sup>123</sup>	Observational	Assist	multicomponent medication review process	Antipsychotics, Benzodiazepines	12157	6 months	Mean prevalence of target Medications; Doses per day per person; Substitutions (prevalence); Discontinuations (proportion); Dose Reductions(proportion); Other Specific Drug Outcome
Wilson et al. (2018) <sup>124</sup>	Observational	Hosp	patient education brochure	Benzodiazepines, Z Drugs	62	1 month	Number of Chronic Medications; Discontinuations; Adverse Drug Withdrawal: Recurrent

							Symptoms; Other Patient-Centered Outcome
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\* Count reflects number of SNFs, not number of patients/participants.

SNF: Skilled nursing or post-acute care facility; Amb: Ambulatory care; Hosp: Hospital; Assist: Assisted living residence



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