

Supplemental Online Content

eAppendix Search strategy and databases

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eTable 3: Summary of conclusions of systematic reviews and results of meta-analyses (Level 1)

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eTable 5: Citation matrix of primary studies included in systematic reviews

eFigure 1: PRISMA diagram summarizing number of studies identified, screened, eligible and included in final review from literature search

eAppendix

Search strategy and databases

Databases: Medline (Ebsco), Embase (Elsevier), CINAHL Complete (Ebsco), APA PsycInfo (Ebsco), Scopus (Elsevier), Web of Science Core Collection (Clarivate Analytics), Cochrane Database of Systematic Reviews (Wiley), DARE (Centre for Reviews & Dissemination), Health Technology Assessment (Centre for Reviews & Dissemination), NHS EED (Centre for Reviews & Dissemination), and Epistemonikos

Medline (EBSCO)

((MH "Aged+") OR (MH "Health Services for the Aged") OR (MH "Geriatric Assessment") OR (MH "Geriatrics") OR (MH "Geriatric Psychiatry") OR (MH "Geriatric Nursing") OR (MH "Geriatric Dentistry") OR (MH "Dental Care for Aged") OR (MH "Homes for the Aged") OR (MH "Nursing Homes+") OR (MH "Housing for the Elderly") OR TI (elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian* OR "older people" OR "older person" OR "older subject" OR "older subjects" OR "older patient" OR "older patients" OR "older age" OR "older aged" OR "older ages" OR "older adult" OR "older adults" OR "older man" OR "older men" OR "older male" OR "older males" OR "older woman" OR "older women" OR "older female" OR "older females" OR "older veterans" OR "older population") OR AB (elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian* OR "older people" OR "older person" OR "older subject" OR "older subjects" OR "older patient" OR "older patients" OR "older age" OR "older aged" OR "older ages" OR "older adult" OR "older adults" OR "older man" OR "older men" OR "older male" OR "older males" OR "older woman" OR "older women" OR "older female" OR "older females" OR "older veterans" OR "older population"))

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AND

(MH "Systematic Review") OR (MH "Systematic Reviews as Topic") OR (MH "Meta-Analysis") OR (MH "Network Meta-Analysis") OR (MH "Meta-Analysis as Topic+") OR TI ("systematic review" OR "systematic literature review" OR “meta analysis” OR “metaanalysis”) OR AB ("systematic review" OR "systematic literature review" OR “meta analysis” OR “metaanalysis”)

Embase

('aged'/exp OR 'elderly care'/exp OR 'geriatric assessment'/exp OR 'geriatrics'/exp OR 'elderly care'/exp OR 'nursing home'/exp OR (elder OR elders OR eldest OR elderly OR geriatric* OR “old age” OR “oldest old” OR “senior citizen” OR “senior citizens” OR “very old” OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian* OR “older people” OR “older person” OR “older subject” OR “older subjects” OR “older patient” OR “older patients” OR “older age” OR “older aged” OR “older ages” OR “older adult” OR “older adults” OR “older man” OR “older men” OR “older male” OR “older males” OR “older woman” OR “older women” OR “older female” OR “older females” OR “older veterans” OR “older population”):ti,ab)

AND

('inappropriate prescribing'/exp OR 'drug utilization review'/mj OR (deprescri* OR “de prescribing” OR “de prescription” OR “inappropriate prescribing” OR “inappropriate prescription” OR “inappropriate prescriptions” OR “over prescribing” OR “inappropriate medications” OR “inappropriate medication”):ti,ab)

OR

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CINAHL Complete (EBSCO)

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(TI=(elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian*)) OR AB=(elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian*)) AND (TI=(deprescri* OR "de prescribing" OR "de prescription" OR "inappropriate prescribing" OR "inappropriate prescription" OR "inappropriate prescriptions" OR "over prescribing" OR "inappropriate medications" OR "inappropriate medication" OR AB=(deprescri* OR "de prescribing" OR "de prescription" OR "inappropriate prescribing" OR "inappropriate prescription" OR "inappropriate prescriptions" OR "over prescribing" OR "inappropriate medications" OR "inappropriate medication")) OR TI=((medication* OR medicin* OR prescription* OR prescrib* OR polypharmacy* OR pharmaceutical* OR drug OR drugs OR aperient OR fiber OR laxative* OR lactulose OR glycerol OR sorbitol OR macrogol OR docusate OR bisacodyl OR senna OR picosulfate OR paraffin OR poloxamer OR "hormone replacement therapy" OR estrogen OR estradiol OR estriol OR tibolone OR "direct thrombin inhibitor" OR bivalirudin OR dabigatran OR warfarin OR anticoagula* OR "factor xa inhibitor" OR "factor xa inhibitors" OR apixaban OR fondaparinux OR rivaroxaban OR pyridoxine OR thiamine OR calcitriol OR cholecalciferol OR colecalciferol OR ergocalciferol OR micronutrient OR vitamin OR mineral OR iron OR ferrous OR calcium OR potassium OR magnesium OR ascorb* OR folic OR folate OR hydroxocobalamin OR cyanocobalamin OR "proton pump inhibitor" OR PPI OR "acid suppression" OR pantoprazole OR omeprazole OR esomeprazole OR lansoprazole OR rabeprazole OR antacid OR cimetidine OR famotidine OR nizatidine OR ranitidine OR fenofibrate OR gemfibrozil OR fibrate OR ezetimibe OR corticosteroid OR glucocorticoid OR steroid OR dihydropyridines OR amlodipine OR diltiazem OR felodipine OR lercanidipine OR nifedipine OR nimodipine OR verapamil OR nitrate OR nitrates OR trinitrate OR isosorbide OR mononitrate OR ivabradine OR nicorandil OR perhexiline OR antipsychotic OR amisulpride OR aripiprazole OR asenapine OR chlorpromazine OR clozapine OR droperidol OR flupenthixol OR fluphenazine OR haloperidol OR olanzapine OR paliperidone OR pericyazine OR quetiapine OR risperidone OR trifluoperazine OR ziprasidone OR zuclopenthixol OR lithium OR buspirone OR diphenhydramine OR doxylamine OR melatonin OR zolpidem OR zopiclone OR benzodiazepine OR alprazolam OR bromazepam OR midazolam OR clobazam OR nitrazepam OR oxazepam OR temazepam OR triazolam OR clonazepam OR diazepam OR flunitrazepam OR lorazepam OR hypnotic OR sedative OR anticholinergic OR darifenacin OR oxybutynin OR tolterodine OR benzhexol OR glycopyrronium OR hyoscine OR bromide OR biperiden OR orphenadrine OR solifenacin OR dopamine OR bromocriptine OR cabergoline OR pergolide OR apomorphine OR pramipexole OR rotigotine OR rasagiline OR selegiline OR amantadine OR entacapone OR levodopa OR anticholinesterase OR donepezil OR memantine OR galantamine OR rivastigmine OR bisphosphonate OR raloxifene OR alendronate OR clodronate OR ibandron* OR pamidronate OR risedronate OR tiludronate OR coledron* OR strontium OR aspirin OR antiplatelet OR clopidogrel OR thienopyridines OR prasugrel OR ticlopidine OR dipyridamole OR celecoxib OR diclofenac OR etoricoxib OR ibuprofen OR indomethacin OR ketoprofen OR ketorolac OR meloxicam OR naproxen OR piroxicam OR NSAID OR "non steroidal anti inflammatory" OR colchicine OR allopurinol OR quinine OR levothyroxine OR thyroxine OR liothyronine OR carbimazole OR propylthiouracil OR iodine OR paracetamol OR acetaminophen OR antiglycaemi* OR biguanide OR metformin OR sulphonylurea OR gliclazide OR glibenclamide OR glimepiride OR glipizide OR pioglitazone OR rosiglitazone OR insulin OR acarbose OR alogliptin OR linagliptin OR saxagliptin OR sitagliptin OR vildagliptin OR antiepilep* OR anticonvulsant OR valproate OR carbamazepine OR barbiturate OR lithium OR lamotrigine OR gabapentin OR phenytoin OR pregabalin OR ethosuximide OR levetiracetam OR topiramate OR vigabatrin OR tiagabine OR antihistamine OR cyclizine OR cyproheptadine OR dexchlorpheniramine OR diphenhydramine OR doxylamine OR pheniramine OR promethazine OR trimeprazine OR cetirizine OR desloratadine OR fexofenadine OR levocetirizine OR loratadine OR diuretic OR thiazide OR frusemide OR

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Centre for Reviews & Dissemination (University of York) – Health Technology Assessment, DARE, NHS EED

MESH term=Deprescriptions = 0

MeSH term = Inappropriate Prescribing = 25 [15 new]

Any field = deprescri* AND (older OR aged OR aging OR elder* OR senior OR geriatric*) = 1 [not new]

Any field=(older OR aged OR aging OR elder* OR senior OR geriatric*) AND Any field=inappropriate* AND Any field=(prescribing OR prescription*) = 26

Epistemonikos

(title:((elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian*)) AND (deprescri* OR "inappropriate prescribing")) OR abstract:((elder OR elders OR eldest OR elderly OR geriatric* OR "old age" OR "oldest old" OR "senior citizen" OR "senior citizens" OR "very old" OR septuagenarian* OR octogenarian* OR octagenarian* OR nonagenarian* OR centarian* OR centenarian* OR supercentenarian*)) AND (deprescri* OR "inappropriate prescribing" OR "inappropriate prescriptions" OR "inappropriate medications" OR overprescri*))

eTable 1: List of articles excluded at full-text, with reasons

	Reference	Author, Year	Reason for Exclusion	Additional Comments
1.	P26 Interventions to improve prescribing quality in care homes: a systematic review ¹	Loganathan, 2010	Published in abstract / poster form only	Conference poster
2.	Computerised Medication Analysis Designed to Minimise Inappropriate Prescribing in Older Hospitalised Patients: A Systematic Review and Meta-Analysis ²	Dalton, 2017	Published in abstract / poster form only	Conference poster
3.	Changing Behaviours: A Systematic Literature Review of Deprescribing Interventions in Older People ³	Hansen, 2017	Published in abstract / poster form only	Conference poster; Full-text is included in our overview
4.	Risk for major and fatal bleeding after discontinuing oral anticoagulation for unprovoked venous thromboembolism: Systematic review and meta-analysis ⁴	Khan F, 2019	Published in abstract / poster form only	Systematic review protocol
5.	A systematic review identifying the impact of patient decision aids in older patients with problematic polypharmacy ⁵	Khan AH, 2019	Published in abstract / poster form only	Conference poster
6.	Polypharmacy, risk of falls in older people and deprescribing: A literature review ⁶	Morgado, 2017	Published in abstract / poster form only	Conference poster
7.	Nonpharmacologic outpatient interventions for benzodiazepine discontinuation in elderly persons ⁷	Arsenault, 2015	Published in abstract / poster form only	Conference poster
8.	Deprescribing strategies in elderly patients or patients with several chronic conditions ⁸	Rodriguez-Perez, 2015	Published in abstract / poster form only	Conference poster
9.	Interventions to improve prescribing at the end-of-life: A systematic review ⁹	Velten, 2011	Published in abstract / poster form only	Conference poster
10.	Does antipsychotic dose reduction result in worsening behavior among nursing home residents with dementia: A systematic review of the literature? ¹⁰	Tjia, 2012	Published in abstract / poster form only	Conference poster
11.	Deprescribing of medications in older patients in the last three months of life: A systematic review ¹¹	Alwidyan, 2020	Published in abstract / poster form only	Conference poster
12.	Inappropriate hospitalisations, aggressive treatments, and insufficient deprescribing: The medicalisation of death from natural causes ¹²	Cardona, 2019	Published in abstract / poster form only	Conference poster
13.	A systematic review and new categorization of clinical aids to improve pharmacotherapy in older patients	Wehling	Published in abstract / poster form only	Article or poster was not found
14.	A systematic review and thematic synthesis of evaluations of pharmacy-led services in care homes across England ¹³	Rathbone, 2020	Published in abstract / poster form only	Conference Poster
15.	A Systematic Review of the Effects of Improvement of Prescription to Reduce the Number of Medications in the Elderly with Polypharmacy ¹⁴	Maeda, 2009	Not in English	

16.	Review of computerized clinical decision support in community pharmacy ¹⁵	Curtain, 2014	Not a systematic review as set out by DARE criteria ¹⁶	
17.	Evidence-Based Strategies for the Optimization of Pharmacotherapy in Older People ¹⁷	Topinkova, 2012	Not a systematic review as set out by DARE criteria ¹⁶	
18.	Medication errors in older adults: a review of recent publications ¹⁸	Aspinall, 2007	Not a systematic review as set out by DARE criteria ¹⁶	
19.	Deprescribing antihyperglycemic agents in older persons: Evidence-based clinical practice guideline ¹⁹	Farrell, 2017	Not a systematic review as set out by DARE criteria ¹⁶	
20.	Review: Minimal interventions (e.g., a letter) reduce long-term benzodiazepine use in primary care ²⁰	Primack, 2012	Not a systematic review as set out by DARE criteria ¹⁶	
21.	Deprescribing in older people ²¹	Liacos, 2020	Not a systematic review as set out by DARE criteria ¹⁶	
22.	Intervention elements to reduce inappropriate prescribing for older adults with multimorbidity receiving outpatient care: A scoping review ²²	Lee, 2020	Not a systematic review as set out by DARE criteria ¹⁶	
23.	Multidisciplinary Medication Review in Long-Term Care: A Review of Clinical Utility, Cost-Effectiveness and Guidelines ²³	Chao, 2019	Not a systematic review as set out by DARE criteria ¹⁶	
24.	Rates, determinants and success of implementing deprescribing in people with type 2 diabetes: A scoping review ²⁴	Oktora, 2020	Not a systematic review as set out by DARE criteria ¹⁶	
25.	The Effect of Interventions to Reduce Potentially Inappropriate Antibiotic Prescribing in Long-Term Care Facilities: a Systematic Review of Randomised Controlled Trials ²⁵	Fleming, 2013	No relevant study population	Age of population not defined in study
26.	Reduced-dose direct oral anticoagulants in the extended treatment of venous thromboembolism: a systematic review and meta-analysis ²⁶	Vasanthamohan, 2018	No relevant study population	Age of population not defined in study
27.	Reduction or discontinuation of antipsychotics for challenging behaviour in adults with intellectual disability: a systematic review ²⁷	Sheehan, 2017	No relevant study population	Age of population <60 years old
28.	Strategies for discontinuation of proton pump inhibitors: a systematic review ²⁸	Haastруп, 2014	No relevant study population	Age of population not defined in study

29.	The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials ²⁹	Rank, 2013	No relevant study population	Age of population <60 years old
30.	Deprescribing Medications for Chronic Diseases Management in Primary Care Settings: A Systematic Review of Randomized Controlled Trials ³⁰	Dills, 2018	No relevant study population	Age of population <60 years old
31.	Minimal interventions to decrease long-term use of benzodiazepines in primary care: a systematic review and meta-analysis ³¹	Mugunthan, 2013	No relevant study population	Age of population <60 years old
32.	Stepping down the dose of inhaled corticosteroids for adults with asthma ³²	Crossingham, 2017	No relevant study population	Age of population <60 years old
33.	The effectiveness of computer system tools on potentially inappropriate medications ordered at discharge for adults older than 65 years of age: a systematic review ³³	Iankowitz, 2012	No relevant intervention	
34.	The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: A systematic review ³⁴	Riordan, 2016	No relevant intervention	
35.	Reducing potentially inappropriate medications in palliative cancer patients: evidence to support deprescribing approaches ³⁵	Lindsay, 2013	No relevant intervention	
36.	Analgesics use and withdrawal in people with dementia - a register-based Danish study and a systematic review ³⁶	Sorensen, 2019	No relevant intervention	
37.	Hospital pharmacists working with geriatric patients in Europe: a systematic literature review ³⁷	Kiesel, 2018	No relevant intervention	
38.	Risk versus risk: a review of benzodiazepine reduction in older adults ³⁸	Paquin, 2014	No relevant intervention	
39.	Discontinuation of lithium augmentation in geriatric patients with unipolar depression: A systematic review ³⁹	Ross, 2008	No relevant intervention	
40.	Discontinuation of alpha-blocker therapy in men with lower urinary tract symptoms: a systematic review and meta-analysis ⁴⁰	van der Worp, 2019	No relevant intervention	
41.	The Effect of Melatonin on Benzodiazepine Discontinuation and Sleep Quality in Adults Attempting to Discontinue Benzodiazepines: A Systematic Review and Meta-Analysis ⁴¹	Wright, 2015	No relevant intervention	
42.	Clinical medication review of polypharmacy reduced unplanned hospitalizations in older adults: A meta-analysis of randomized clinical trials ⁴²	Mizokami, 2019	No relevant intervention	
43.	The feasibility of Chinese massage as an auxiliary way of replacing or reducing drugs in the clinical treatment of adult type 2 diabetes: A systematic review and meta-analysis ⁴³	Zhang, 2020	No relevant intervention	

44.	Long-Term Drug Therapy and Drug Discontinuations and Holidays for Osteoporosis Fracture Prevention A Systematic Review ⁴⁴	Fink, 2019	No relevant intervention	
45.	Polypharmacy and mobility outcomes ⁴⁵	Ali, 2020	No relevant intervention	Includes interventions with element of deprescribing, not all clearly deprescribing
46.	Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies ⁴⁶	Hill-Taylor, 2019	No outcome of interest	Not a clear deprescribing outcome
47.	Deprescribing interventions and their impact on medication adherence in community-dwelling older adults with polypharmacy: a systematic review ⁴⁷	Ulley, 2019	No outcome of interest	Adherence not an outcome of interest
48.	Effectiveness of interventions targeting antibiotic use in long-term aged care facilities: A systematic review and meta-analysis ⁴⁸	Raban, 2020	No outcome of interest	
49.	Withdrawal versus continuation of long-term antipsychotic drug use for behavioural and psychological symptoms in older people with dementia ⁴⁹	Van Leeuwen, 2018	No outcome of interest	Not a clear deprescribing outcome
50.	Impact of pharmacist-led home medicines review services on drug-related problems among the elderly population: a systematic review ⁵⁰	Gudi, 2019	No relevant control group	
51.	Interventions for reducing benzodiazepine use in older people: meta-analysis of randomised controlled trials ⁵¹	Gould, 2014	No relevant control group	
52.	Discontinuation of Preventive Medicines in Older People with Limited Life Expectancy: A Systematic Review ⁵²	Narayan, 2017	No relevant control group	
53.	Deintensification of hypoglycaemic medications-use of a systematic review approach to highlight safety concerns in older people with type 2 diabetes ⁵³	Abdelhafiz, 2018	Fewer than 2 primary studies of interest	
54.	Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials ⁵⁴	Forsetlund, 2011	Fewer than 2 primary studies of interest	
55.	Psychosocial interventions for reducing antipsychotic medication in care home residents ⁵⁵	Richter, 2012	Fewer than 2 primary studies of interest	
56.	Health Outcomes of Deprescribing Interventions Among Older Residents in Nursing Homes: A Systematic Review and Meta-analysis ⁵⁶	Kua, 2019	Fewer than 2 primary studies of interest	
57.	Antihypertensive withdrawal for the prevention of cognitive decline ⁵⁷	Jongstra, 2018	Fewer than 2 primary studies of interest	

58.	Process, impact and outcomes of medication review in Australian residential aged care facilities: A systematic review ⁵⁸	Chen, 2019	Fewer than 2 primary studies of interest	
59.	Discontinuation of Long-Term Antipsychotic Drug Use for Behavioral and Psychological Symptoms in Older Adults Aged 65 Years and Older With Dementia ⁵⁹	Van Leeuwen, 2018	Duplicate study	Duplicate of #36 ⁴⁹ , published separately

Reasons for exclusion were set out *a priori* in a hierarchical fashion as follow: 1. Published in abstract / poster form only, 2. Not in English, 3. Not a systematic review as set out by DARE criteria¹⁶, 4. No relevant study population, 5. No relevant intervention, 6. No outcome of interest, 7. No relevant control group, 8. Fewer than 2 primary studies of interest and 9. Duplicate study.

eTable 2: Study characteristics of included systematic reviews

Authors (Year Published)	Databases and Time Frame Searched	# Stu die s (No. of Parti cip ants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Stu die s (Design)	No. of Parti cip ants (Mean Age in years ^b)
Kaur et al (2009) ⁶¹	<ul style="list-style-type: none"> PubMed, Cochrane databases, International Pharmaceutical Abstracts, EMBASE and CINAHL 1996 to September 2008 	24 (1,559, 623)	<ul style="list-style-type: none"> Setting: not stated Age 65+ 	<ul style="list-style-type: none"> Aim: improve inappropriate prescribing, target medication^c not stated Intervention type: various Facilitator of intervention: not stated 	Not stated	Inappropriate prescribing	Critically low	3 (3 RCTs ⁶²⁻⁶⁴)	13,660 (Not stated)
Coon et al (2014) ⁶⁵	<ul style="list-style-type: none"> MEDLINE, EMBASE, Social Policy and Practice, PsycINFO, CDSR and CENTRAL, CINAHL, AMED and British Nursing Index, Science Citation Index Expanded and Social Science Citation Index Inception to November 2013 	23 (>19,300) ^d	<ul style="list-style-type: none"> Setting: community residential care With dementia 	<ul style="list-style-type: none"> Aim: reduce inappropriate prescribing of antipsychotics Intervention type: various Facilitator of intervention: health professionals (e.g. GP, community psychiatrists, pharmacists) 	Not stated	Change in medication use	Low	5 (5 RCTs ⁶⁶⁻⁷⁰)	3,601 (Not stated)
Castelino et al (2009) ⁷¹	<ul style="list-style-type: none"> MEDLINE, International Pharmaceutical Abstracts, and EMBASE 1992 to 2008 	12 (3,958)	<ul style="list-style-type: none"> Setting: not stated Age 65+ 	<ul style="list-style-type: none"> Aim: reduce suboptimal prescribing of various drugs / drug classes Intervention type: no restrictions Facilitator of intervention: pharmacists 	Not stated	Suboptimal prescribing	Critically low	3 (3 RCTs ^{63, 64, 72})	1,269 (Not stated)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Verrue et al (2009) ⁷³	<ul style="list-style-type: none"> MEDLINE (PubMed), International Pharmaceutical Abstracts and EMBASE January 1987 to May 2008 	8 (7,299)	<ul style="list-style-type: none"> Setting: nursing homes Age 65+ No specific disease/pathology 	<ul style="list-style-type: none"> Aim: improve the quality of prescribing, target medication^c not stated Intervention type: no restrictions Facilitator of intervention: pharmacists 	Not stated	Not stated	Critically low	6 (5 RCTs ^{69, 74-77} , 1 non-RCT ⁷⁸)	7,035 (Not stated)
Rankin et al (2018) ⁷⁹	<ul style="list-style-type: none"> CENTRAL, Health Technology Assessment Database, NHS Economic Evaluation Database, MEDLINE Ovid, Embase Ovid and CINAHL EBSCO November 2013 to February 2018 	32 (28,672)	<ul style="list-style-type: none"> Setting: any Age 65+ Having >1 long term medical condition Receiving polypharmacy (≥4 prescribed medicines) 	<ul style="list-style-type: none"> Aim: improve appropriate polypharmacy Intervention type: no restrictions Facilitator of intervention: not stated 	Usual care	<ul style="list-style-type: none"> Primary outcomes Medication appropriateness PIMs Potential prescribing omissions Hospital admissions Secondary outcomes^e 	Low	10 (9 RCTs ⁸⁰⁻⁸⁸ , 1 non-RCT ⁸⁹)	1,663 (64 - 85)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Black et al (2017) ⁹⁰	<ul style="list-style-type: none"> MEDLINE, EMBASE, and the Cochrane Library, clinicaltrials.gov, the World Health Organization Clinical Trials Registry, UpToDate, and Google Scholar 1946 to July 2015 	2 (6,352)	<ul style="list-style-type: none"> Setting: any Age 18+ Taking antihyperglycemic medications for T2DM 	<ul style="list-style-type: none"> Aim: deprescribe at least one antihyperglycemic medication Intervention type: no restrictions Facilitator of intervention: not stated 	Continuing antihyperglycemic medications	<ul style="list-style-type: none"> Hypoglycemia Falls Adverse drug reactions Frequency of blood glucose testing Blood glucose levels HbA1C levels Pill burden Emergency room visits and hospitalizations Quality of life and patient satisfaction Length of stay in hospital Microvascular complications Macrovascular outcomes Polyuria, hyperglycemia, and/or sleep disturbances 	Critically low	2 (2 CBAs ^{91, 92})	6,352 (77 - 84)
Nakham et al (2020) ⁹³	<ul style="list-style-type: none"> CINAHL, Ovid MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) January 2010 to February 2019 	8 (1,061)	<ul style="list-style-type: none"> Setting: not stated Age 65+ On long-term medication (> 12 weeks) 	<ul style="list-style-type: none"> Aim: reduce anticholinergic burden Intervention type: no restrictions Facilitator of intervention: not stated 	Usual care	<ul style="list-style-type: none"> Medication use Patient outcomes such as falls Cost outcomes 	Critically low	4 (4 RCTs ⁹⁴⁻⁹⁷)	423 (76 - 85)
Monteiro et al (2019) ⁹⁸	<ul style="list-style-type: none"> MEDLINE, CENTRAL, EMBASE, and Web of Science Inception to February 2018 	16 (>266,562) ^d	<ul style="list-style-type: none"> Setting: any Age 65+ 	<ul style="list-style-type: none"> Aim: reduce PIPs or PIMs Intervention type: computerized decision support tools Facilitator of intervention: not stated 	No restrictions	<ul style="list-style-type: none"> Outcomes categorized as PIP or PIM-related. Number of prescriptions Adverse drug reactions Potential drug-drug interactions 	Critically low	3 (3 RCTs ^{62, 99, 100})	94,786 (75 - 82)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Seidu et al (2019) ¹⁰¹	<ul style="list-style-type: none"> MEDLINE, Embase, Web of Science, and Cochrane data-bases Inception to October 2018 	10 (26,558)	<ul style="list-style-type: none"> Setting: any Age 65+ With T2DM 	<ul style="list-style-type: none"> Aim: deintensify antidiabetic medication and other therapies Intervention type: no restrictions Facilitator of intervention: not stated 	usual care or continuing medications	<ul style="list-style-type: none"> Measures of glycaemia Admission rates Hospitalizations Complications Mortality Quality of life, and patient satisfaction 	Low	2 (2 cohort studies ^{91, 92})	6,352 (77 - 84)
Dou et al (2019) ¹⁰²	<ul style="list-style-type: none"> Ovid, PubMed, Academic Search Complete, Web of Science 1990 to not stated ("Present") 	11 (1,575)	<ul style="list-style-type: none"> Setting: not stated Age 60+ Using BDZs ≥3 months 	<ul style="list-style-type: none"> Aim: withdraw long-term BDZs Intervention type: Medication withdrawal Facilitator of intervention: not stated 	Standard treatment	BDZs withdrawal success	Critically low	10 (10 RCTs ¹⁰³⁻¹¹²)	1,478 (60 - 75)
Sheehan et al (2018) ¹¹³	<ul style="list-style-type: none"> Medline, PsycINFO, EMBASE, and CINAHL Plus Inception to February 2018 	26 studies in 27 articles (8,556)	<ul style="list-style-type: none"> Setting: any Any population 	<ul style="list-style-type: none"> Aim: optimize psychotropic medications Intervention type: medication review Facilitator of intervention: not stated 	Not stated	Outcomes of psychotropic medication optimization	Critically low	3 studies in 4 articles (3 RCTs ¹¹⁴⁻¹¹⁷)	652 (79 - 85)
Dalton et al (2018) ¹¹⁸	<ul style="list-style-type: none"> PubMed, EMBASE, Medline, Web of Science, CINAHL, Cochrane Central Register of Controlled Trials, PsycInfo and ClinicalTrials.gov Inception to October 2017 	8 (>48,204) ^d	<ul style="list-style-type: none"> Setting: hospital Age 65+ 	<ul style="list-style-type: none"> Aim: reduce PIP Intervention type: computer generated recommendation Facilitator of intervention: not stated 	Usual care or non-exposed	Primary outcomes: <ul style="list-style-type: none"> Reductions in PIP or patients with PIP. Secondary outcomes ^f	Critically low	5 (2 RCTs ^{119, 120} , 1 cohort study ¹²¹ , 2 CBAs ^{122, 123})	>21,730 (73.5 - 81.3)*

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Kallio et al (2018) ¹²⁴	• CINAHL, MEDLINE (Ovid), Scopus, International Pharmaceutical Abstracts, and Cochrane Library • January 2000 to February 2016	16 (7,340)	• Setting: outpatient • Age 65+	• Aim: describe the outcomes of medication reviews, target medication ^c not stated • Intervention type: medication reviews • Facilitator of intervention: Community pharmacists	No restrictions	No restrictions	Critically low	3 (3 RCTs ^{125- 127})	3,143 (Not stated)
Thillainade- san et al (2018) ¹²⁸	• Ovid MEDLINE, Embase, Informit, International Pharmaceutical Abstracts, Scopus, PsycINFO, the Cochrane Central Register of Controlled Trials (CENTRAL) and CINAHL • 1 January 1996 up to and including April 2017	9 (2,522)	• Setting: hospital • Older adults (no specific age defined)	• Aim: reduce PIM • Intervention type: no restrictions • Facilitator of intervention: includes pharmacist, physician, and prescriber	Usual care	Primary outcome: • Reduction in PIMs Secondary outcomes ^d	Critically low	9 (9 RCTs ^{63, 81, 89, 129- 134})	2,522 (75 - 87)
Reeve et al (2017) ¹³⁵	• PubMed, Embase, Informit, International Pharmaceutical Abstracts, Scopus, PsychINFO, Cochrane Central Register of Controlled Trials and CINAHL • January 1995 to July 2015	7 (1,214)	• Setting: community, hospital or aged care • Age 65+ • On long term BZDs and/or Z- drugs (≥ 4 weeks)	• Aim: deprescribe long- term use of BZDs and/or Z-drugs • Intervention type: no restrictions • Facilitator of intervention: not stated	Not stated	• Number of participants continuing vs. stopping BZD or Z-drug use • Clinical outcomes: • Adverse drug withdrawal reactions • Return of condition/ loss of benefit	Critically low	5 (5 RCTs ^{107, 136-139})	1,023 (73- 82)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Wilsdon et al (2017) ¹⁴⁰	<ul style="list-style-type: none"> PubMed, MEDLINE (Ovid), Embase (Ovid), the Cochrane Library, ProQuest Dissertations and Theses Global, and Google Inception to January 2017 	21 (>164,180) ^d	<ul style="list-style-type: none"> Setting: hospital, community dwelling or aged care facilities. Age 65+ Inappropriate PPI use 	<ul style="list-style-type: none"> Aim: deprescribe inappropriate PPI Intervention type: no restrictions Facilitator of intervention: not stated 	No restrictions	Primary outcome: <ul style="list-style-type: none"> Inappropriate PPI use Secondary outcomes ^h	Critically low	4 (3 RCTs ^{133, 134, 141} , 1 cohort study ¹⁴²)	71,306 (82 - 87)
Page et al (2016) ¹⁴³	<ul style="list-style-type: none"> EbscoHost (CINAHL Plus, Health Source: Nursing/Academic Edition, Academic Search Premier), Ovid (Medline, DARE), Scopus, Web of Science, Elsevier (Embase) and ProQuest (Dissertations and Theses Global), National Institutes of Health Trials Register, Australian New Zealand Clinical Trials Registry and European Union Clinical Trials Register Inception to February 2015 	116 (34,143)	<ul style="list-style-type: none"> Setting: any setting Age 65+ Prescribed ≥1 regular medication 	<ul style="list-style-type: none"> Aim: deprescribe ≥ 1 regular prescription medications Intervention type: no restrictions Facilitator of intervention: health care professionals 	No comparator or usual care	Primary outcome: <ul style="list-style-type: none"> Mortality Secondary outcomes ⁱ	Critically low	65 (53 RCTs ^{64, 81, 86, 94, 107, 132, 136, 137, 141, 144-187} , 6 non-RCTs ¹⁸⁸⁻¹⁹³ , 6 cohort studies ^{92, 194-198})	16,336 (65 - 86)

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Clyne et al (2016) ¹⁹⁹	<ul style="list-style-type: none"> PubMed, Embase, Scopus, and the Cochrane library databases Time frame was not stated 	12 (156,529)	<ul style="list-style-type: none"> Setting: community dwelling Age 65+ 	<ul style="list-style-type: none"> Aim: improve PIP, target medication^c not stated Intervention type: no restrictions Facilitator of intervention: not stated 	Usual care or alternative intervention	Change in PIP	Critically low	4 (4 RCTs ^{62, 64, 127, 200})	14,105 (Not stated)
Walsh et al (2016) ²⁰¹	<ul style="list-style-type: none"> Medline, PubMed, EMBASE, Centre for reviews and dissemination databases, Cochrane database of systematic reviews, CINAHL, Web of Science, Science Direct, ClinicalTrials.gov, metaRegister of Controlled Trials, ProQuest Dissertations and Theses, and Index to Theses in Great Britain and Ireland Inception up to and including June 2014 	5 (1,651)	<ul style="list-style-type: none"> Setting: hospital Age 65+ Or any age with dementia 	<ul style="list-style-type: none"> Aim: improve quality of prescribing, target medication^c not stated Intervention type: no restrictions Facilitator of intervention: pharmacists 	No restrictions	Reduction of PIP	Critically low	3 (3 RCTs ^{63, 130, 131})	1,388 (81.9 - 87.1)*
Pruskowski et al (2019) ²⁰²	<ul style="list-style-type: none"> The Cochrane Library (Wiley), Cumulative Index to Nursing and Allied Health (CINAHL), MEDLINE via PubMed, and EMBASE Inception to November 2017 	13 (2,195)	<ul style="list-style-type: none"> Setting: not stated Age 65+ With life-limiting conditions 	<ul style="list-style-type: none"> Aim: deprescribe prescription or over-the-counter medication Intervention type: no restrictions Facilitator of intervention: not stated 	Usual care	Primary outcome: <ul style="list-style-type: none"> Quality of life Secondary outcomes ⁱ	Critically low	9 (9 RCTs ^{141, 146, 151, 152, 161, 171, 172, 203, 204})	1,884 (74 - 84)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Shrestha et al (2019) ²⁰⁵	<ul style="list-style-type: none"> PubMed, Embase, CINHAL, PsychInfo, Google scholar Inception to February 2019 	9 (1,375)	<ul style="list-style-type: none"> Setting: any Age 65+ With life-limiting illness and limited life expectancy up to 2 years 	<ul style="list-style-type: none"> Aim: deprescribe inappropriate medications Intervention type: no restrictions Facilitator of intervention: health care professionals 	Usual care or any head-head intervention	<ul style="list-style-type: none"> Medication appropriateness Clinical measures Mortality, QOL, Falls, Sleep quality, Bowel function, Cognitive function, Performance status and Symptoms status. Costs 	Critically low	4 (3 RCTs ^{141, 161, 206, 1} , 1 non-RCT ¹⁹⁶)	972 (74 - 84)*
Hansen et al (2018) ²⁰⁷	<ul style="list-style-type: none"> MEDLINE, EMBASE, The Cochrane Central Register of Controlled Trials, Web of Science, Academic Search Complete, Google Scholar, OpenSIGLE, ClinicalTrials.gov, International Standard Registered Clinical/social Study Number (ISRCTN), WHO International Clinical Trials Registry Platform (ICTRP) and the Australian New Zealand Clinical Trials Register (ANZCTR) search date: December 14 2016 	25 (20,812)	<ul style="list-style-type: none"> Setting: any Age 65+ 	<ul style="list-style-type: none"> Aim: deprescribe existing drugs or reduce inappropriate prescribing, target medication^c not stated Intervention type: no restrictions Facilitator of intervention: not stated 	Either active interventions or inactivity, e.g. sham or no intervention	<ul style="list-style-type: none"> Primary outcomes: <ul style="list-style-type: none"> Number of total and inappropriate prescriptions and/or drugs Proportion of participants with a reduction in number of total and inappropriate prescriptions and/or drugs Implementation of recommendations Secondary outcomes^k 	Critically low	19 (19 RCTs ^{63, 64, 81, 107, 131, 141, 144, 147, 206, 208-217})	6,583 (61 - 89)

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Thio et al (2018) ²¹⁸	<ul style="list-style-type: none"> PubMed and EMBASE Between 2005 and 2017 	27 reporte d in 26 articles (8,773)	<ul style="list-style-type: none"> Setting: primary care or nursing home Age 18+ On long-term medication (>4 weeks) 	<ul style="list-style-type: none"> Aim: withdraw ≥ 1 long-term medications Intervention type: no restrictions Facilitator of intervention: not stated 	Continuing medication	<ul style="list-style-type: none"> Number of patients who successfully stopped medication. Patients who experienced relapse of symptoms or restarted medication Early dropout of the study 	Critically low	23 (23 RCTs ¹⁴¹ , 151, 161, 162, 165, 171, 173-175, 177, 182, 183, 186, 203, 219- 227)	8,146 (62 - 89)*
Hoyle et al (2018) ²²⁸	<ul style="list-style-type: none"> PubMed, Scopus, ProQuest, CENTRAL, EMBASE, and CINAHL Inception to 25 July 2017 	14 (2,852)	<ul style="list-style-type: none"> No population characteristics stated Setting: Nursing homes 	<ul style="list-style-type: none"> Aim: reduce antipsychotic and/or BDZ use Intervention type: professional and organization interventions defined by Cochrane EPOC review group Facilitator of intervention: not stated 	Not stated	Clinical outcomes as: <ul style="list-style-type: none"> Behavioral and psychological symptoms Quality of life Falls 	Critically low	10 (6 RCTs ⁶⁷ , 114, 115, 229-231, 2 non- RCTs ⁶⁸ , 70, 1 ITS ²³² , 1 CBA ¹⁹¹)	2,236 (Not stated)

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Johansson et al (2016) ²³³	<ul style="list-style-type: none"> Ovid Medline, OVID EMBASE, OVID All evidence-based medicine reviews – Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Methodology Register, American College of Physicians (ACP) Journal Club, Database of Abstracts of Reviews of Effects, Health Technology Assessment, National Health Service Economic Evaluation • 1946 to 13 July 2015 	25 (11,181)	<ul style="list-style-type: none"> • Setting: any • Patients with polypharmacy: ≥4 prescribed or nonprescribed drugs • Studies with 80% of study population taking ≥4 drugs 	<ul style="list-style-type: none"> • Aim: reduce polypharmacy • Intervention type: no restrictions • Facilitator of intervention: not stated 	No intervention or usual care	Primary outcomes: <ul style="list-style-type: none"> • Mortality • Hospitalization • Change in number of drugs Secondary outcomes ^l	Critically low	25 (21 RCTs ⁶⁴ , 77, 86, 125, 126, 147, 200, 206, 208, 210-213, 216, 234-240, 4 non-RCTs ⁷⁸ , 197, 215, 241)	11,181 (70 - 88)
Nishtala et al (2008) ²⁴²	<ul style="list-style-type: none"> MEDLINE, Cochrane Central Register of Control Trials, Cinahl, EMBASE , International Pharmaceutical Abstracts and PsycINFO • January 1980 to April 2007 	11 (13,010)	<ul style="list-style-type: none"> • Setting: long-term care facilities • Age 65+ 	<ul style="list-style-type: none"> • Aim: optimize the use of psychotropic drugs • Intervention type: medication reviews and/or educational intervention • Facilitator of intervention: not stated 	Not stated	Primary outcome: <ul style="list-style-type: none"> • Proportion of residents using one or more psychotropic drugs Secondary outcome ^m	Critically low	3 (3 RCTs ⁶⁹ , 75, 243)	6,395 (Not stated)

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Tjia et al (2013) ²⁴⁴	<ul style="list-style-type: none"> MEDLINE, EMBASE, and International Pharmaceutical Abstracts January 1966 to September 2012 	36 (13,906)	<ul style="list-style-type: none"> Setting: assisted living, nursing home, hospital, or hospice Age 65+ With an indication of frailty or disability 	<ul style="list-style-type: none"> Aim: discontinue unnecessary daily medications for chronic conditions Intervention type: no restrictions Facilitator of intervention: not stated 	Not stated	Reductions in the number of unnecessary medications	Critically low	10 (9 RCTs ^{63, 64, 67, 69, 74, 75, 131, 241, 245} , 1 cohort study ²⁴⁶)	8,331 (65+)*
Parr et al (2008) ²⁴⁷	<ul style="list-style-type: none"> PsycLIT, MEDLINE and EBASE 1840 to 2007 	32 (15,787)	<ul style="list-style-type: none"> Setting: General practice or outpatient On long term BZDs (≥ 3 months) 	<ul style="list-style-type: none"> Aim: discontinue BDZs Intervention type: brief interventions, gradual dose reduction and psychological interventions. Facilitator of intervention: not stated 	adjunctive treatment with routine care or routine care alone	Cessation rates for each condition	Critically low	5 (5 RCTs ¹⁰⁵)	4,936 (62 - 71)
Iyer et al (2008) ²⁴⁸⁻²⁵²	<ul style="list-style-type: none"> PubMed Between 1966 to 2007 	32 (9,475)	<ul style="list-style-type: none"> Setting: any Age 65+ 	<ul style="list-style-type: none"> Aim: withdraw a particular class of medications completely, target medication^c not stated Intervention type: no restrictions Facilitator of intervention: not stated 	Continuing medications for RCTs No restrictions on control for other study designs	Clinically relevant outcome (not specified)	Critically low	4 (4 RCTs ¹⁵⁶⁻¹⁵⁹)	448 (Not stated)

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Bloomfield et al (2020) ²⁵³	<ul style="list-style-type: none"> MEDLINE, Embase, the Cumulative Index of Nursing and Allied Health (CINAHL), and the Cochrane Library 1990 to February 2019 	38 trials reported in 47 papers (419,902)	<ul style="list-style-type: none"> Setting: community-dwelling Age 65+ 	<ul style="list-style-type: none"> Aim: deprescribe medications, target medication² not stated Intervention type: comprehensive medication review, education and feedback, or computerized decision support Facilitator of intervention: not stated 	Not stated	Primary outcomes: <ul style="list-style-type: none"> Quality of life All-cause mortality Hospitalizations Falls Adverse drug withdrawal events Major adverse cardiac events Delirium PIMs 	Critically low	18 (18 RCTs ^{62, 64, 72, 83, 84, 107, 203, 211, 217, 234, 254-261})	19,948 (72 - 83)
Almutairi et al (2020) ²⁶²	<ul style="list-style-type: none"> MEDLINE, PubMed, Google scholar, PsycINFO Inception to May 2019 	25 studies reported in 28 papers (22,989)	<ul style="list-style-type: none"> Setting: aged care facility, nursing homes, residential continuing care hospitals Age 60+ 	<ul style="list-style-type: none"> Aim: increase the appropriateness of medications used, target medication² not stated Intervention type: no restrictions. Facilitator of intervention: health professional 	Not stated	<ul style="list-style-type: none"> Medication appropriateness Residents' clinical outcomes (not specified) 	Critically low	9 (9 RCTs ^{67, 69, 75-77, 86, 206, 213, 230})	8,443 (65+)

Authors (Year Published)	Databases and Time Frame Searched	# Stu- die s (No. of Parti- cipants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Particip- ants (Mean Age in years ^b)
Hart et al (2020) ²⁶³	<ul style="list-style-type: none"> PubMed and EMBASE On or before June 30, 2019 	14 (8,300)	<ul style="list-style-type: none"> Setting: not stated Age 60+ with a fall-related injury or a history of falls. 	<ul style="list-style-type: none"> Aim: reduce or discontinue FRIDs Intervention type: no restrictions Facilitator of intervention: not stated 	Not stated	<ul style="list-style-type: none"> Prevalence of FRID use among older adults with fall-related injury FRIDs that were most frequently prescribed Whether FRID use was reduced following the fall-related healthcare episode Which interventions have reduced falls or FRID use in older adults with a history of falls. 	Critically low	3 (3 RCTs ^{203, 264, 265})	997 (76 - 85)
Earl et al (2020) ²⁶⁶	<ul style="list-style-type: none"> CINAHL, MEDLINE From 2008 to 2018 	26 studies and 1 SR (> 89,047) ^d	<ul style="list-style-type: none"> Setting: Not stated Older adults (no specific age defined) 	<ul style="list-style-type: none"> Aim: Deprescribe to reduce polypharmacy and use of STOPP interventions to reduce PIMs Intervention type: no restrictions Facilitator of intervention: not stated 	Not stated	<ul style="list-style-type: none"> Reduction of preventable ADEs Polypharmacy PIMs Other relevant outcomes (not specified) 	Critically low	10 (9 RCTs ^{99, 100, 107, 213, 236, 254, 260, 267, 268} , 1 quasi-experimental ²⁶⁹)	84,424 (65+)*

Authors (Year Published)	Databases and Time Frame Searched	# Studies (No. of Participants)	Setting(s) and Population Characteristics	Intervention (Aim, Intervention type, Facilitator of intervention)	Comparison	Outcomes ^a	AMSTAR 2 ⁶⁰	Primary Studies of Interest from SR	
								# Studies (Design)	No. of Participants (Mean Age in years ^b)
Reeve et al (2020) ²⁷⁰	<ul style="list-style-type: none"> CRS-Web, CENTRAL, MEDLINE, EmbaseOvid, ClinicalTrials.gov, World Health Organisation International Clinical Trials Registry Platform. Search date: 22 May 2019 	6 (1,192)	<ul style="list-style-type: none"> Setting: community, residential aged care facilities or hospital. Age 50+ With hypertension or required primary prevention of CVD Prescribed ≥ 1 antihypertensive medication 	<ul style="list-style-type: none"> Aim: withdrawal of antihypertensive medication Intervention type: medication withdrawal Facilitator of intervention: not stated 	Continuation of antihypertensive medication	Primary outcomes: <ul style="list-style-type: none"> Mortality Myocardial infarction Adverse drug reactions and adverse drug withdrawal reactions Secondary outcome ^d	Critically low	5 (5 RCTs ^{151, 156, 158, 159, 271})	832 (60-82)

This table reports key study characteristics of included systematic reviews (n=34). Information on setting and population characteristics, intervention, comparison and outcomes are based on the PICOT question reported in their methodology. We include both information obtained at the systematic review level, as well as information specific to primary studies of our interest within each systematic review (in the rightmost 2 columns of the table).

Abbreviations: RCT: Randomized controlled trials; non-RCT: non-randomized controlled trials; CBA: controlled-before-after studies; ITS: interrupted time series; PIMs: Potentially inappropriate medications; T2DM: Type 2 Diabetes mellitus; HbA1c: glycated hemoglobin; PIPs: Potentially inappropriate prescriptions; BZD: Benzodiazepines; Z-drugs: nonbenzodiazepine drugs; PPI: proton pump inhibitor; CVD: Cardiovascular disease; SR: Systematic Review; CDS: Computerized Decision Support

^a This represents either primary outcomes only or all outcomes of the systematic review if no primary and secondary outcomes were specified.

^b Represented in range of mean ages of participants in included primary studies, if reported by systematic reviews. *Systematic reviews where there are some primary studies that did not report mean ages are indicated with an asterisk.

^c Target medications could refer to a specific medication class (e.g. benzodiazepines), potentially inappropriate medications or prescriptions.

^d indicates that one or more primary studies did not report their sample size.

Secondary outcomes:

^e Medication-related problem, adherence to medication, and quality of life.

^f Patient outcomes and acceptance rates of recommendations.

^g Mortality, falls, cognitive function, adverse drug withdrawal events, quality of life, and hospitalizations.

^h Mortality, hospitalization rates, and recurrence of peptic ulcer disease or adverse events.

ⁱ Adverse drug withdrawal events, psychological and physical health outcomes, quality of life, and medication usage.

^j Satisfaction with care, emergency department visits and hospitalizations.

^k Change in MAI score

^l New morbidity, change in quality of life, changes of physical and mental functioning, adverse drug event, adverse drug reaction, medication error, inappropriate medication, adverse event after discontinuation of medication (safety), process of care (feasibility), User or patient satisfaction, adherence to medication, resource utilization (e.g. use of healthcare resources), costs (e.g. reduction of drug costs, hospital costs)/cost-effectiveness.

^m Cognitive function, depression, and falls.

ⁿ Systolic and diastolic BP, hospitalization, stroke, success rate of withdrawal from antihypertensive drugs over the short term (12 months or less) and long term (greater than 12 months), quality of life of participants, carers, families or a combination, and Falls.

eTable 3: Summary of conclusions of systematic reviews and results of meta-analyses (Level 1)

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
Single Medication Class				
Anticholinergics	Nakham et al. (2020) ⁹³	Not concluded	Concluded; Evidence found; Evidence with mixed effects <ul style="list-style-type: none"> • Mixed effect on reducing anticholinergic burden. 	
Antihyperglycemics	Black et al. (2017) ⁹⁰	Concluded; Evidence not found <ul style="list-style-type: none"> • Limited evidence available regarding deprescribing antihyperglycemic medications 	Concluded; Evidence not found	
	Seidu et al. (2019) ¹⁰¹	Concluded; Evidence found; Evidence with no effect <ul style="list-style-type: none"> • Majority of studies reported no deterioration in HbA1c levels, hypoglycemic episodes, falls or hospitalizations. • No significant differences observed among comparison groups for adverse events and mortality) 	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Significant evidence for achieving deintensification. 	
Antihypertensives	Reeve et al. (2020) ²⁷⁰	Concluded; Evidence found; Evidence with no effect <ul style="list-style-type: none"> • No significant increase in mortality, CVD or stroke 	Concluded; Evidence found; Evidence with mixed effects <i>Positive effects</i> <ul style="list-style-type: none"> • Withdrawal is feasible. <i>Evidence not found</i> <ul style="list-style-type: none"> • There is an absence of data on falls and quality of life. 	
Proton Pump Inhibitors	Wilsdon et al. (2017) ¹⁴⁰	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Some interventions effective at deprescribing inappropriate medicines. 	

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
Psychotropics	Coon et al. (2014) ⁶⁵	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • May be effective in short-term reducing inappropriate prescribing of antipsychotics. 	
	Dou et al. (2019) ¹⁰²	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Evidence of success discontinuing benzodiazepines. 	<p>Favors interventions Outcome: Reduction in medication use Percentage of participants completely tapered off benzodiazepines</p> <ul style="list-style-type: none"> • CBT intervention studies (n=3), OR 1.93 (1.13, 3.29) • Education intervention studies (n=3), OR 5.94 (3.99, 8.83) <p>No effect Outcome: Reduction in medication use Percentage of participants completely tapered off benzodiazepines</p> <ul style="list-style-type: none"> • Melatonin intervention studies (n=3), OR 1.16 (0.63, 2.14)
	Hoyle et al. (2018) ²²⁸	Concluded; Evidence found; Evidence with no effect <ul style="list-style-type: none"> • Little evidence for deleterious effects from interventions to reduce antipsychotic or benzodiazepine medications 	Concluded; Evidence not found <ul style="list-style-type: none"> • Clinical and economic outcomes remain underreported. 	
	Nishtala et al. (2008) ²⁴²	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Significant effect on reducing psychotropic prescribing or use. 	<p>Favors interventions Outcome: Medication use</p> <ul style="list-style-type: none"> • Proportion of residents on hypnotic drugs (n=5), OR 0.576 (0.419, 0.793) • Proportion of residents on antipsychotic drugs (n=5, OR 0.813 (0.635, 1.039)

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
	Parr et al. (2009) ²⁴⁷	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Significant evidence for effectiveness in reducing benzodiazepines. 	<p>Favors interventions <u>Outcome: Reduction in medication use</u> Proportion of patients ceased benzodiazepines, by intervention</p> <ul style="list-style-type: none"> • Brief intervention vs routine care with individual random allocation (n=3), OR 4.37 (2.28, 8.40) • Brief intervention vs routine care with practices random allocation (n=2), OR 2.21 (1.92, 2.55) • Psychological intervention vs routine care (n=3), OR 3.38 (1.86, 6.12) • Psychological intervention and gradual dose reduction (GDR) vs GDR alone at post-cessation (n=7), OR 1.82 (1.25, 2.67) • Psychological intervention and GDR vs GDR alone at follow-up (n=6), OR 1.88 (1.19, 2.97) <p>No effect <u>Outcome: Reduction in medication use</u> Proportion of patients ceased benzodiazepines, by intervention</p> <ul style="list-style-type: none"> • Abrupt substitution of substitutive pharmacotherapy vs abrupt reduction alone (n=3), OR 1.69 (0.60, 4.74) • Substitutive pharmacotherapy and GDR vs GDR alone at post-cessation (n=14), OR 1.30 (0.97, 1.73) • Substitutive pharmacotherapy and GDR vs GDR alone at follow-up (n=5), OR 1.30 (0.77, 2.20) <p>Favors comparison <u>Outcome: Reduction in medication use</u> Proportion of patients ceased benzodiazepines, by intervention</p> <ul style="list-style-type: none"> • Abrupt substitution of substitutive pharmacotherapy vs GDR alone (n=3), OR 0.30 (0.14, 0.64)

<p>Reeve et al. (2017)¹³⁵</p>	<p>Concluded; Evidence found; Evidence with no effect</p> <ul style="list-style-type: none"> • Most studies found no difference in sleep quality and no significant adverse drug withdrawal reactions when tapering or substitution was used. 	<p>Concluded; Evidence found; Evidence with mixed effect</p> <p><i>No effect</i></p> <ul style="list-style-type: none"> • Withdrawal success variable, benefits and sustainability unclear. <p><i>Evidence not found</i></p> <ul style="list-style-type: none"> • Limited evidence available on clinical outcomes. 	<p>No effect</p> <p><u>Outcome: Mortality</u></p> <ul style="list-style-type: none"> • All-cause mortality (n=4), OR 2.08 (0.79, 5.46) • Cardiovascular mortality (n=1), OR 2.04 (0.21, 20.19) <p><u>Outcome: Clinical or patient-centered outcomes</u></p> <ul style="list-style-type: none"> • Myocardial infarction (fatal and non-fatal) (n=2), OR 1.86 (0.19, 17.98) • Stroke (fatal + nonfatal + TIA) (n=3), OR 1.44 (0.25, 8.35) • Quality of life (n=1), OR -0.10 (-0.35, 0.15) <p><u>Outcome: Hospitalization</u></p> <ul style="list-style-type: none"> • Hospitalization (n=1), OR 0.83 (0.33, 2.10) <p>Favors comparison</p> <p><u>Outcome: Surrogate biomarkers outcomes</u></p> <ul style="list-style-type: none"> • Systolic blood pressure (n=5), OR 9.75 (7.33, 12.18) <ul style="list-style-type: none"> <u>Subgroup analysis</u> Duration <ul style="list-style-type: none"> • Less than 12 months (n=3), OR 9.17 (6.62, 11.71) • 12 months or longer (n=2), OR 15.30 (7.48, 23.12) Drug type <ul style="list-style-type: none"> • Diuretics (n=4), OR 10.85 (7.92, 13.78) • Other (n=1), OR 7.40 (3.10, 11.70) • Diastolic blood pressure (n=5), OR 3.50 (1.82, 5.18) <ul style="list-style-type: none"> <u>Subgroup analysis</u> Duration <ul style="list-style-type: none"> • Less than 12 months (n=3), OR 2.68 (0.87, 4.49) • 12 months or longer (n=2), OR 8.70 (4.15, 13.25) Drug type <ul style="list-style-type: none"> • Diuretics (n=4), OR 4.42 (2.03, 6.81) • Other (n=1), OR 2.60 (0.24, 4.96) <p><u>Outcome: Reduction in medication use</u></p> <ul style="list-style-type: none"> • Resumption due to hypertension or other clinical reasons (n=3), OR 3.23 (1.86, 5.61)
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Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
	Sheehan et al. (2018) ¹¹³	Not concluded	<p>Concluded; Evidence found; Evidence with mixed effects</p> <p><i>Positive</i></p> <ul style="list-style-type: none"> • Potential to contribute to psychotropic medication optimization <p><i>No effect</i></p> <ul style="list-style-type: none"> • No evidence suggesting improved clinical and patient important outcomes. 	<p>Favors interventions</p> <p><u>Outcome: Reduction in medication use</u></p> <ul style="list-style-type: none"> • Reduction in psychotropic medications (n=3) ,OR 0.24 (0.14, 0.39) <p>No effect</p> <p><u>Outcome: Reduction in medication use</u></p> <ul style="list-style-type: none"> • Change in psychotropic medications (n=1), OR 0.39 (0.12, 1.19)
Polypharmacy				
Appropriateness (PIP/PIM etc.)	Almutairi et al. (2020) ²⁶²	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Could improve medication appropriateness. 	<p>Favors interventions</p> <p><u>Outcome: Medication appropriateness</u></p> <ul style="list-style-type: none"> • Medication appropriateness (n=10), RR 0.71 (0.60, 0.84) <p>No effect</p> <p><u>Outcome: Medication appropriateness</u></p> <ul style="list-style-type: none"> • Mean difference in change of MAI score (n=2), MD -0.67 (-0.97, -0.37) <p><u>Subgroup analyses</u></p> <p>Intervention</p> <ul style="list-style-type: none"> • Medication review (n=4), RR 0.62 (0.41, 0.93) – favors intervention • Multidisciplinary team meetings (n=1), RR 0.97 (0.92, 1.03) • Staff education (n=4), RR 0.66 (0.43, 1.01) • Computerised clinical decision, RR 0.78 (0.64, 0.95) – favors intervention <p><u>Outcome: Hospital admissions</u></p> <ul style="list-style-type: none"> • Hospital admission (n=9), RR 1.00 (0.93, 1.06) <p><u>Outcome: Clinical and patient-centered outcomes</u></p> <ul style="list-style-type: none"> • Mortality (n=10), RR 0.98 (0.86, 1.11) • Falls (n=8), RR 1.06 (0.89, 1.26)

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
				<ul style="list-style-type: none"> • QoL (n=3), MD 0.16, (-0.13, 0.45) • BPSD (n=2), RR 0.68 (0.44, 1.06)] • Cognitive function (n=2), MD 0.69 (-1.25, 2.64) <p><u>Outcome: Adverse Drug Events</u></p> <ul style="list-style-type: none"> • ADEs (n=2), RR 1.04 (0.96, 1.13)
	Bloomfield et al. (2020) ²⁵³	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Some evidence for reduction in mortality, use of PIMs. 	<p>Favors interventions</p> <p><u>Outcome: All-cause Mortality</u></p> <ul style="list-style-type: none"> • Comprehensive medication review RCTs (n=12), OR 0.74 (0.58, 0.95) <p>No effect</p> <p><u>Outcome: Hospitalizations</u></p> <ul style="list-style-type: none"> • Comprehensive medication review RCTs (n=6), OR 1.07 (0.92, 1.26)
	Castelino et al. (2009) ⁷¹	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Promising results for prescribing optimisation. 	
	Clyne et al. (2016) ¹⁹⁹	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Some interventions appear beneficial in reducing inappropriate prescribing 	
	Dalton et al. (2018) ¹¹⁸	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Can be effective in reducing potentially inappropriate prescribing 	<p>Favors interventions</p> <p><u>Outcome: Potentially Inappropriate Medications</u></p> <ul style="list-style-type: none"> • Reduction in the proportion of patients prescribed PIMs post-intervention (n=3), OR 0.60 (0.38, 0.93)
	Earl et al. (2020) ²⁶⁶	Not concluded	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Some statistically significant differences in polypharmacy or PIMs. 	

<p>Hansen et al. (2018)²⁰⁷</p>	<p>Not concluded</p>	<p>Concluded; Evidence found; Evidence with positive effects</p> <ul style="list-style-type: none"> • Effective in reducing number of drugs taken and improving inappropriate prescribing. 	<p>Favors interventions</p> <p><u>Outcome: Drug use</u></p> <ul style="list-style-type: none"> • Mean number of drugs (n=8), MD -0.96 (-1.53, -0.38) • Change in number of drugs (n=11), MD -0.74 (-1.26, -0.22) <p><u>Subgroup analysis</u></p> <p>Setting</p> <ul style="list-style-type: none"> • Outpatient setting (n=9), MD -0.80 (-1.40, -0.21) • Hospital setting (n=2), MD -0.50 (-1.36, 0.37) – No effect <p>Target person</p> <ul style="list-style-type: none"> • Patient-centred interventions (n=4), MD -1.01 (-2.00, -0.03) • Healthcare professional-centred interventions (n=7), MD -0.51 (-0.80, -0.22) <p>RoB assessment</p> <ul style="list-style-type: none"> • Low RoB random sequence (n=8), MD -0.73 (-1.50, 0.03) – No effect • High RoB allocation concealment (n=3), MD -0.74 (-1.14, -0.34) <p><u>Outcome: Prescribing Appropriateness</u></p> <ul style="list-style-type: none"> • Mean difference in change in MAI score per participant (n=5), MD -5.04 (-7.40, -2.68) • No. of inappropriate drugs (n=7), OR 0.59 (0.38, 0.91) <p><u>Subgroup analysis</u></p> <p>RoB assessment</p> <ul style="list-style-type: none"> • Low RoB allocation concealment (n=3), OR 0.48 (0.20, 1.16) – No effect • High RoB allocation concealment (n=4), OR 0.67 (0.45, 1.01) – No effect <p>No effect</p> <p><u>Outcome: Prescribing Appropriateness</u></p> <p>Mean difference in number of inappropriate drugs (n=3), MD -0.19 (-0.40, 0.02)</p>
<p>Iyer et al. (2008)²⁴⁸</p>	<p>Concluded; Evidence found; Evidence with no effect</p>	<p>Concluded; Evidence found; Evidence with positive effects</p>	

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
		<ul style="list-style-type: none"> Medications may be withdrawn without causing harm or, when symptoms recurred after medication withdrawal, that these could be easily treated by recommending the medications. 	<ul style="list-style-type: none"> Some evidence for specific medicine class withdrawal in some people. 	
	Kallio et al. (2018) ¹²⁴	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> Seem to reduce drug related problems. 	
	Kaur et al. (2009) ⁶¹	Not concluded	Concluded; Evidence found; Evidence with mixed effects <ul style="list-style-type: none"> Mixed effect on reducing inappropriate prescribing 	
	Monteiro et al. (2019) ⁹⁸	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> Some significance of positive impact on potentially inappropriate medicines. 	
	Pruskowski et al. (2019) ²⁰²	Concluded; Evidence found; Evidence with no effects <ul style="list-style-type: none"> No significant difference in additional ED visits or hospitalisations 	Concluded; Evidence found; Evidence with no effects <ul style="list-style-type: none"> No effect found on quality of life (QoL) or satisfaction with care 	

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
	Rankin et al. (2018) ⁷⁹	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Improves appropriate polypharmacy • May be slightly beneficial in reducing potential prescribing omissions. 	<p><i>Favors interventions</i></p> <p><u>Outcome: Medication appropriateness</u></p> <ul style="list-style-type: none"> • Comparison of MAI scores from baseline to follow-up (n= 5), MD -4.76, (-9.20, -0.33) <p><u>Sensitivity analyses</u></p> <ul style="list-style-type: none"> • Comparison of MAI scores from baseline to follow-up (n=4), MD -5.16, (-11.04, 0.72)]* • Comparison of MAI scores from baseline to follow-up (n=3), MD -0.50 (-2.27, 1.28)]* <p><u>Outcome: Potentially inappropriate medications</u></p> <ul style="list-style-type: none"> • Number of PIMs (n=7), SMD -0.22, (-0.38, -0.05) • Proportion of patients with one or more PIM (n=11), RR 0.79, (0.61, 1.02)* <p><u>Sensitivity analyses</u></p> <ul style="list-style-type: none"> • Proportion of patients with one or more PIM (n= 10) – favors intervention [RR 0.79, (0.61, 1.02)]* • Proportion of patients with one or more PIM (n= 9), RR 0.88, (0.72, 1.09)]* <p><u>Outcome: Potential prescribing omissions</u></p> <ul style="list-style-type: none"> • Number of potential prescribing omissions (n=2), SMD -0.81 (-0.98, -0.64) • Proportions of patients with one or more potential prescribing omissions (n=5), RR 0.40 (0.18, 0.85) <p>*In this review, authors conclude that there is effect as long as the majority of the 95% CI lies in the region where intervention is favored.</p>

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
	Shrestha et al. (2019) ²⁰⁵	Not concluded	Concluded; Evidence found; Evidence with mixed effects <i>Positive</i> <ul style="list-style-type: none"> • Can improve medication appropriateness <i>No effect</i> <ul style="list-style-type: none"> • Limited evidence available, but has potential for mortality reduction and cost savings 	
	Thillainadesan et al. (2018) ¹²⁸	Concluded; Evidence found; Evidence with no effects <ul style="list-style-type: none"> • No notable harm observed in intervention groups [appear to be safe] 	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • Can reduce potentially inappropriate medicines. 	
	Thio et al. (2018) ²¹⁸	Concluded; Evidence found; Evidence with negative effects <ul style="list-style-type: none"> • Evidence of relapse of symptoms. 	Concluded; Evidence found; Evidence with mixed effects <i>Positive</i> <ul style="list-style-type: none"> • Evidence of success stopping medication. <i>No effect</i> <ul style="list-style-type: none"> • Equivocal for clinical outcomes. 	
	Tjia et al. (2013) ²⁴⁴	Not concluded	Concluded; Evidence not found <ul style="list-style-type: none"> • Few rigorous intervention studies on reducing medications in frail older adults 	
	Verrue et al. (2009) ⁷³	Not concluded	Concluded; Evidence found; Evidence with mixed effects <ul style="list-style-type: none"> • Mixed evidence for effectiveness on pharmacotherapy in the nursing home setting. 	

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
	Walsh et al. (2016) ²⁰¹	Not concluded	Concluded; Evidence found; Evidence with positive effects <ul style="list-style-type: none"> • May have improvements in prescribing appropriateness in certain contexts. 	Favors interventions <u>Outcome: Medication Appropriateness</u> <ul style="list-style-type: none"> • Summated MAI scores at discharge (n=4), MD -5.27 (-8.44, -2.11) <u>Sensitivity analysis</u> Summated MAI scores at discharge including study at high risk of bias (n=5), MD -5.91 (-8.95, -2.87) <ul style="list-style-type: none"> • Change in summated MAI scores from admission to discharge (n=4), MD -7.45 (11.14, -3.76)
Falls Risk-Increasing Drugs	Hart et al. (2020) ²⁶³	Not concluded	Concluded; Evidence found; Evidence with no effects <ul style="list-style-type: none"> • Limited evidence suggesting no reduction in overall FRID use following the fall-related healthcare encounter 	
Polypharmacy	Johansson et al. (2018) ²³³	Not concluded	Concluded; Evidence found; Evidence with no effects <ul style="list-style-type: none"> • No convincing evidence that the strategies assessed are effective in reducing polypharmacy or have an impact on clinically relevant endpoints • Strategies to reduce polypharmacy had no effect on all-cause mortality 	No effect <u>Outcome: Mortality</u> All pooled studies (n=18), OR1.02 (0.84, 1.23) <u>Subgroup analysis</u> <ul style="list-style-type: none"> • Only RCTs (n=16), OR1.05 (0.85, 1.29) • Studies with short follow-up 2-6 months (n=8), OR1.13 (0.86, 1.50) • Studies with long follow-up 12-18 months (n=10), OR 0.93 (95%CI: 0.69, 1.24)

Page et al. (2016)¹⁴³

Concluded; Evidence found; Evidence with **no** effects

- Some medications can be deprescribed without adverse changes in the specific health outcomes the medications were intended to treat

Concluded; Evidence found; Evidence with **positive** effects

- Feasible to reduce polypharmacy
- May improve longevity.

Favors intervention

Outcome: Mortality

All pooled non-randomized studies (n=2), OR 0.32 (0.17, 0.60)

Outcome: Falls

Number of falls per participant (n=3) – favors intervention [MD -0.11 (95% CI: -0.21, -0.02)]

Outcome: Effect on medication regimen

- Reduction of total number of medications (n=2), MD -0.99 (-1.83, -0.14)
- Reduction of PIMs (n=3), MD -0.49 (-0.70, -0.28)

No effect

Outcome: Mortality

All pooled randomized studies (n=10), OR 0.82 (0.61, 1.11)

Subgroup analysis

Intervention type

- Randomized studies with only patient-specific interventions (n=8), OR 0.62 (0.43, 0.88) – **favors intervention**
- Randomized studies with educational programs interventions (n=2), OR 1.21 (0.86, 1.69)

Age

- Randomized studies with patients ≥ 80 years (n=7), OR 0.98 (0.74, 1.31)
- Randomized studies with patients < 80 years (n=3), OR 0.64 (0.40, 1.04) – **favors intervention**

Dementia status

- Randomized studies with participants living with dementia (n=5), OR 0.89 (0.63, 1.27)
- Randomized studies with cognitively-intact people (n=5), OR 0.64 (0.36, 1.13)

No. of medications

Medication Category	Authors (Year Published)	Conclusions of Systematic Reviews related to Harm from Interventions	Conclusions of Systematic Reviews related to Benefits from Interventions	Meta-analysis Results [Statistic (95% Confidence Interval)]
				<ul style="list-style-type: none"> • Randomized studies of deprescribing of single medication class - antipsychotics (n=5), OR 0.59 (0.33, 1.07) <p><u>Outcome: Falls</u></p> <ul style="list-style-type: none"> • Risk of experiencing at least one fall (n=5), OR 0.65 (0.40, 1.05) <p><u>Outcome: Adverse drug withdrawal events</u></p> <ul style="list-style-type: none"> • Adverse drug withdrawal events associated with deprescribing of antipsychotics (n=3), OR 1.24 (0.51, 3.01) • Change in the neuropsychiatric index associated with deprescribing of antipsychotics (n=3), OR 2.65 (0.52, 4.77) • Successful withdrawal of deprescribing of benzodiazepines (n=3), OR 1.38 (0.21, 9.08) • Non-vertebral fractures of deprescribing bisphosphonates, OR 0.94 (0.50, 1.78) <p><i>Favors control</i></p> <p><u>Outcome: Surrogate biomarkers outcomes</u></p> <ul style="list-style-type: none"> • Systolic blood pressure when deprescribing diuretics (n=3), MD 9.73 (8.13, 11.33) • Diastolic blood pressure when deprescribing diuretics (n=3), MD 3.99 (3.04, 4.94)

This table aggregates conclusions made by authors of systematic reviews, based on their evidence synthesis process. We categorized their conclusions on three levels – (1) whether outcomes of harm or benefit was clearly evaluated; (2) if evaluated, whether evidence was found or not; (3) if evidence found, what was that evidence? Where appropriate, a summary of the evidence found is provided.

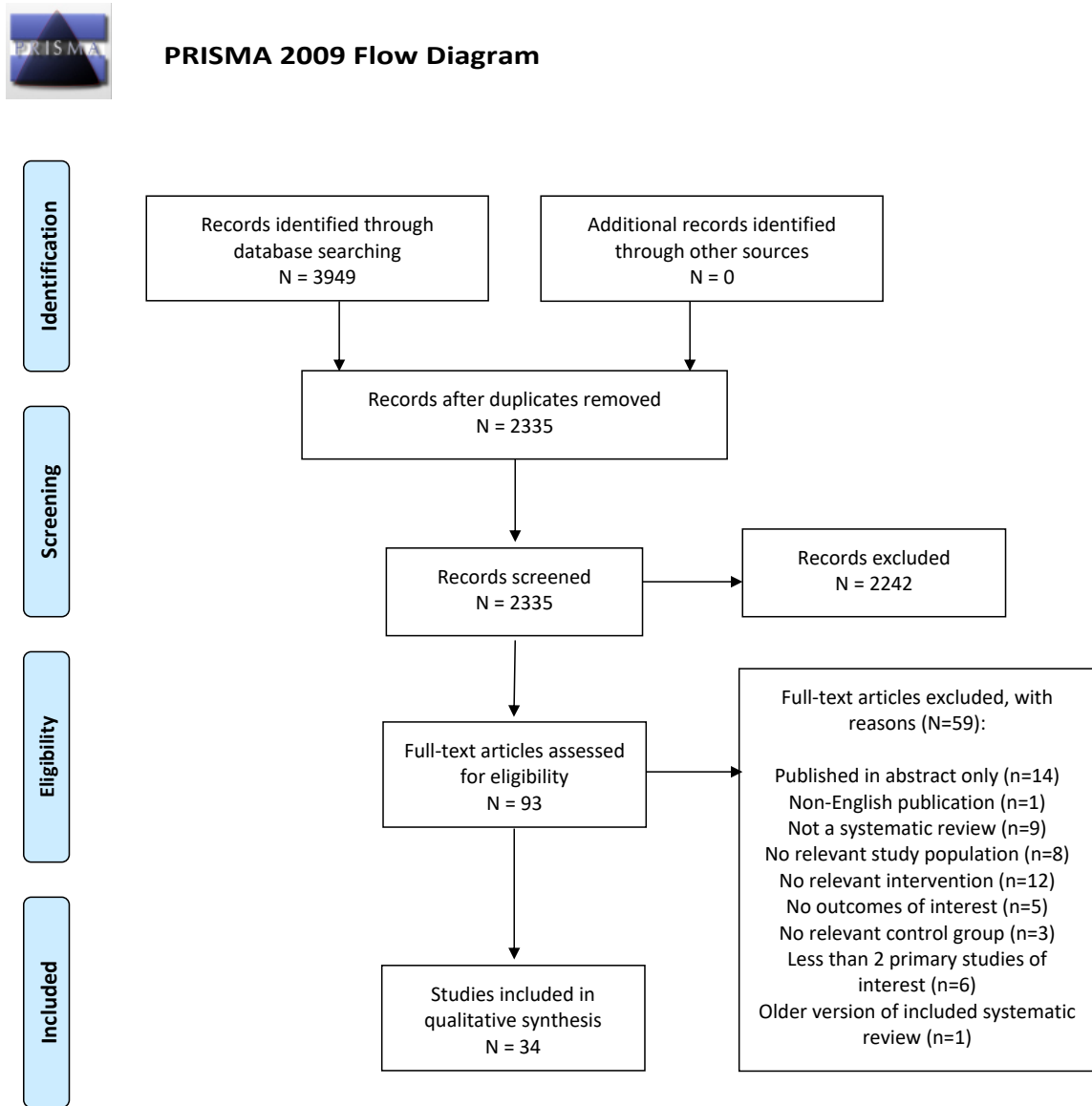
Abbreviations: CI: confidence interval; HbA1c: glycated hemoglobin; MD: mean difference; OR: odds ratio; RR: risk ratio; SMD: standardized mean difference

eTable 4: AMSTAR-2 quality assessment of included systematic reviews

	AMSTAR 2 ⁶⁰ Domains																Confidence Rating
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Kaur 2009 ⁶¹	x	x	x	x	x	x	x	x	x	x	NA	NA	x		NA		Critically low
Coon 2014 ⁶⁵		-	x	-			x	-		x	NA	NA			NA		Low
Castelino 2009 ⁷¹	x	x	x	x	x	x		-	x	x	NA	NA	x		NA	x	Critically low
Verrue 2009 ⁷³	x	x	x	x	x	x	x	-	x	x	NA	NA	x	x	NA		Critically low
Rankin 2018 ⁷⁹				-						x	x						Low
Black 2017 ⁹⁰			x	-			x			x	NA	NA	x		NA		Critically low
Nakham 2020 ⁹³			x	-			x	-	-	x	NA	NA	x		NA		Critically low
Monteiro 2019 ⁹⁸	x	-	x				x	-	x	x	NA	NA			NA		Critically low
Seidu 2019 ¹⁰¹				-			x			x	NA	NA		x	NA		Low
Dou 2019 ¹⁰²		x	x	x	x	x	x			x	x	x			x		Critically low
Sheehan 2018 ¹¹³		-	x	-		x	x				x	x		x	x		Critically low
Dalton 2018 ¹¹⁸				-			x	-		x					x		Critically low
Kallio 2018 ¹²⁴		x	x	x		x	x		x	x	NA	NA	x		NA		Critically low
Thillainadesan 2018 ¹²⁸		x	x	x		x	x			x	NA	NA			NA		Critically low
Reeve 2017 ¹³⁵	x	x	x	x			x	x		x	NA	NA		x	NA		Critically low
Wilsdon 2017 ¹⁴⁰				-			x		-	x	NA	NA	x		NA		Critically low
Page 2016 ¹⁴³			x	x								x			x		Critically low
Clyne 2016 ¹⁹⁹		x	x	-		x	x			x	NA	NA			NA		Critically low
Walsh 2016 ²⁰¹		-	x	-			x	x		x					x		Critically low
Pruskowski 2019 ²⁰²		-	x	x			x			x	NA	NA	x	x	NA		Critically low
Shresta 2019 ²⁰⁵			x	x		x	x			x	NA	NA	x	x	NA		Critically low
Hansen 2018 ²⁰⁷				-			x	x		x					x		Critically low
Thio 2018 ²¹⁸		x	x	-			x	-		x	NA	NA			NA		Critically low
Hoyle 2018 ²²⁸		-	x	x		x	x	x		x	NA	NA			NA		Critically low
Johansson 2018 ²³³		x		-					x	x	x	x	x	x	x		Critically low
Nishtala 2008 ²⁴²		x	x	x		x		x	x	x		x	x	x	x	x	Critically low
Tjia 2013 ²⁴⁴		x	x	x			x	x	x	x	NA	NA	x		NA		Critically low
Parr 2009 ²⁴⁷		x	x	x		x	x	x	x	x	x	x	x	x	x		Critically low
Iyer 2008 ²⁴⁸		x	x	x	x		x	-	x	x	NA	NA	x	x	NA		Critically low
Bloomfield 2020 ²⁵³				x			x				x			x	x		Critically low
Almutairi 2020 ²⁶²			x	x	x		x	x		x		x	x				Critically low
Hart 2020 ²⁶³		x	x	x			x	x		x	NA	NA	x	x	NA		Critically low
Earl 2020 ²⁶⁶	x	x	x	x	x	x	x	-	x	x	NA	NA	x	x	NA		Critically low
Reeve 2020 ²⁷⁰			x												x		Low

x denotes a weakness in that domain, while – denotes a partial weakness in that domain. Shaded columns represent domains considered critical by Shea et al⁶⁰. One critical flaw results in an overall confidence rating of low, while more than one critical flaw results in an overall confidence rating of critically low.

eFigure 1: PRISMA diagram summarizing number of studies identified, screened, eligible and included in final review from literature search



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