HTA Austria
Austrian Institute for
Health Technology Assessment
GmbH

Structured Medication Review for Polypharmacy

Systematic Review

Appendix

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Content

List of figures

List of tables

1 Appendix

1.1 RQ1: Evidence on effectiveness, safety, organisational aspects and costs of structured medication reviews

1.1.1 Literature selection

literature selection from 492 records

A total of 492 records were available for literature selection. The literature was reviewed independently by two researchers (RJ, JK). Differences were resolved through discussion and consensus or by involving a third researcher. The selection process is shown in Figure A-1:

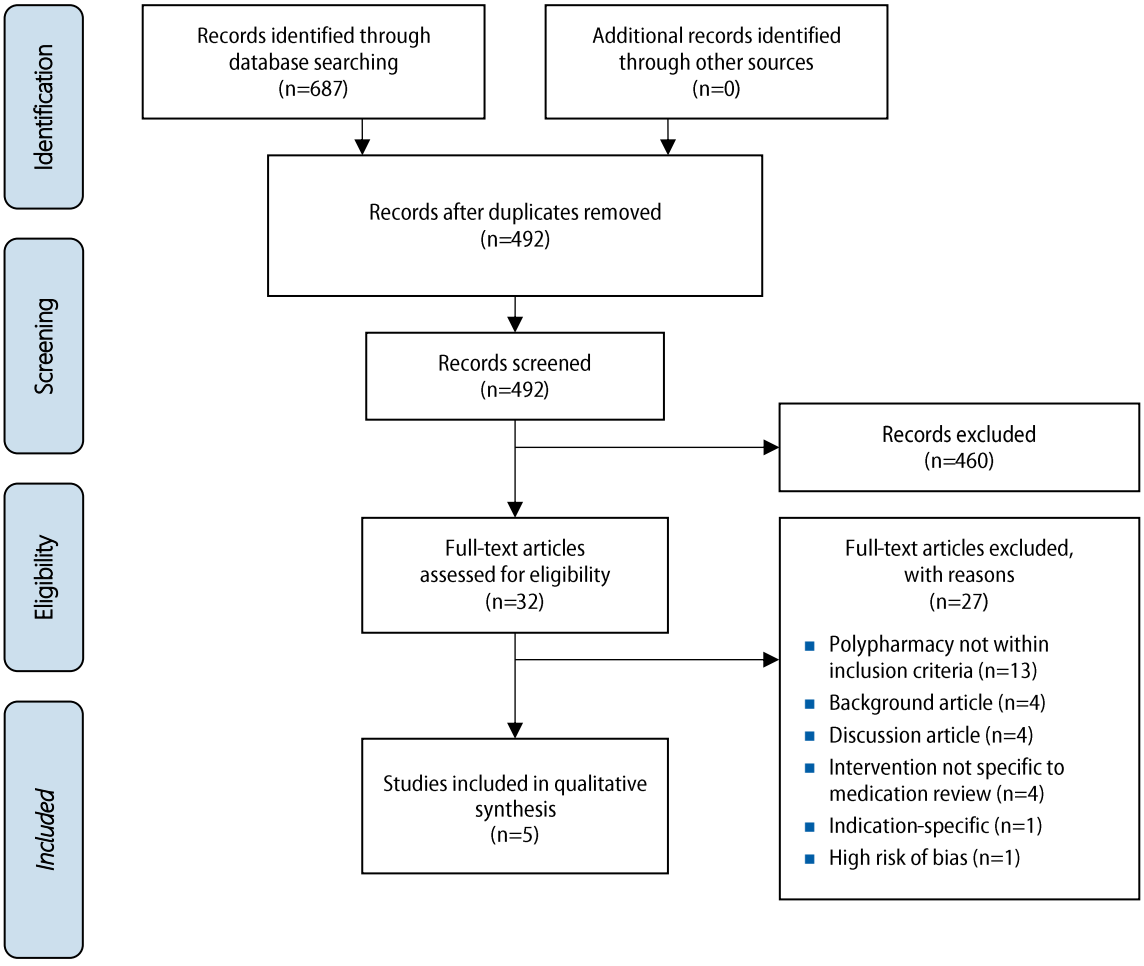

Figure A- 1: Literature selection process (PRISMA Flow Diagram)

Table A- 1: Fulltext articles excluded due to unspecific inclusion criteria in regard to population or intervention

Author, Year [Reference]	Study type	Exclusion reason
Ali 2020 [1]	Systematic review	Intervention not specific to medication review
Bezerra 2022 [2]	Systematic review	Intervention not specific to medication review
Bloomfield 2020 [3]	Systematic review	Polypharmacy not within inclusion criteria
Carollo 2024 [4]	Systematic review	Polypharmacy not within inclusion criteria
Chua 2024 [5]	Umbrella review	Polypharmacy not within inclusion criteria
Clarkson 2023 [6]	Systematic review	Polypharmacy not within inclusion criteria
Cole 2023 [7]	Systematic review	Intervention not specific to medication review
Degen 2025 [8]	Systematic review	Polypharmacy not within inclusion criteria
Earl 2020 [9]	Systematic review	Intervention not specific to medication review
Goncalves 2025 [10]	Systematic review	Polypharmacy not within inclusion criteria
Kroon 2021 [11]	Umbrella review	Polypharmacy not within inclusion criteria
Linsky 2025 [12]	Systematic review	Polypharmacy not within inclusion criteria
Masnoon 2024 [13]	Systematic review	Polypharmacy not within inclusion criteria
Okeowo 2023 [14]	Systematic review	Polypharmacy not within inclusion criteria
Quek 2024 [15]	Systematic review	Polypharmacy not within inclusion criteria
Seppala 2021 [16]	Systematic review	Polypharmacy not within inclusion criteria
Zhou 2023 [17]	Systematic review	Polypharmacy not within inclusion criteria

1.1.2 Umbrella reviews

Table A- 2: Data extraction table for umbrella reviews on interventions for people with polypharmacy

Author, Year	Ali et al., 2022 [18]	Keller et al., 2024 [19]
Study methods		
Title	Interventions to address polypharmacy in older adults living with multimorbidity: Review of reviews	Cumulative update of a systematic overview evaluating interventions addressing polypharmacy
Study design	Umbrella review (Review of reviews)	Umbrella review (Systematic overview)
Population	■ Adults with chronic conditions taking five or more medications, or as indicated in the study	■ Adults (age ≥ 18 years)
Intervention	Any polypharmacy intervention that may include the following: role (i.e., pharmacist), a program (medication optimisation clinic), tools, decision aids, or computer support systems to deprescribe, taper, or optimize medications. A polypharmacy intervention may be explicit (e.g., polypharmacy questionnaire) or implicit (e.g., medication review by a pharmacist) in nature	Interventions addressing polypharmacy, such as: administering type I, type II, type III medication reviews; deprescribing; patient education and counseling; case conferences with interdisciplinary teams; identifying potentially inappropriate medications or potential prescribing omissions; use of pharmacogenomics; health care professional education and clinical decision support; simplifying medication regimes; using guidelines or tools or medication management tools
Comparator	Usual care or standard approaches to medication management	NR
Outcomes	■ Clinical outcomes: mortality (all-cause), morbidity (hospitalisation, adverse events related to medication), health related quality of life ■ Disease-specific risk factors: improvements in cognitive functioning, blood pressure, glucose control, mood, medication adherence, mobility, falls, fatigue, instrumental activities of daily living, frailty, fractures, medication burden	■ clinical and functional outcomes, ■ medication-related process outcomes (e.g, reduction in PIMs or PPOs, increase in medication appropriateness or medication adherence), ■ health care use and economic outcomes, and ■ acceptability of the intervention among patients and clinicians.
Setting	Community-based; primary care, nursing homes; interventions that could be conducted in the primary care setting	No restrictions
Included study type	Systematic reviews	Systematic reviews (with or without meta-analyses)
Additional inclusion criteria	NR	■ SR should have an a priori defined protocol ■ Definition of polypharmacy in review or term in the search strategy
Additional exclusion criteria	■ Pregnant women, children; adults in long-term care or nursing homes	SRs focusing on: ■ low- to middle-income countries ■ antibiotic stewardship ■ only about inappropriate prescribing or medication adherence ■ only one medication class
Systematic search period	From inception to April 2019	From 2017 to October 2022[1]
Characteristics of included studies		
Number of included studies per study type	Total: 5 SR Narrative syntheses (n=2): included 4 and 5 studies Meta-analyses (n=3): included studies 4, 12 and 25 studies	14 SRs (7 meta-analyses) With a total of 179 unique studies (80% cited only in one SR) Number of included studies per SR: 7 – 58 (mean: 16) Included only RCTs (n=4) Included RCTs and observational studies (n=10)

[1] Also included systematic reviews from a previous overview article with a search period from January 2004 to February 2017.

Author, Year	Ali et al., 2022 [18]	Keller et al., 2024 [19]
Risk of bias in included studies	AMSTAR 2 rating: Low (n=3); Moderate (n=1); High (n=1) Evidence quality as assessed by included SRs: Rating per outcome: low to very low	AMSTAR 2 rating[2]: Mean (SD): 10.8 (2.8) of 16 Meta-analyses: 12.6 (2.8) of 16 Narrative: 9 (1.5) of 16 Evidence quality as assessed by included SRs: Rating per outcome: low to very low
Total of included participants	Range: 1925 – 61006	NR
Patient characteristics	■ Mean age range: 64.4 – 87.7 ■ Male percentage range: 20 – 100% ■ chronic conditions of participants asthma, diabetes, dyslipidemia, hypertension, cardiovascular disease, and dementia (n=1); NR (n=4) ■ The mean number of medications taken daily by participants ranged from 5.7 to 9.4.	■ focus on adults aged ≥ 65 years (n=10) ■ inclusion criterion presence of multimorbidity or having at least 1 chronic disease (n=5) ■ focus on patient populations with psychiatric diagnoses (n=1) ■ focused on patient populations with cardiometabolic chronic diseases (i.e., stroke, heart disease, or type 2 diabetes) (n=1)
Intervention characteristics	■ explicit screening tools (criteria-based tools, e.g. Beers criteria, STOPP/START (Screening Tool of Older Persons' Prescriptions and Screening Tool to Alert to Right Treatment) criteria, ■ implicit screening approaches (judgment- or expert opinion–based tools), e.g. Medication Appropriateness Index. ■ The operational components of the polypharmacy interventions largely included extended pharmacist consultations, medication reviews, and patient education.	■ Medication reviews ■ Pharmacogenetic testing ■ Physician- or patient-focused educational programs ■ Guidelines or criteria (Beers Criteria, STOPP/START) ■ Tools based on guidelines ■ Consultancy services ■ Multidisciplinary teams ■ Home safety checklists ■ Computerised clinical decision support ■ Geriatric assessments
Setting	Acute care hospitals, long-term care facilities, primary care, urgent care centres, outpatient clinics, community and centralised pharmacies, home health care	■ primary care, outpatient care or community setting (n=12) ■ only hospital setting (n=1) ■ nursing homes or other long-term care facilities (n=8)
Follow-up	6 weeks – 18 months (n=2)	NR across studies
Effectiveness		
Drug-related problems (adverse effects, interactions) identified with the intervention	NR	NR
Change in number of drugs or dose	NR	5 SRs: ■ With meta-analysis (n=1): reduction in the total number of medications (mean difference [MD], −0.99; 95% CI, −1.83 to −0.14) ■ Narrative (n=4): reduction (n=1), mixed effects (n=2), null effect (n=1)
Potentially inappropriate medications	Significant reductions in potentially inappropriate prescribing across all 5 SRs	5 SRs: With meta-analysis (n=2): ■ significant reduction in the number of PIMs (standardized MD [SMD], −0.22; 95% CI, −0.38 to −0.05 (but no significant difference in the proportion of patients with at least 1 PIM (risk ratio [RR], 0.79; 95% CI, 0.61-1.02) (n=1)

[2] The authors did not report AMSTAR 2 rating as "low", "moderate" or "high", but provided sum scores.

Author, Year	Ali et al., 2022 [18]	Keller et al., 2024 [19]
		■ significant reduction in the number of PIMs: MD, −0.49; 95% CI, −0.70 to −0.28) (n=1) Narrative (n=3): all mixed-effects Medication appropriatenss 6 SRs: ■ Improvement (n=4), mixed effects (n=2)
Potential prescribing omissions	NR	2 SRs: ■ meta-analysis (n=1): significant reduction in the number of PPOs (SMD, −0.81; 95% CI, −0.98 to −0.64) and a reduction in the proportion of patients with at least 1 PPO (RR, 0.40; 95% CI, 0.18-0.85).13 ■ narrative (n=1): included 1 study in which PPOs decreased
Safety		
Morbidity	NR	NR
Adverse drug events and adverse drug withdrawal events due to the intervention	3 SRs: No significant differences between polypharmacy and usual care	Medication-related problems, including adverse drug reactions and drug-drug interactions: 8 SRs: Reduction (n=3), mixed effects (n=4), null effect (n=1) Falls: Meta-analysis: ■ incidence of falls (n=1): non-significant RR of 0.87 (95% CI, 0.57-1.31) for ■ risk of experiencing at least 1 fall (n=1): OR of 0.65 (95% CI, 0.40-1.05) ■ with a fall risk incidence (n=1) of 1.04 (95% CI, 0.86-1.26) and a risk difference of 0.01 (95% CI, −0.06 to 0.09) ■ rate of falls (n=2): null effect in one SR (rate ratio, 0.98; 95% CI, 0.63-1.51), while the other did not conduct a pooled analysis, but found a reduction based on 1 study ■ number of falls (n=5): MD of −0.11 (95% CI, −0.21 to 0.02) (n=1); null effect with only one study included (n=3); reduction (n=1) Narrative (n=5): Reduction (n=2), mixed effects (n=1), null effects (n=2)
Mortality	3 SRs: no differences between intervention and usual care (of these, 1 SR: trend towards reduced mortality for longer follow-up period)	5 SRs: Null effect (n=4), mixed effects (n=1) Meta-analysis (n=2) ■ OR of 1.02 in all studies examining all-cause mortality (95% CI, 0.84-1.23), an OR of 0.93 (95% CI, 0.69-1.24) among studies with longer follow-up periods (12-18 months), an OR of 1.13 (95% CI, 0.86-1.50) among studies with shorter follow-up periods (2-6 months), and an OR of 1.05 (95% CI, 0.85-1.29) among randomised clinical trials (n=1) ■ OR of 0.82 (95% CI, 0.61-1.11) among randomised studies and an OR of 0.32 (95% CI, 0.17-0.60) among nonrandomised studies (n=1)
Hospitalisations	* Reported as composite outcome	10 SRs (hospitalisations and/or readmissions): Meta-analysis (n=2):

Author, Year	Ali et al., 2022 [18]	Keller et al., 2024 [19]
		■ slight increase for low-intensity intervention (RR, 1.22, 95% CI, 1.07-1.38) and reduction for high-intensity intervention (RR, 0.86; 95% CI, 0.79-0.95) (n=1); ■ null effect with regard to hospitalisations (RR, 0.88; 95% CI, 0.78-1.00) (n=1) Narrative (n=8): ■ mixed (n=5), null effects (n=2), decreased effect (n=1)
Emergency department visits	* Reported as composite outcome	4 SRs: Meta-analysis (n=1): ■ reduction in ED visits (RR 0.68; 95% CI, 0.48-0.96) (n=1) Narrative (n=3): ■ null-effect (n=1)*; reduction (n=1)*, mixed-effects (n=1) *both SRs only included one study for this outcome
Composite outcomes	Hospitalisations and emergency department visits: 4 SRs: Benefit (n=2) in terms of fewer hospitalisations and emergency department visits, when compared with usual care[3]	NR
Organisational domain		
Professional groups involved	The primary polypharmacy interventions in most of the studies in included reviews were led by pharmacists (and 2 of 5 reviews limited their foci to pharmacist-led interventions), while a few also reported physician-led or multidisciplinary team–led interventions (involving GPs, geriatricians, pharmacists, and residential care staff).	Medication reviews: ■ Pharmacist-led (n=12) ■ Physician-led (n=6) ■ Nurse-led (n=3) ■ Unspecified (n=2) ■ Multi-disciplinary interventions (n=6)
Time requirements	NR	NR
Influence on the relationship between healthcare providers	NR	NR
Patient domain		
Adherence to therapy	Improved medication adherence across all 5 SRs	5 SRs: Increase (n=2), mixed effects (n=3)
Health literacy	NR	NR
Health-related quality of life	5 SRs: No significant improvements when compared to usual care	8 SRs: Increase in individuals receiving the intervention (n=1), mixed effects (n=4), null effects (n=3)
Influence on the relationship between patients and healthcare providers	NR	2 SRs reported on outcomes assessing the acceptability of the intervention among patients and clinicians. These included acceptance or adoption of the medication-related recommendations: ■ Positive acceptability (n=1), wide variation (16%-99%) of intervention adoption rates (n=1)

[3] Type of findings (mixed or null) not reported for the other two SRs.

Author, Year	Ali et al., 2022 [18]	Keller et al., 2024 [19]
Economic domain		
Healthcare costs	2 SRs: polypharmacy interventions reduced the use of health care resources and expenditure.	4 SRs: reduction in health care costs associated with polypharmacy interventions 1 SR: no significant change in nearly every study that examined this outcome
Cost analyses	NR	1 SR: ■ estimates of the cost per quality-adjusted life-year gained ranged from £11 885 to £32 466 (€13,466 to €36,805) in the UK and Ireland ■ The cost per PIM avoided was estimated at €1,269 (95% CI, €1400 to €6,302)
Implementation factors		
Facilitators	Assessing the feasibility and practicality of implementation in primary care settings and effective models for interprofessional teamwork is essential initial groundwork.	NR
Barriers	In studies looking at pharmacist-led interventions, a lack of an effective operationalized pathway for teamwork or communication between health professionals conducting medication reviews and the prescriber may have influenced any effect. Similarly, one review of the STOPPSTART tool concluded that success depended heavily on the implementation of the tool. Interprofessional barriers: lack of information sharing (ie, access to patients' clinical information); lack of collaboration across multidisciplinary teams, particularly for pharmacist-led interventions where the pharmacists' recommendations were not at times implemented by corresponding health care providers.	NR
Study conclusion		
Author's conclusion	Polypharmacy interventions are **associated with reductions in PIP** and **improved medication adherence**. However, there is **limited evidence of their effectiveness for clinical outcomes of importance to patients**. Findings from this review highlight the importance of further high-quality research on polypharmacy intervention characteristics, as these are complex interventions. Understanding the influence of the intervention characteristics on clinical and intermediate outcomes will help guide and refine clinical practice. Further, **understanding the implementation** of these intervention characteristics **may be just as, if not more important than, studying the characteristics themselves.**	While the evidence base for polypharmacy-related interventions has expanded since 2019, gaps in research persist. Understanding the most useful interventions for specific high-risk populations remains a key priority. Our updated systematic overview reveals **mixed findings** on interventions addressing polypharmacy. They show **promise in reducing potentially inappropriate medications and prescribing omissions** but **limited evidence in reducing mortality, hospitalizations, readmissions, or falls.**

Abbreviations: CI – confidence interval; ED – emergency department; MD – mean difference; N – number; NR – not reported; OR – odds ratio; PIM – potentially inappropriate medication; PPO – potential prescribing omission; RCT – randomised controlled trial; RR – risk ratio; SD – standard deviation; SMD – standardized mean difference; SR – systematic review; START – Screening tool to alert to right treatment; STOPP – Screening tool of older persons' potentially inappropriate prescriptions; UK – United Kingdom

1.1.3 Systematic reviews

Table A- 3: Data extraction table for systematic reviews on medication reviews for people with polypharmacy

Author, Year	Bülow et al., 2023 [20]	Omuya et al., 2023 [21]	Tasai et al., 2021 [22]
Study methods			
Title	Medication review in hospitalised patients to reduce morbidity and mortality	A systematic review of randomised-controlled trials on deprescribing outcomes in older adults with polypharmacy	Impact of medication reviews delivered by community pharmacist to elderly patients on polypharmacy: A meta-analysis of randomized controlled trials
Study design	Systematic review	Systematic review	Systematic review
Population	■ Hospitalised adult patients	■ 65 years or older ■ Five or more prescription or regular medications/drugs	■ 65 years or older ■ Four or more prescribed medications
Intervention	■ Any medication review of a patient's pharmacotherapy delivered by a healthcare professional with the aim of optimising medication use and improving health outcomes. ■ Evaluation of each medication's relevance, benefit and harms in relation to the patient ■ Intervention results in a recommendation or a direct change in the medication	■ Deprescribing interventions had to examine the complete medication profile	■ Medication review delivered by community pharmacists
Comparator	■ Usual care, or ■ comparing two or more types of medication reviews	■ Usual care (which could include medication review if this was a usual practice in the study setting)	NR[4]
Outcomes	Primary outcomes: ■ Mortality (all-cause) Secondary outcomes: ■ Mortality (due to adverse drug events) ■ Hospital readmissions (all-cause, or due to adverse drug events) ■ Hospital emergency department contacts (all-cause, or due to adverse drug events) ■ Adverse drug events (defined as when someone is harmed by a medication) ■ Health-related quality of life	Minimum of two outcomes: ■ measurement whether the intervention attempted to reduce the participant's number or dose of drugs ■ additional clinical and/or economic outcome	Measured one of the following outcomes: ■ Hospitalisation ■ Emergency department visit ■ Quality of life ■ Adherence
Setting	Inpatient setting	NR	Community pharmacy setting
Included study type	RCTs	RCTs	RCTs
Additional inclusion criteria	■ Any language ■ Published or unpublished ■ Randomisation on an individual level or an aggregated level (i.e. cluster-randomised trials)	NR	■ Studies were included irrespective of language of publication

[4] Not reported within inclusion criteria. However, in description of results, the control group is referred to as "those who received usual care".

Author, Year	Bülow et al., 2023 [20]	Omuya et al., 2023 [21]	Tasai et al., 2021 [22]
Additional exclusion criteria	■ Trials of outpatients ■ Patients solely seen in the emergency department (i.e. not admitted to a hospital) ■ Paediatric patients ■ Trials aimed solely at increasing a patient's knowledge about current medication, improving adherence or reducing costs; ■ Trials in which the results of medication review were to be primarily implemented after discharge from hospital (e.g. intervention consisting of a letter to the patient's general practitioner); ■ Trials reviewing only portions of a patient's medication related to a specific condition or to a single class of medications (e.g. only diabetes medications or antidepressants were reviewed).	■ Articles not in English ■ Articles that did not have a clear intervention to reduce drugs ■ Articles that did not meet the inclusion criteria	NR
Systematic search period	From January 2014 to January 2022[5]	From inception to April 2022	From inception to January 2018
Characteristics of included studies			
Number of included studies per study type	25 RCTs; randomised at individual level (n=22) or cluster-randomised (n=3). Of these, 21 studies were included in quantitative synthesis (meta-analysis)[6]	14 RCTs	4 RCTs[7] included in qualitative synthesis; of these 3 studies were included in quantitative synthesis (meta-analysis)
Risk of bias in included studies	No overall risk of bias reported. Domain-specific risk of bias assessments within systematic review full-text (Figure 3).	Low risk of bias (n=7), unclear risk of bias (n=6), high risk of bias (n=1)	Low risk of bias (n=3), unclear risk of bias (n=1)
Total of included participants	15,076 participants	8,813 participants (4,414 IG vs. 4,399 CG)	4,633 participants (Number of participants in IG vs. CG: NR)
Patient characteristics	■ Patients aged 65 years or older (n=9), 70 years or older (n=2), 75 years or older (n=2), 80 years or older (n=1) ■ Mean trial participant age around 75 years (range of means: 53 to 87 years) ■ Mean proportion of women 55% (range of means: 40% to 71%) ■ Mean number of medications per participant: 9 medications (range of means: 7 to 16 medications)	Patients aged 65 years and older. Frailty, average age, and mean number of drugs varied depending on the health care setting where investigators conducted their research.	Patient mean age ranging from 74 to 75.9 years. Polypharmacy definition within included studies: four medications (n=1), five medications (n=2) or six medications (n=1)

[5] Publications prior to 2014 were identified in previous versions of the Cochrane review.

[6] Four trials were not included in any of the meta-analyses due to incomplete data or methodological issues; instead, the results from these studies were reported descriptively only.

[7] Of the four RCTs included in the review, one was not included in the quantitative meta-analysis because no sufficient data could be retrieved as the authors reported quality of life measured by the 36-Item Short Form Health Survey (SF-36) in the form of line graph illustration with the differences between groups and p-values for only two SF-36 domains.

Author, Year	Bülow et al., 2023 [20]	Omuya et al., 2023 [21]	Tasai et al., 2021 [22]
Intervention characteristics	■ Compared medication review with standard care (n=20), or comparing two different types of medication reviews with standard care (n=4), or comparing two different types of medication reviews (n=1) <u>Content of the medication reviews:</u> ■ Non-criteria based (n=19) ■ Published criteria (n=6), including STOPP criteria (n=2)[8], computerised decision support system encompassing the STOPP/START criteria, i.e. SENATOR software (n=1), or the STRIP software (n=1), or the STOPPFrail criteria (n=1), or a web-based clinical decision support system (MiniQ) (n=1) <u>Co-interventions:</u> ■ The intervention group received co-interventions (e.g. discharge counselling or written information to a primary care physician) in addition to a basic medication review (n=19) ■ No co-interventions, i.e. interventions were basic medication reviews (n=6) <u>Implementation:</u> ■ Written recommendation to the prescribing physicians (n=6), or ■ discussed with the prescribing physicians (n=8), or ■ both discussed and written down (n=6), or ■ no specification on medication review delivery (n=5)	■ Deprescribing interventions used medication reviews, interdisciplinary interventions, staff education and computerised systems ■ Most common drugs deprescribed: anticholinergics, proton pump inhibitors and antiplatelet drugs. ■ Criteria used: STOPP/START or STOPPFrail criteria (n=5), Beers criteria (n=2), other guides, templates and other decision support tools (n=4)	■ Clinical medication review, which included assessing and resolving DRPs (n=4) ■ Pharmacists had access to patients' medical records (n=4) <u>Detail of medication review:</u> ■ Identify DRP and provide (a) educating the patient about their drug regimen and their medical condition(s); (b) implementing compliance-improving strategies such as drug reminder charts; and (c) rationalising and simplifying drug regimens in collaboration with the patient's GP (n=1) ■ Assessment of the medicines therapy including identifying DRPs, preparing a care plan to help resolve the drug therapy problems (recommendations to the prescriber, patient and making other necessary referrals) and then ongoing follow-up with the patient (n=1) ■ Medication review with follow-up, the pharmacist agreed with patients on certain therapeutic objectives to be reached regarding their pharmacotherapy, resolve, or improve the identified DRPs and negative outcomes associated with medication (n=1) ■ Comprehensive medication review and DRP assessment, attempted to resolve as many DRPs as possible through patient education and/or physician notification (n=1)
Setting	■ Departments of internal medicine (n=9), ■ cardiology department (n=1), ■ nephrology department (n=1), ■ surgical departments (n=2), ■ acute admission departments (n=3), ■ general medicines service (n=1), ■ both internal medicine and surgical departments (n=4), ■ tertiary medical referral hospital (n=2), ■ without department specification (n=2) <u>Regional variation:</u> United States (n=2), Canada (n=1), Brazil (n=1), South Korea (n=1), Europe (n=18), Multinational (n=2)	■ Primary care or outpatient sites (n=8) ■ Nursing home/long-term care facilities (n=3) ■ Community pharmacies (n=2) ■ Hospital (n=1) <u>Regional variation:</u> Europe (n=11), North America (n=2), Asia (n=1)	■ Community pharmacy setting (n=4) <u>Regional variation:</u> All studies were conducted in high-income western countries, which included European countries: Denmark, Germany, the Netherlands, Northern Ireland, Portugal, Republic of Ireland, and Sweden (n=1), New Zealand (n=1), Spain (n=1), and United States (n=1)
Follow-up	Range from 1 to 20 months	Range from 1.5 months to 24 months	Range from 6 months (n=3) to 18 months (n=1)

[8] Of these two trials, one also used the START criteria

Effectiveness			
Drug-related problems (adverse effects, interactions) identified with the intervention	Medication reviews that resulted in a recommendation for medication changes: Range from 58% to 91% (n=5)	NR	NR
Change in number of drugs or dose	NR	■ More drugs reduced in IG vs. CG (n=12, statistically significant in n=10) ■ Higher reduction of dose of drugs in IG vs. CG, without statistical significance (n=1) ■ No statistically significant difference between groups (n=1)	NR
Potentially inappropriate medications	NR	NR	NR
Potential prescribing omissions	NR	NR	NR
Safety			
Morbidity	NR	NR	NR
Adverse drug events and adverse drug withdrawal events due to the intervention	Adverse drug events (n=1): RR 1.08, 95% CI 0.53 to 2.18 Falls (n=2): RR 0.69, 95% CI 0.33 to 1.46 HR 0.96, 95% CI 0.79 to 1.15 Falls and non-vertebral fractures (n=1): RR 0.90, 95% CI 0.48 to 1.69 for falls RR 0.23, 95% CI 0.03 to 1.95 for non-vertebral fractures Adverse events and adverse drug events as composite outcome (n=1): NR[9]	Adverse drug events: ■ Restart of deprescribed medications (n=6), ranging from 9.6% to 34.3% of the medications stopped Adverse drug withdrawal events: ■ Adverse drug withdrawal events and adverse drug events (n=2), of which one study had adverse drug withdrawal events in 1.81%, requiring restart of those medications Falls: Primary outcome: ■ No statistically significant difference in IG vs. CG (n=2) Including secondary outcomes: ■ No statistically significant difference in IG vs. CG (n=5) ■ Statistically significant decrease in IG vs. CG (n=1)	NR
Mortality	All-cause mortality (n=18 with 10,108 participants): Median follow-up 6 months (range 1 to 20 months) Illustrative comparative risk (95% CI)*: Assumed risk with standard care: High-risk population*: 200 per 1000 Very high-risk population*: 400 per 1000	Including secondary outcomes: ■ No statistically significant difference in IG vs. CG (n=8) ■ Statistically significant fewer deaths in IG vs. CG (n=1) ■ Higher number of deaths in IG vs. CG, without statistical significance (n=1)	NR

[9] Authors state that they were unable to get separate data on adverse drug events and therefore did not include data for this outcome.

	Corresponding risk with medication review: High-risk population*: 194 per 1000 (174 to 216) Very high-risk population*: 388 per 1000 (332 to 432) Relative effect (95% CI): RR 0.96 (0.87 to 1.05) Certainty of the evidence (GRADE): Low Mortality due to adverse drug events (n=1): 6 months follow-up: RR 0.69, 95% CI 0.24 to 1.96		
Hospitalisations	All-cause hospital readmissions (n=17 with 9,561 participants): Median follow-up 6 months (range 1 to 12 months) Illustrative comparative risk (95% CI)*: Assumed risk with standard care: High-risk population*: 500 per 1000 Very high-risk population*: 650 per 1000 Corresponding risk with medication review: High-risk population*: 465 per 1000 (445 to 490) Very high-risk population*: 605 per 1000 (579 to 637) Relative effect (95% CI): RR 0.93 (0.89 to 0.98) Certainty of the evidence (GRADE): Moderate Hospital readmissions due to adverse drug events (n=8): Follow-up 6 months, dichotomous data (n=6): RR 0.75, 95% CI 0.58 to 0.98; I^2 = 63% Follow-up 6 months, continuous data (n=1): MD 0.00, 95% CI -0.20 to 0.20 Follow-up 12 months, continuous data (n=2): MD -0.18, 95% CI -0.26 to -0.10, I^2 = 0%	Primary outcome: ■ Statistically significant decrease in IG vs. CG (n=1) ■ No statistically significant difference in IG vs. CG (n=4) Including secondary outcomes: ■ No statistically significant difference in IG vs. CG (n=8) ■ Statistically significant fewer hospitalisations in IG vs. CG (n=2)	All-cause hospitalisation: Reduced risk of hospitalisation in IG vs. CG (n=3) RR = 0.88; 95% CI = 0.78-1.00 No heterogeneity: I^2 = 0.0%, p=0.828
Emergency department visits	All-cause hospital emergency department contacts (n=8 with 3,527 participants): Median follow-up 3[10] months (range 1 to 12 months) Illustrative comparative risk (95% CI)*: Assumed risk with standard care:	Secondary outcome: ■ No statistically significant difference in IG vs. CG (n=2) ■ Statistically significant fewer visits in IG vs. CG (n=1)	Reduced risk of emergency department visits in IG vs. CG (n=2) RR = 0.68; 95% CI = 0.48-0.96 (n=2) Substantial heterogeneity: I^2 = 76.3%, p=0.040

[10] Within the summary of findings table, three months are reported. However, within the narrative summary of results, a median follow-up of six months is stated.

	High-risk population*: 300 per 1000 Very high-risk population*: 400 per 1000 Corresponding risk with medication review: High-risk population*: 249 per 1000 (204 to 309) Very high-risk population*: 332 per 1000 (272 to 412) Relative effect (95% CI): RR 0.84 (0.68 to 1.03) Certainty of the evidence (GRADE): Low Hospital emergency department contacts due to adverse drug events (n=1): Follow-up 12 months, dichotomous outcome: RR 0.45, 95% CI 0.14 to 1.45 Follow-up 12 months, continuous outcome: MD -0.03, 95% CI -0.07 to 0.01		
Composite outcomes	Composite hospital readmissions and hospital emergency department (n=2)[11]: RR 1.02, 95% CI 0.65 to 1.61 RR 1.31, 95% CI 0.69 to 2.45	Primary outcome: Composite mortality with hospitalisation: ■ No statistically significant difference in IG vs. CG (n=2)	NR
Organisational domain			
Professional groups involved	■ Performed by a pharmacist (n=13), or ■ by a team of pharmacists and pharmacy technicians (n=2), or ■ by a physician (n=4), or ■ by a pharmacist and/or a physician specialised in clinical pharmacology (n=3), or ■ by a team of cardiovascular pharmacy residents and cardiologists (n=1), or ■ by a trained research physician and pharmacist (n=1), or ■ by a pharmacist, who collaborated with a physician and sometimes a nurse (n=1)	■ In interprofessional teams, pharmacists played a key role analysing the presence of PIMs in a variety of hospital, nursing home and clinic-based studies and took the lead in two community pharmacy-based studies	■ Participating pharmacists were trained to ensure comparative competency in providing medication review to study patients (n=4) ■ Collaboration with general practitioners was included in study intervention protocols (n=2) Pharmacist training: Trained to provide the structured pharmaceutical care program to intervention patients (n=1); completed at least 5 of the 20 care plans required for full accreditation as a comprehensive pharmaceutical care practitioner (n=1); 3-day training on the provision of the service (n=1); 90-minute training on the study background and methods (n=1)

[11] Results reported descriptively and not included in meta-analyses, as the separate data could not be obtained from the authors.

Time requirements	NR	Intervention was performed either once (n=13) or continuously with follow-up throughout the study period (n=1)	Community pharmacists provided medication review six times for 44.6±29.8 minutes during the 6-month study period (n=1) Community pharmacists provided medication review two times (at study begin and at 3 months) without reporting the duration of minutes per intervention (n=1) Community pharmacists provided medication review for only once in the first month for 30-60 minutes throughout the 6-month study period (n=1)
Influence on the relationship between healthcare providers	Medication review recommendations that were subsequently implemented: Range from 15% to 93% (n=16)	Medication review recommendations that were subsequently implemented: Level of acceptance by the primary physician ranged from 24.3% to 87.8% (n=6)	Collaboration with healthcare professional: Rationalizing and simplifying drug regimens in collaboration with the patient's general practitioner (n=1); the pharmacist met with the general practitioner after the patient consultation (n=1); suggested interventions to patients and/or general practitioner (n=1); DRPs were sent to the physician via a standard facsimilie form or telephone (n=1)
Patient domain			
Adherence to therapy	NR	NR	Participants' self-report: Statistically significant higher change from nonadherence to adherence in IG vs. CG (15.2% and 12.2%, p=0.028)
Health literacy	NR	NR	NR
Health-related quality of life	Health-related quality of life (n=4 with 392 participants): Median follow-up 3 months (range 3 to 6 months) Relative effect (95% CI): SMD 0.10 (-0.10 to 0.30)[12] Certainty of the evidence (GRADE): Very low	Primary outcome: ■ Statistically significant increase in IG vs. CG for HRQOL (n=4)[13] ■ No statistically significant difference in IG vs. CG for HRQOL (n=1) Including secondary outcomes: ■ No statistically significant difference in IG vs. CG for HRQOL (n=6) ■ Statistically significant increase in IG vs. CG at 4 months, but not at 13 months for HRQOL (n=1) ■ No statistically significant difference within IG, but statistically significant drop within CG for "self-rated health" (n=1)	Meta-analysis could not be conducted due to insufficient reported numerical findings from one study. SF-36 (n=2): No significant differences between IG vs. CG in any of the eight dimensions of the SF-36 over time (area under the curve summary measure analysed; independent t test; p>0.05 (n=1) No significant differences in IG between baseline and 6 months; statistically significant lower scores in IG vs. CG for the SF-36 domains of emotional role (13.4 unit difference, p=0.024) and social functioning (7.7 unit difference, p=0.019); (n=1) Visual analog scale (VAS) and utility score (EuroQol-5D-3L questionnaire); (n=1):

[12] The authors state that values > 0 favour medication reviews. 0.2 represents a small effect, 0.5 a moderate effect and 0.8 a large effect.

[13] In one of these studies, the EQ-Visual Analogue Scale had a significant positive difference for the IG and no difference in the EuroQol-5D 5L.

			Statistically significant improvement within IG after 6 months: 0.0528±0.20 in the utility score (p<0.001) and 4.97±15.29 in the VAS score (p<0.001). Reduction (statistically not significant) in within CG after 6 months: 0.0022±0.24 in the utility score (p=0.815) and 0.90±15.19 in the VAS score (p=0.127). Difference between IG vs. CG: 0.0550±0.01 in the utility score (95% CI = 0.0306-0.0794) 5.87±0.85 in the VAS score (95% CI = 4.20-7.54)
Influence on the relationship between patients and healthcare providers	NR	Team recommended discontinuation of an average of 4.5 drugs per subject, patients stopped taking only 1.5 drugs on average (n=1)	Collaboration with patient: The pharmacist suggested interventions to patients and/or general practitioner (n=1)
Economic domain			
Healthcare costs	Formal health economic analysis (n=1): No difference in overall societal cost between the groups; analysis authors' conclusion: the costs of the additional time used on medication reviews, patient interviews and follow-ups outweighed the decrease in costs of readmissions	Lower cost of medications in IG vs. CG (n=3)	NR
Cost analyses	Estimated cost of a medication review: 24 to 170 United States Dollars per participant (n=4)	Cost-utility analysis estimating the incremental cost-effectiveness ratio: Reduction in the mean incremental total cost and increase in the mean incremental quality adjusted life years (n=1)	Incremental cost-effectiveness ratio of a medication review with follow-up service (n=1), results NR
Implementation factors			
Facilitators	NR	Overview of facilitators: ■ When patients were reluctanct to stop medications, the assurance from clinicians that the medication would be restarted if there is an adverse event was reassuring. ■ Importance of ensuring patients' contribution to the medication decisions. ■ Interprofessional collaboration to reach consensus on medications to be deprescribed. Investigator reported facilitators within included studies: ■ Adaptability & physician acceptance (n=2) ■ Follow-up with patients (n=2) ■ Patient goals focused (n=4) ■ Interprofessional collaboration (n=4) ■ Staff got pre-education (n=1) ■ Clinical examination and test results (n=1) ■ Specialist/Brown Bag Medication Review (n=3) ■ Self-efficacy (n=1) ■ Pharmacist reviews/develops recommendation (n=1)	NR

Barriers	NR	Overview of barriers: ■ The most common barriers were clinician time constraints, reluctance of patients and providers to adopt recommendations, lack of clinician knowledge and incomplete interprofessional team involvement. ■ Not reaching interprofessional consensus. Investigator reported barriers within included studies: ■ Lack of adaptability & physician acceptance (n=2) ■ Complexity of intervention (n=2) ■ Patient frailty (n=3) ■ Patient's resistance (n=3) ■ Lack of interprofessional collaboration (n=1) ■ Physician computerised decision support (n=1) ■ Lack of knowledge and beliefs (n=1) ■ Lack of self-efficacy (n=1) ■ Lack of reflecting and evaluating (n=1)	NR
Study conclusion			
Author's conclusion	**Implications for practice:** This systematic review provides evidence that **medication reviews for hospitalised elderly polypharmacy patients likely reduce hospital readmissions and may reduce emergency department contacts**. However, the **beneficial effect** of reviewing patients' medication **does not seem to expand to increased survival**, and the **effect on quality of life is very uncertain**. Based on our data, it **seems reasonable to implement medication reviews in some form for hospitalised patients to prevent readmission**. However, it is **uncertain which form of medication review is most effective**. **Implications for research:** **Future trials** of medication reviews should ensure a **high implementation rate**, **long follow-up** and assess the **impact of different types of co-interventions on intervention effects**. For example, by using a **factorial design**. The evidence for an effect on **health-related quality of life** is limited and future trials should include this **important outcome**, preferably using a **generalisable measure (e.g. EQ-5D)** and try to **minimise risk of attrition bias from loss to follow-up**. Furthermore, **risk of contamination bias** is an important issue when investigating the effect of medication reviews and use of a **cluster-randomised design** may minimise such bias. However, such trials should **appropriately adjust for clustering** and **transparently report their methodology** so that data may be included in future meta-analyses.	This systematic review analysed the outcomes from 14 RCT deprescribing studies reviewing the complete medication profiles of older adults with polypharmacy taking at least 5 prescriptions or regularly used medications. While this review focused **broadly across all health care settings, almost all studies found deprescribing succeeded in reducing drugs and/or doses without risking safety as measured by mortality, hospitalisation, emergency room visits or falls as primary outcomes**. Similar findings have emerged from systematic reviews of deprescribing within a single type of setting. **Four out of the five studies using HRQOL** as a primary outcome found a **positive impact from deprescribing**. In addition, **all four studies which examined the economic outcomes** of deprescribing found **positive outcomes regarding a lower cost of medications in the intervention group** compared to the control group. **One cost-utility analysis** estimated the incremental cost-effectiveness ratio and reported a **reduction in the mean incremental total cost** and an **increase in the mean incremental Quality Adjusted Life Years** as a result of the deprescribing intervention. Given the small number of studies in this area, it is important to investigate the economic effects of deprescribing further.	The current evidence demonstrates that medication reviews performed by community pharmacists, **specifically comprehensive clinical reviews**, for older people with polypharmacy **regimens reduce the risk of ED visits**. This service **should be considered** because one of the enhanced services community pharmacists can provide to **improve patients' safety**. However, **further research is needed** to clarify the impact of community pharmacists' medication reviews on other aspects such as **quality of life and medication adherence** where there are **insufficient evidence to determine pooled estimates** on these outcomes.

		Finally, these studies quite legitimately focused on measuring outcomes. However, **it is time also to systematically study** the process of deprescribing interventions to understand more about **the components of interventions and their implementation** which most influence deprescribing outcomes. Adding this research agenda to the RCT outcome studies has the potential to improve deprescribing outcomes, implementation, maintenance and dissemination internationally.	

** The basis for the assumed risk with standard care is based on published trial data. The "very high-risk" estimates are based on the included trials with the highest risk in the control group at 12 months follow-up for mortality, hospital readmissions and emergency department contacts. The "high-risk" estimates are based on the included trials with the lowest risk (albeit still a high-risk, hospitalized population) in the control group at 12 months follow-up for mortality and hospital readmissions and emergency department contacts. The corresponding risk with medication review (and its 95% CI interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*

Abbreviations: CI – confidence interval; CG – control group; DRP – drug-related problems; ED – emergency department; GP – general practitioner; HR – hazard ratio; HRQOL – health-related quality of life; IG – intervention group; n – number; MD – mean difference; NR – not reported; PIM – potentially inappropriate medications; RCT – randomised controlled trial; RR – relative risk; SF-36 – short form health survey; SMD – standardised mean difference; START criteria – Screening tool to alert to right treatment; STOPP criteria – Screening tool of older persons' potentially inappropriate prescriptions; STOPPFrail – Screening tool of older persons prescriptions in frail adults with limited life expectancy; STRIP software – Systematic tool to reduce inappropriate prescribing; VAS – visual analog scale; vs. – versus

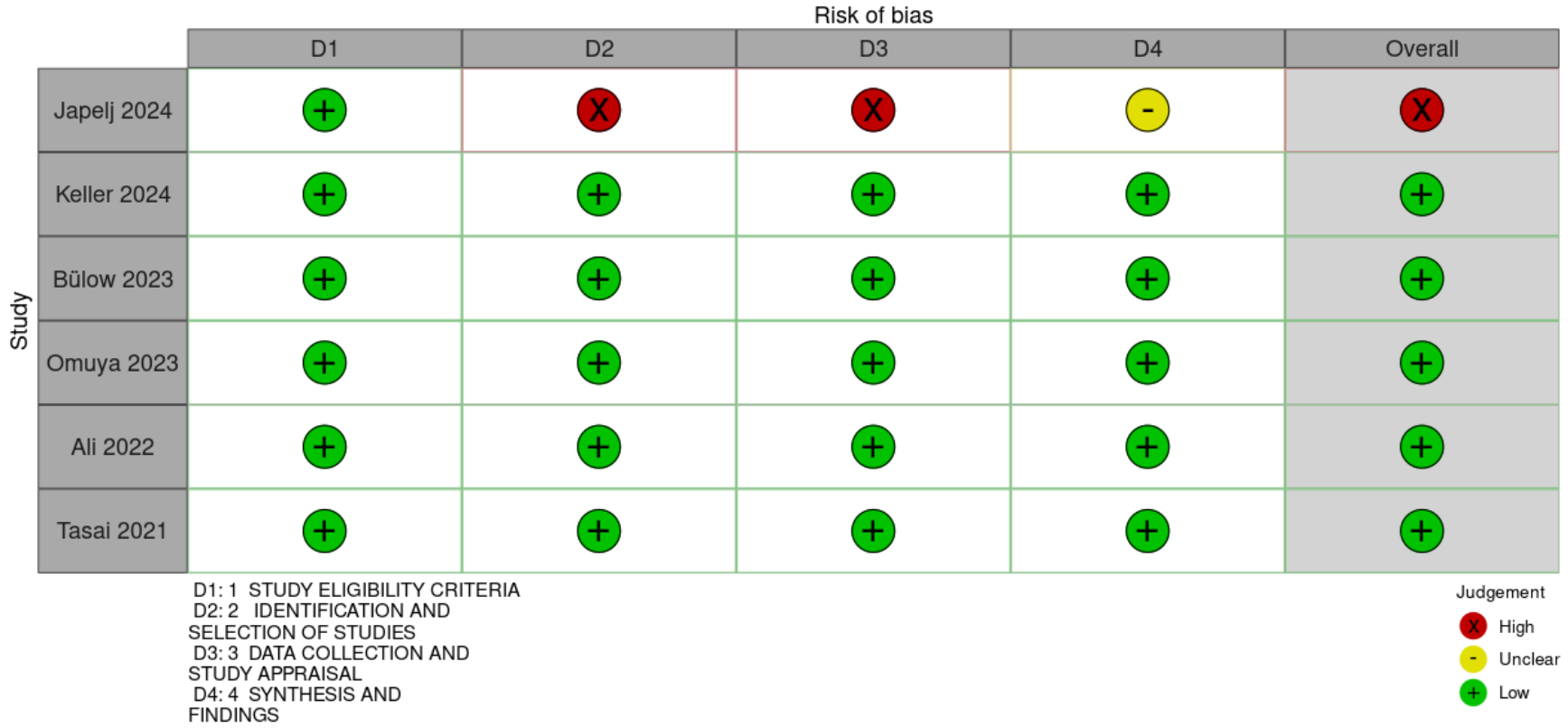

Figure A- 2: ROBIS Risk of bias assessment of umbrella reviews and systematic reviews

Japelj et al. 2024 [23]: Only one database searched, no other search methods, unspecified selection criteria, no information on screening process provided. No risk of bias assessment using standardised tools. Keller et al. 2024 [19]; Bülow et al 2023 [20]; Omuya et al 2023 [21]; Ali et al 2022 [18]; Tasai et al 2021 [22]

Study ID	Balsom 2020	Bernsten 2021	Bladh 2011	Blum 2021	Bonetti 2018	Bonnerup 2014	Bryant 2011	Campins 2017	Cateau 2021	Cossette 2017	Curtin 2020	Dalleur 2014	Farris 2014	Gallagher 2011	Gillespie 2009	Graabaek 2019	Gustafsson 2017	Jodar-Sanchez 2015	Juanes 2018	Kempen 2021	Kornholt 2022	Kua 2021	Lea 2020	Lenander 2014	Lenssen 2018	Lisby 2010	Lisby 2015	Mahlknecht 2021	McCarthy 2022	Nielsen 2017	O'Mahony 2020	Ravn-Nielsen 2018	Rieckert 2020	Romskaug 2020	Schnipper 2006	Scullin 2007	Song 2021	SUREPILL 2015	Touchette 2012	Verdoorn 2019	Williams 2004
Bülow 2023			■	■	■	■				■	■	■	■	■	■	■	■		■	■			■		■	■	■			■	■	■			■	■	■	■			
Omuya 2023	■							■	■		■							■			■	■		■				■	■				■	■						■	■
Tasai 2021		■					■											■																					■		

Figure A- 3: Overview of primary study overlap among included systematic reviews

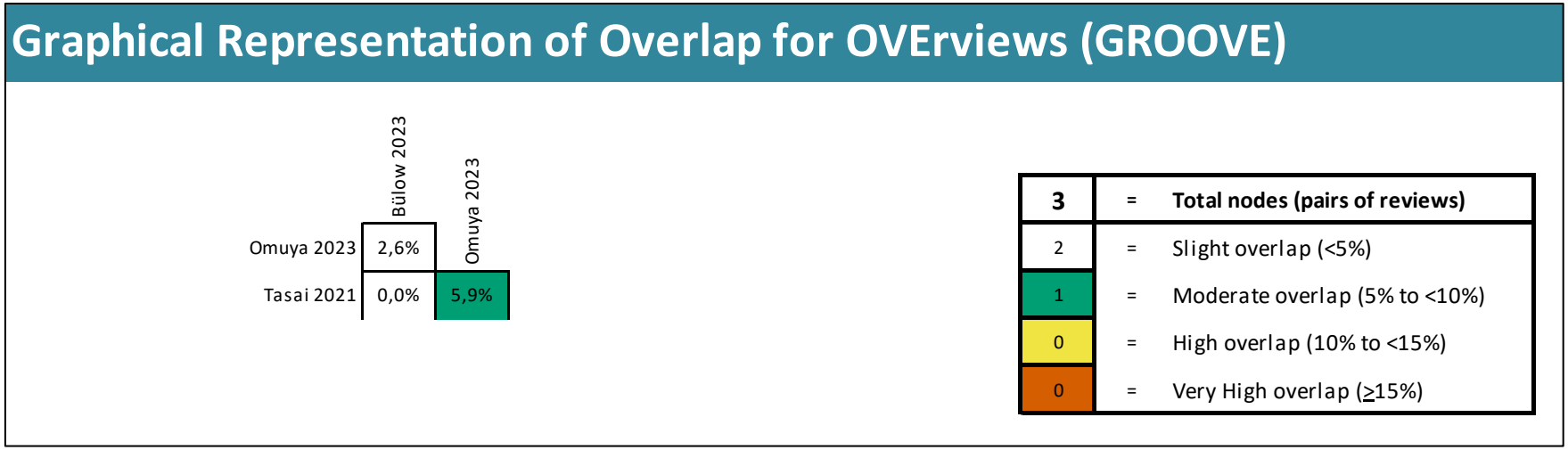

Figure A- 4: Graphical Representation of Overlap for Overviews using the GROOVE tool

1.1.4 Medical guidelines

Table A- 4: Guidelines on multimorbidity and polypharmacy (Guidelines 1-3)[14]

Title (Year) [Reference]	S2e-Leitlinie Schutz vor Über- und Unterversorgung - gemeinsam entscheiden - Living Guideline (2025) [24]	S3-Leitlinie Multimorbidität – Living guideline (2024) [25]	S3-Leitlinie Umfassendes Geriatrisches Assessment (Comprehensive Geriatric Assessment CGA) bei hospitalisierten Patientinnen und Patienten (2024) [26]
Professional association	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V. (DEGAM)	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V.	Deutsche Gesellschaft für Geriatrie (DGG)
Recommendations regarding the intervention (structured medication reviews, medication analyses, deprescribing)	**Es werden ausgewählte Empfehlungen aus der 3. Aktualisierung der Leitlinie „Multimedikationen“[15] aufgeführt:** **1-6**. Die **Medikation soll strukturiert bewertet werden, z. B. mittels eines Instrumentes, wie dem modifizierten Medikationsangemessenheitsindex**, unter besonderer Berücksichtigung von ■ PIM-Listen/anticholinerger Last, QTc –Zeit verlängernden Medikamenten, ■ Unterversorgung, ■ Adhärenz. *Empfehlungsgrad: A, LoE: V* **3.12.** Der Medikationsplan soll stets vollständig und aktuell sein, der bundeseinheitliche Medikationsplan (BMP) ist das bevorzugte Format. Die Koordination liegt beim **Hausarzt/hauptbehandelnden Arzt. Der Medikationsplan ist bei jeder Konsultation und in der Apotheke vorzulegen.** *Empfehlungsgrad: A; LoE: V*	5.2 Krankheitsmanagement 5.2.1 Multimedikation Evidenzbasiertes Statement: Aufgrund der heterogenen Studienlage kann kein einheitliches Vorgehen für ein Deprescribing empfohlen werden.[16] Konsensbasierte Empfehlung: Bei jeder Konsultation soll die Anzahl und Dosierung der Medikamente („pillcount“) erfasst werden mit Prüfung auf nicht-indizierte, UAW auslösende oder miteinander interagierende Medikamente (Medikamentenreview). Gegebenenfalls soll ein Absetzen oder eine Dosisreduktion („Deprescribing“) erfolgen.[17]	**Not mentioned as specific intervention**; no mention of the role of pharmacists in medication optimisation; no recommendation on interdisciplinary teams. Konsensbasiertes Statement: Ein comprehensive geriatric assessment beinhaltet mindestens die folgenden Dimensionen: Selbsthilfefähigkeit, Mobilität, kognitive Funktion inklusive Delir, Affekt, Ernährung und soziale Situation. Weitere Dimensionen können unter anderem sein: Sensorik, Dysphagie, Kommunikationsfähigkeit inklusive Sprache und Sprechen, Inkontinenz, Schmerz, Schlaf, Sucht, Spiritualität, **Multimorbidität und Polypharmazie**

[14] Information extracted from medical guidelines was retained in the original language to preserve original wording.

[15] Here available as the current version: “S3-Leitlinie Hausärztliche Leitline: Multimedikation (2022)“ https://register.awmf.org/de/leitlinien/detail/053-043

[16] Qualität der Evidenz: Niedrig bis sehr niedrig. Starker Konsens: Ja (n=14), Nein (n=0), Enthaltungen (n=0)

[17] Starker Konsens: Ja (n=14), Nein (n=0), Enthaltungen (n=0)

	5.1. Vom **koordinierenden Arzt** sollte sichergestellt werden, dass **jeder Patient/jede Patientin mit Multimedikation einen aktuellen Medikationsplan hat.** *Empfehlungsgrad: B; LoE: V*		
Patient selection criteria	There is no specific recommendation, as to what patients should receive a structured medication review. The guidline itself defines polyphamacy ("Multimedikation") as two or more, also self-prescribed, medications.	Meta-Algorithmus (Abbildung 2): Zum umfassenden Krankheitsmanagement, unter **übergreifendem Management** zählt unter anderem **Medikamentenreview.** Zum **Ausschluss von abwendbar gefährlichen Verläufen**, bei **unerwünschten Arzneimittelwirkungen** (Gastrointestinale Blutungen, Hypokaliämie/ Hyponatriämie, Leberwert-/ Kreatinin-Anstieg, Stürze, Benommenheit/ Schwindel, Hyper-/ Hypoglykämie) wird **Medikamentenreview** als Maßnahme angegeben.	NR
Setting	The guideline focuses on the primary care setting.	The guideline focuses on the primary care setting as the central point for managing multimorbidity and providing medication review. Other settings: The guideline highlights the cooperation with other sectors (Nursing homes, pharmacies, hospitals).	3.2.1 Empfehlung: Zur optimalen Versorgung älterer Patient:innen **in der Notaufnahme sollte** sich die Auswahl eines Screeninginstruments an der Komplexität dieser Patient:innen orientieren und die Dimensionen Kognition (Demenz, Delir), Selbsthilfefähigkeit und Mobilität (Sturzrisiko) sowie eine **Überprüfung von Polypharmazie** und das Erfragen der Wertvorstellungen und **Präferenzen der Patient:innen** beinhalten. Vertrauenswürdigkeit der Evidenz nach GRADE: nicht zutreffend Konsensstärke: 100% (starker Konsens)
Other information	Guideline outlines some relevant recommendations from the 3rd version of the "S3-Leitlinie Hausärztliche Leitlinie: Multimedikation". Recommendation numbers correspond to those in the original guideline.	The guideline contains a "Tool-Box" referencing instruments for optimising medication, such as the "Hausärztliche Leitlinie Multimedikation", „DEGAM S1-Handlungsempfehlung Medikamentenmonitoring", Priscus List, Beers-List, Forta-List, "Medikationsplan", "Gesundheitsfragebogen für Patienten", Sturzprävention in der Gesundheitsversorgung – Sturzrisiko erkennen".	The guideline focuses on comprehensive geriatric assessments, which professional groups are involved, the relevant dimensions of a comprehensive geriatric assessment, as well as the optimal duration of this intervention.

Abbreviations: LoE – Level of Evidence

Table A- 5: Guidelines on multimorbidity and polypharmacy (Guidelines 4-6)

Title (Year) [Reference]	**S2k-Leitlinie Arzneimitteltherapie bei Multimorbidität - Living Guideline (2023) [27]**	**Italian guidelines on management of persons with multimorbidity and polypharmacy (2022) [28]**	**S3-Leitlinie Hausärztliche Leitlinie: Multimedikation (2021) [29]**
Professional association	Deutsche Gesellschaft für Innere Medizin e.V. (DGIM)	Not applicable	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V. (DEGAM)
Recommendations regarding the intervention (structured medication reviews, medication analyses, deprescribing)	**Not mentioned as specific intervention**; no mention of the role of pharmacists in medication optimisation; no recommendations on interdisciplinary teams or specific settings for medication reviews Indirect reference: The guideline mentions the need for regular systematic review and consolidation of drug therapy in cases of multimorbidity, but without providing specific methods or implementation recommendations.	Review question 4: Effective interventions for reducing polypharmacy and optimizing drug treatment. Recommendation. **Interventions to reduce polypharmacy and optimize drug treatment must be based on a comprehensive, multidimensional assessment** with, whenever possible, a **multidisciplinary approach, active involvement of the person and/or caregivers, and identification of inappropriate prescribing through standard criteria and/or the use of digital support tools for deprescribing**. It is essential to follow the patient up to assess compliance with any intervention that has been initiated, and to detect and manage deprescriptionrelated symptoms. Strength of the recommendation: Strong. Review question 5: What is the clinical and cost-effectiveness of interventions to reduce polypharmacy? Recommendation: Interventions to reduce the number of drugs and optimize drug treatment are recommended to reduce the risk of falls in older persons with multimorbidity and/or polypharmacy. Such interventions should be based on a **comprehensive assessment of the patient, preferably using a multidisciplinary approach, the assessment of inappropriate prescribing using standard criteria and/or digital tools to support deprescribing**, the estimation of cumulative drug toxicity, the assessment of fall risk, and the active involvement of the patient and/or caregiver.	Die Leitlinie **empfiehlt** die Durchführung einer **strukturierten Medikationsanalyse**, die hier „**Medikationsüberprüfung**" genannt wird: Die Mandatsträger haben im Konsensusprozess empfohlen, den Begriff Medikationsreview durch Medikationsüberprüfung zu ersetzen. Hierunter ist im Folgenden immer ein Prozess zu verstehen, der eine **Bestandaufnahme der Medikation, ihre Bewertung und daraus folgende Schritte für das Medikationsmanagement** umfasst. Evidenzbasierte Empfehlung: 2-1: Patientinnen und Patienten **sollen** zu ihren bevorzugten Therapiezielen befragt werden. Hierbei sollte herausgefunden werden, wie sich die **persönliche Prioritätensetzung** hinsichtlich der folgenden Aspekte darstellt: ■ Verbesserung oder Erhalt der Lebensqualität ■ Selbstständige Lebensführung / Unabhängigkeit ■ Verbesserung oder Erhalt der Funktionsfähigkeit ■ Überleben / Prognoseverbesserung ■ Schmerzlinderung ■ Weitere Symptomverbesserung (Übelkeit, Kurzatmigkeit, Schwindel etc.) ■ Stellenwert der Belastung durch die Therapie: Empfehlunsgrad: A (hoher Empfehlungsgrad); Evidenzgrad: IIIa (Evidenz aus einem systematischen Review mit/ohne Meta-Analysen von Fall-Kontroll-Studien); Ergebnis Konsensverfahren: 100%

		Strength of the recommendation: Strong.	
Patient selection criteria	There is no specific recommendation, as to what patients should receive a structured medication review. Zielgruppe: Patient:innen mit Multimorbidität und Multimedikation	Tool to identify people with multimorbidity who are at risk of unplanned hospital admission? Recommendation. The **Frailty Index** can be used to identify persons with multimorbidity at risk of unplanned hospital admissions. Strength of the recommendation: Weak. Risk tool to identify people with multimorbidity who are at risk of reduced life expectancy: Recommendation: Among patients hospitalized or discharged from hospital, validated tools such as **the Clinical Frailty Scale (CFS), Frailty Index, and Multidimensional Prognostic Index (MPI) are recommended for** identifying those with multimorbidity and limited life expectancy. Strength of the recommendation: **Strong.** Recommendation: In community-dwelling persons, the **Charlson Comorbidity Index, Frailty Index, and gait speed test** can be used to identify those with multimorbidity and limited life expectancy. Strength of the recommendation: Weak.	Evidenzbasierte Empfehlungen: 0-1: Bei Patientinnen und Patienten mit **Multimedikation**[18] (≥ 5 dauerhaft[19] angewendete Arzneimittel) und **Multimorbidität** (≥ 3 chronische Erkrankungen) **sollte mindestens einmal jährlich** eine **Medikationsüberprüfung** mit Bestandsaufnahme und Bewertung der Medikation) erfolgen. Empfehlungsgrad: B (mittlerer Empfehlungsgrad); Evidenzgrad: V (Evidenz aufgrund von Expertenkonsens); Ergebnis Konsensverfahren: 92% 0-2: Bei Patientinnen und Patienten mit Multimedikation und Multimorbidität mit zusätzlichen Risiken oder Ereignisse (z.B. Stürze, Krankenhausaufenthalt) sollte eine anlassbezogene Medikationsüberprüfung (mit Bestandsaufnahme und Bewertung der Medikation) durchgeführt werden. Empfehlungsgrad: B (mittlerer Empfehlungsgrad); Evidenzgrad: V (Evidenz aufgrund von Expertenkonsens); Ergebnis Konsensverfahren: 100% 0-3: Sie sollten für Ihre Praxis (z.B. in Ihrem Qualitätsmanagement-system) festlegen, wie Sie Patienten mit diesen Kriterien (s. Empfehlung 0-1 und 0-2) für eine Medikationsüberprüfung erkennen und wo Sie dokumentieren, wann die nächste Medikationsüberprüfung spätestens stattfinden soll. Empfehlungsgrad: B (mittlerer Empfehlungsgrad); Evidenzgrad: V (Evidenz aufgrund von Expertenkonsens); Ergebnis Konsensverfahren: 100%
Setting	Die Leitlinie betrifft Arzneimitteltherapie im ambulanten und stationären Behandlungssektor, sowie bei Sektor übergreifender Behandlung.	No specific setting defined, mention that interventions should be based on an **multidisciplinary approach** whenever possible (see recommendations 4 and 5 above – strength of recommendation: Strong).	Primäres Setting: Hausarztpraxis Schnittstellen zu anderen Versorgungsbereichen: Apotheke:

[18] In der Leitlinie wird im Kontext von Interaktionen und Kontraindikationen unter Multimedikation die Verordnung von 5 und mehr Wirkstoffen verstanden. Steht die Adhärenz und Handhabbarkeit der Therapie im Vordergrund wird die Anzahl der unterschiedlichen Verordnungen betrachtet.

[19] dauerhaft bedeutet in der Literatur eine Anwendung von 90 und mehr Tagen; für die Identifikation der Zielgruppe wird eine Bedarfsmedikation hierbei nicht berücksichtigt, diese jedoch in die Medikationsüberprüfung einbezogen.

			Evidenzbasierte Empfehlungen: 4-1: Hausärzte sollen mit Apotheken einen Kommunikationsweg vereinbaren, um Fragen im Rahmen der Medikationsabgabe zu klären. Empfehlungsgrad: A (hoher Empfehlungsgrad); Evidenzgrad: Ia (Evidenz aus einem systematischen Review mit/ohne Meta-Analysen von mehreren randomisierten, kontrollierten Studien); Ergebnis Konsensverfahren: 100%. 4-2 Hausärzte sollen ihren Patientinnen und Patienten mit Multimedikation empfehlen eine Stammapotheke[20] aufzusuchen, die zur Arzneimittelanwendung persönlich berät, die gesamte Medikation dokumentiert, Interaktionen prüft und somit Arzt und Patienten unterstützt, den Überblick über die Medikation zu behalten. Empfehlunsgrad: A (hoher Empfehlungsgrad); Evidenzgrad: Ia (Evidenz aus einem systematischen Review mit/ohne Meta-Analysen von mehreren randomisierten, kontrollierten Studien); Ergebnis Konsensverfahren: 82%. 4-3: In der Praxis soll der Patientin/dem Patienten vermittelt werden, dass es für ihn von Nutzen sein kann, wenn sie/er sich mit allen Rezepten, bei OTC-Bedarf und bei Fragen oder Problemen der Arzneimittelanwendung an die Stammapotheke wendet. Empfehlungsgrad: A (hoher Empfehlungsgrad); Evidenzgrad: Ia (Evidenz aus einem systematischen Review mit/ohne Meta-Analysen von mehreren randomisierten, kontrollierten Studien); Ergebnis Konsensverfahren: 90%. Ambulant: Hausbesuche sind eine gute Gelegenheit, um sich einen Überblick über die vorhandenen Arzneimittel, die Handhabung der Medikation (Verwendung von Tages- oder Wochen-Dosetten, Blister) und über Anwendungsprobleme zu verschaffen.

[20] Als Stammapotheke wird eine Apotheke bezeichnet, in der der Patient den überwiegenden Teil seiner Rezepte einlöst und auch für die Selbstmedikation aufsucht („Apotheke des Vertrauens“). Die Stammapotheke stellt das Pendent zum Hausarzt da, der Begriff Hausapotheke ist jedoch inhaltlich als Bezeichnung für die zuhause gelagerten Arzneimittel besetzt.

			<u>Stationär/Krankenhaus:</u> Die Leitlinie thematisiert den Informationsfluss beim Übergang vom und ins Krankenhaus und betont die Wichtigkeit einer korrekten Medikationsübergabe. <u>Kooperation mit Pflegeberufen und pflegenden Angehörigen:</u> Die Kooperation mit professionell Pflegenden und pflegenden Angehörigen wird als essenziell beschrieben, um die Medikation im Alltag sicherzustellen. Visiten im Pflegeheim werden als relevanter Zeitpunkt für die Überprüfung genannt.
Other information	The guideline focuses on specific drug interactions and combinations (e.g. avoidance of certain active ingredients in older patients, dangerous drug combinations)	Review question 1 outlines important principles for assessing, prioritising and managing care for people with multimorbidity. Further information of deprescribing specific medications are available for: antihypertensive drugs, proton pump inhibitors, statins, antiplatelets, and vitamin D. A *medication review* as such is not specifically named but deprescribing procedures are described.	The guideline provides further recommendations: Recommendations 1-1 to 1-6 in regard to the delivery of the intervention (e.g., further information that should be collected during medication review, including relatives and healthcare professionals (provided the patient gives consent), evaluating the therapy burden with screening questions, explore suitable options for reducing therapy burden, usage of the medication appropriateness index (MAI). Recommendations 3-1 to 3-12 in regard to proposed regulation and communication (e.g. avoiding undertreatment and overtreatment, taking into account non-pharmacological measures, keeping the medication regimen simple to avoid errors) Recommendations 5-1 to 5-5 in regard to medication use and self-management Recommendations 6-1 to 6-4 in regard to monitoring and follow-up.

Abbreviations: LoE – Level of Evidence

Table A- 6: AGREE II Quality assessment check of included guidelines

Quality Assessment Check	S2e-Leitlinie Schutz vor Über- und Unterversorgung - gemeinsam entscheiden - Living Guideline (2025) [24]	S3-Leitlinie Multimorbidität – Living guideline (2024) [25]	S3-Leitlinie Umfassendes Geriatrisches Assessment (Comprehensive Geriatric Assessment CGA) bei hospitalisierten Patientinnen und Patienten (2024) [26]	S2k-Leitlinie Arzneimitteltherapie bei Multimorbidität - Living Guideline (2023) [27]	Italian guidelines on management of persons with multimorbidity and polypharmacy (2022) [28]	S3-Leitlinie Hausärztliche Leitlinie: Multimedikation (2021) [29]
Domain 2: Stakeholder Involvement						
4. The guideline [document] development group includes individuals from all the relevant professional groups.	12	14	14	14	14	14
5. The views and preferences of the target population (patients, public, etc.) have been sought.	13	12	13	12	13	12
6. The target users of the guideline [document] are clearly defined.	14	14	14	13	12	14
Domain 3: Rigour of Development						
7. Systematic methods were used to search for evidence.	12	14	13	11	13	14
8. The criteria for selecting the evidence are clearly described.	12	13	13	11	11	14
9. The strengths and limitations of the body of evidence are clearly described.	9	14	13	14	7	13
10. The methods for formulating the recommendations are clearly described.	12	13	13	13	12	14

Quality Assessment Check	S2e-Leitlinie Schutz vor Über- und Unterversorgung - gemeinsam entscheiden - Living Guideline (2025) [24]	S3-Leitlinie Multimorbidität – Living guideline (2024) [25]	S3-Leitlinie Umfassendes Geriatrisches Assessment (Comprehensive Geriatric Assessment CGA) bei hospitalisierten Patientinnen und Patienten (2024) [26]	S2k-Leitlinie Arzneimitteltherapie bei Multimorbidität - Living Guideline (2023) [27]	Italian guidelines on management of persons with multimorbidity and polypharmacy (2022) [28]	S3-Leitlinie Hausärztliche Leitlinie: Multimedikation (2021) [29]
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	12	13	13	13	13	13
12. There is an explicit link between the recommendations and the supporting evidence.	11	13	13	13	10	14
13. The guideline has been externally reviewed by experts prior to its publication.	4	11	14	14	12	13
14. A procedure for updating the guideline is provided.	14	14	14	13	6	14
Domain 6: Editorial Independence						
22. The views of the funding body have not influenced the content of the guideline.	12	12	12	14	13	14
23. Competing interests of guideline development group members have been recorded and addressed.	8	8	13	14	10	14
Overall quality of this guideline/document	Domain 2: 92% Domain 3: 73% Domain 6: 67%	Domain 2: 94% Domain 3: 93% Domain 6: 67%	Domain 2: 97% Domain 3: 94% Domain 6: 88%	Domain 2: 92% Domain 3: 90% Domain 6: 100%	Domain 2: 92% Domain 3: 71% Domain 6: 79%	Domain 2: 94% Domain 3: 97% Domain 6: 100%

1.2 RQ2: Implementation of structured medication review in selected countries

1.2.1 Austria

Category	Austria
Included document(s), Year (Reference)	■ Effects of a community pharmacy-based structured medication review on drug-related problems in all-comers with polypharmacy: a randomized, controlled, double-blind, parallel-group trial (2025) [30] ■ ELGA: eMedikation (2026) [31] ■ About ELGA (2026) [32] ■ Alle Arzneimittel im Blick: Pilotprojekt Medikationsanalyse (2026) [33] ■ Medikationsanalyse: Alle Arzneimittel im Blick (2026) [34] ■ Fortbildungen Apotheker (2026) [35] ■ Klinische Pharmazie – Medikationsanalyse (2026) [36] ■ Neue Dienstleistung in der Apotheke kann Gesundheit von 500.000 Menschen verbessern (2024) [37] ■ Leistungsspektrum der öffentlichen Apotheken im österreichischen Gesundheitssystem – Bestandsaufnahme, Analyse und Ausblick (2023) [38]
Medication review type	■ Type 2a (structured evaluation of medicines via patient interview)
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Community pharmacies; trial with 14 participating pharmacies in Vienna
Process ■ Duration of conversation, frequency	Frequency: ■ Baseline assessment; re-assessment at 3-4 months; optional second review with final assessment at 6-9 months Duration of conversation: ■ not reported
Patient selection ■ Usage of selection criteria	■ Adults (≥18 years) ■ Intake of ≥8 active ingredients ■ Patients were excluded if they previously received a medication review
Methods ■ Questionnaires or screening tools used	■ PCNE DRP framework ■ Study-specific software with automated pDDI database (austriacodex: https://mein.apoverlag.at/austriacodex) ■ Further criteria (e.g. MAI/STOPP/START) not reported
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	Clinical components: ■ Assessed DRPs including clinically relevant pDDIs (with severity grading), duplicate prescriptions, dosage errors (deviates from prescription or SmPC), inappropriate therapy duration, contraindicated medications, lack of effect, tolerability issues, improper storage, inappropriate pharmaceutical form, problems with use/application Patient-centred components: ■ Therapy adherence and health literacy assessed and targeted; administration technique/problems with use recorded System-related components: ■ ELGA e-Medikation supports checking for potential interactions and avoiding duplicate prescriptions; generic alternatives not reported.

Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Community pharmacists (patient- and assessor-blind design; independent pharmacist assessor); physicians not systematically involved Qualifications/additional training: ■ 28 pharmacists trained in structured sessions for the study software (lectures, case studies, individual feedback) ■ The Austrian Chamber of Pharmacists offers workshops on medication reviews and webinars on deprescribing ■ The Postgraduate Center of the University of Vienna offers a certificate program that provides fundamental knowledge of pharmaceutical disease management and insights into extended medication review and medication management. The certificate enables independent Type 2a medication reviews.
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ Study-specific software (trial) + ELGA e-Medikation enables pharmacies to store dispensings and view e-medication lists. Link to electronic health record: ■ ELGA e-Medikation provides an e-medication list accessible to pharmacies; entries (prescribed and dispensed medicines) are available for 18 months; pharmacies can retrieve the list for interaction checks and store dispensings/OTC items (via e-card). Automated detection of DRPs: ■ software featured a pDDI database that automatically detected drug-drug interactions with severity grading
Costs ■ Costs per intervention, savings potential	Remuneration: ■ Not established; the Austrian Chamber of Pharmacists advocates establishing the service as an insurance-funded benefit (Kassenleistung). Costs per intervention: ■ Not reported Savings potential: ■ ELGA page notes potential to avoid duplicate prescriptions and check interactions; trial reported reductions in DRPs.
Implementation notes	■ randomised, controlled, patient- and assessor-blind, parallel-group trial in Vienna; 220 randomised; 198 completed Part 1; trial registration ISRCTN14052916; ethics approval (Medical University of Vienna 2029/2021); software-guided workflow ELGA e-Medikation: prescribed and dispensed medicines visible to ELGA health service providers; pharmacies can access lists and record dispensings/OTC items; contracted physicians are required to save prescriptions in e-Medikation; this obligation applies to private physicians from 1 Jan 2026. Dec 2024 OTS release states the Chamber advocates establishing the service as an insurance-funded benefit.

Abbreviations: DRP – drug-related problem; ELGA – "Elektronische Gesundheitsakte" (Electronic Health Record in Austria); MAI – Medication Appropriateness Index; PCNE - Pharmaceutical Care Network Europe; pDDI – potential drug-drug interaction; SmPC - Summary of Product Characteristics; START - Screening Tool to Alert to Right Treatment; STOPP - Screening Tool of Older Person's Prescriptions; OTC – over the counter; OTS – "Originaltextservice" (Press Release Service of the Austrian Press Agency)

1.2.2 Belgium

Category	Belgium
Included document(s), Year (Reference)	■ Medicatienazicht door de huisapotheker: een nieuw initiatief (2023) [39] ■ Implementation study of an intermediate medication review in Belgian community pharmacies (2025) [40] ■ Qualitative study of medication review in Flanders, Belgium among community pharmacists and general practitioners (2021) [41] ■ Tarief farmaceutische verstrekkingen (2025) [42]
Medication review type	■ Type 2a ('Medicatienazicht' by the huisapotheker)
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Community pharmacies (huisapotheker) ■ Private consultation space required
Process ■ Duration of conversation, frequency	Frequency: ■ eligible patients can receive 1 review every 2 years; an extra review may be reimbursed on GP prescription (R/GGG Medicatienazicht) Duration of conversation: ■ The preparation of the first interview took between 30 min and 2 h depending on the number of chronic medicines. This time decreased with the pharmacist's experience acquired during the project. After some interviews, pharmacists were more comfortable with the tools and acquired a systematic method to prepare for the interviews. However, they considered that 30 min was the minimum time required. The first interviews lasted between 20 min and 1 h, with a maximum of 2 h for some patients. The second interview, including the treatment plan delivery and the presentation of the proposed interventions, was shorter and took approximately 10–20 min. Finally, the follow-up interview lasted less than 5 min and was provided at the counter or by phone.
Patient selection ■ Usage of selection criteria	■ Home-dwelling patients chronically taking ≥5 reimbursed medicines; service performed by the patient's designated 'huisapotheker'
Methods ■ Questionnaires or screening tools used	■ STOPP/START screening lists cited for older adults; ■ APB PHIL referenced; ■ GHeOPS tool ■ no MAI reported
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	Clinical components: ■ Identify medicine-related problems including clinically relevant interactions, dose/duration issues, duplicate therapies, drugs without indication Patient-centred components: ■ Assess therapy adherence and daily use; engage patient; provide updated medication scheme System-related components: ■ Avoid duplication and clinically relevant interactions ■ Generic alternatives not reported
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Community pharmacist (huisapotheker) leads; collaboration with GP is essential; certain interventions require GP agreement Qualifications/additional training: ■ Not reported (BCFI mentions educational materials and APB guidance)
Digital tools	Digital documentation: ■ Mandatory documentation in APB 'e-form Medicatienazicht'; report shared with the GP

■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Link to electronic health record: ■ Use of Gedeeld Farmaceutisch Dossier (GFD) for medication history; report sent to GP via eHealthBox (secure messaging) Automated detection of DRPs: ■ Not reported
Costs ■ Costs per intervention, savings potential	Remuneration: ■ Reimbursed by RIZIV when APB e-form report is shared with the GP; tariff per medication review (Art. 6/2) = €98.63 excl. VAT (€104.55 incl. VAT) as of 1 Jan 2025. Costs per intervention: ■ Not reported Savings potential: ■ Not reported
Implementation notes	■ Started 1 Apr 2023 nationwide; initiation possible by huisapotheker/patient/after MFO/nurse/caregiver/GP; National code Medicatienazicht 5522-032 used for tariffing; pilot and qualitative studies provide context on earlier implementation and time/resource barriers Tariff indexed 1 Jan 2025 (RIZIV circular), Medicatienazicht listed under Art. 6/2.

Abbreviations: APB - Algemene Pharmaceutische Bond (General Pharmaceutical Association); APB PHIL – APB - Pharmacie / Huisarts Interface Liaison; BCFI - Belgisch Centrum voor Farmacotherapeutische Informatie (Belgian Centre for Pharmacotherapeutic Information); DRP – drug-related problem; GFD – Gedeeld Farmaceutisch Dossier (Shared Pharmaceutical Record); GHeOPS - Ghent Health Optimization and Prescription Screening; GP – general practitioner; MAI – Medication Appropriateness Index; MFO - Multidisciplinair Farmaceutisch Overleg (multidisciplinary pharmaceutical meeting); R/GGG – Risicoanalyse/Geïntegreerd Gestructureerd Gesprek (risk assessment/integrated structured interview); RIZIV - Rijksinstituut voor Ziekte- en Invaliditeitsverzekering (Belgian National Institute for Health and Disability Insurance); START - Screening Tool to Alert to Right Treatment; STOPP - Screening Tool of Older Person's Prescriptions

1.2.3 Germany

Category	Germany
Included document(s), Year (Reference)	■ ABDA Leitlinie Medikationsanalyse (2019) [43] ■ Leistungsbeschreibung Medikationsberatung im Rahmen der pharmazeutischen Dienstleistungen (2022) [44] ■ Pharmazeutische Dienstleistungen bei Polymedikation (2022) [45] ■ Apotheken – Arznei-, Heil- und Hilfsmittel (2023) [46] ■ Arbeitshilfe zur Vereinbarung Medikationsberatung (2022) [47] ■ Mustervereinbarung und Abrechnungsgrundlagen pharmazeutische Dienstleistungen (2021) [48] ■ Technische Anlage 1 – Anhang 3 Pharmazeutische Dienstleistungen (2021) [49] ■ Checkliste Polymedikation (2022) [50] ■ DRKS00026247 – Medikationsanalyse in Apotheken (2022) [51] ■ Arzneiverordnung in der Praxis – Medikationsanalyse (2018) [52]
Medication review type	■ Type 2a (ABDA Leitlinie Medikationsanalyse)
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Pharmacies ■ service may also be delivered in the patient's home environment
Process ■ Duration of conversation, frequency	Frequency: ■ It consists of two appointments. Service once every 12 months; earlier if ≥3 new/other medicines within 4 weeks are added as long-term therapy (then 12-month clock restarts). Duration of conversation: ■ Between 30 – 90 minutes.
Patient selection ■ Usage of selection criteria	■ Use of ≥5 medicines in long-term therapy (≥28 days)
Methods ■ Questionnaires or screening tools used	■ Structured patient interview via brown-bag review; use of data capture form and documentation of 'arzneimittelbezogene Probleme (ABP)' per ABDA/BAK guideline; pharmaceutical AMTS check including (pseudo)duplicates, interactions, dosing errors, storage errors, adherence issues. ■ No MAI/STOPP/START reported.
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	Clinical components: ■ Check for (pseudo)duplicate therapy, interactions, unsuitable dosing interval/time, unsuitable dosage form, application problems, adverse effects/intolerances, non-adherence, inappropriateness of self-medication (incl. over/underdosing, contraindications), improper storage Patient-centred components: ■ Patient interview; assess use/application problems and adherence; agree on measures; provide updated medication plan System-related components: ■ Not reported
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Licensed pharmacists; collaboration with treating physician as needed; ATHINA-trained pharmacists offer medication analyses in public pharmacies. Qualifications/additional training:

	■ Only licensed pharmacists ('approbierte Apotheker') may provide the service and must complete training based on the Bundesapothekerkammer curriculum 'Medikationsanalyse, Medikationsmanagement als Prozess'; accepted equivalents: ATHINA, ARMIN, Apo-AMTS, BA KlinPharm (Medikationsmanager), Weiterbildung Geriatrische Pharmazie, Weiterbildung Allgemeinpharmazie.
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ Complete documentation retained in the pharmacy (service documentation; signed agreement and receipt; confidentiality release if applicable); result report to the treating physician; updated medication plan may be stored on eGK or in other TI media (ePA). Link to electronic health record: ■ Medication plan may be stored on eGK / ePA; physician report can be sent via KIM. Automated detection of DRPs: ■ Not reported
Costs ■ Costs per intervention, savings potential	Remuneration: ■ €90.00 net per completed service; billed with PZN 17716808 (standard) or PZN 17716814 (after major therapy changes). Costs per intervention: ■ €90.00 net Savings potential: ■ Not reported
Implementation notes	■ Personal contact required; reimbursable in pharmacy or patient's home; prioritisation applies if quarterly cap exceeded (§129 SGB V framework). Written agreement with the insured person is required (long or short version); patients sign to confirm eligibility and receipt; agreements retained for 4 years; Brown-bag conversation should take place in a separate/ screened area; service can be provided for eligible residents in nursing homes. Billing via DAV Nacht- und Notdienstfonds (NNF); quarterly settlement. For GKV, the §300 SGB V dataset must include: IK of pharmacy, KVNR, IK of insurer, payer name, Sonderkennzeichen (SPZN), factor=1, tax=0, co-pay=0, Gesamtbrutto=0.00, Fonds-IK 661100401 as BSNR and LANR, insured data as on eGK, and date of service as document date. ARMIN (AOK PLUS model project, Sachsen/Thüringen) comprises three modules: 'Wirkstoffverordnung', 'Medikationskatalog', and 'Medikationsmanagement'. DRKS00026247 describes a completed non-interventional evaluation (actual N=15,072) with primary endpoints including hospitalisation, mortality, misuse, adherence, and interactions; inclusion (for MM module): AOK PLUS insured, outpatient (not permanently in nursing homes), enrolled in MM with chosen ARMIN GP and pharmacy, and concurrent ≥5 systemic long-term medicines (≥6 months).

Abbreviations: ABDA – "Bundesvereinigung Deutscher Apothekerverbände" (National Umbrella Organisation representing German Pharmacists); ABP – "arzneimittelbezogene Probleme" (drug-related problems); AMTS – Arzneimitteltherapiesicherheit (Medication Therapy Safety); Apo-AMTS - ARMIN – "Arzneimittelinitiative Sachsen-Thüringen"; ATHINA – "Arzneimitteltherapiesicherheit in Apotheken" (program that trains community pharmacists to perform structured medication reviews); BAK – "Bundesapothekerkammer" (German Federal Chamber of Pharmacists); DRP – drug-related problem; eGK – elektronische Gesundheitskarte (Patient's health insurance card); ePA – elektronische Patientenakte (National electronic patient record); KIM – "Kommunikation im Medizinwesen" (electronic transmission of medical documents); MAI – Medication Appropriateness Index; START - Screening Tool to Alert to Right Treatment; STOPP - Screening Tool of Older Person's Prescriptions; TI - Telematikinfrastruktur" (National digital health infrastructure)

1.2.4 Netherlands

Category	Netherlands
Included document(s), Year (Reference)	■ Module Medicatiebeoordeling (2019) [53] ■ KNMP-richtlijn Polyfarmacie bij ouderen (2012) [54] ■ LESA Organisatie van zorg bij Chronische Medicatie (2022) [55] ■ KNMP-richtlijn Medicatiebewaking (2020) [56] ■ KNMP-richtlijn Patiëntendossier (2020) [57] ■ Hoofdstuk 6 – Medicatiebeoordeling in de praktijk (2014) [58] ■ A survey on the implementation of clinical medication reviews in community pharmacies within a multidisciplinary setting (2024) [59] ■ Clinical medication review in community pharmacies: a systematic review (2015) [60]
Medication review type	■ Clinical medication review (MBO/medicatiebeoordeling); structured method recommended (STRIP). ■ Type label (e.g., 2a/3) not explicitly stated in the guideline.
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Primary care: collaboration between GP (huisarts) and community pharmacist (openbaar apotheker)
Process ■ Duration of conversation, frequency	<u>Frequency:</u> ■ Not routine for all older adults; proactive MBO advised for high-risk group. Selection-based rather than fixed interval. <u>Duration of conversation:</u> ■ Not reported
Patient selection ■ Usage of selection criteria	■ Primarily choose patients with highest risk of FTPs: ≥75 years with chronic use of ≥10 medicines (hyperpolypharmacy) and/or established frailty; also triggers include recent hospital admission, unexplained fall, cognitive decline, poor adherence, kidney function loss, lack of social network, etc.
Methods ■ Questionnaires or screening tools used	■ Structured method: STRIP; patient pre-visit questionnaire recommended to elicit problems, questions and wishes; use of patient-defined treatment goals; STOPP/START Criteria to identify DRP. PROMISE questionnaire referenced in underpinning evidence; Goal Attainment Scaling (GAS) used in studies. Adds the Amsterdam Tool for Clinical Medication Review (checklist of 124 DRPs across 20 sections + semi-structured patient-interview script); patient-reported PROMISE symptoms used in Dutch CMR research; structured questionnaires commonly used during anamnesis.
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique)	<u>Clinical components:</u> ■ Identify and resolve FTPs: interactions, (pseudo)duplicate therapy, dosing/dose-interval issues, inappropriate duration, contraindications, inappropriate dosage form, adverse effects and lack of effect. <u>Patient-centred components:</u> ■ Shared discussion with patient (and/or caregiver); assess adherence and personal treatment goals; provide written medication changes. <u>System-related components:</u> ■ Guideline emphasizes coordinated data across GP, pharmacy and hospital for a complete, up-to-date list; ■ generic alternatives/cost analyses not reported.

■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ GP and community pharmacist jointly perform the review; geriatrician or specialist eldercare physician can be consulted as needed. Qualifications/additional training: ■ Not reported
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ Documentation in patient record per professional standards (patient dossier). Link to electronic health record: ■ Not reported Automated detection of DRPs: ■ Pharmacy information system medicatiebewakingsmodule supports signaling of FTPs (KNMP Medicatiebewaking).
Costs ■ Costs per intervention, savings potential	Remuneration: ■ Not reported Costs per intervention: ■ Not reported Savings potential: ■ Not reported
Implementation notes	■ 2019 module revises prior 2012 approach; focuses MBO on those with high risk; STRIP recommended; selection criteria centered on ≥75 years with ≥10 medicines and/or frailty; recommendations include giving a pre-visit questionnaire, setting measurable personal goals, and documenting agreements in the patient record. Nationwide survey (2024) reports mean of ~56 CMRs/pharmacy (range 0–300); 90% often/always use a structured questionnaire; labs requested sometimes/often; barriers: lack of time and suboptimal collaboration with medical specialists; responsibilities often shared between pharmacist and GP for patient selection and conduct.

Abbreviations: CMR – Comprehensive Medication Review; DRP – drug-related problem; FTP – "Farmacotherapeutisch Probleem" (drug-related problem); GAS – Goal Attainment Scaling; GP – general practitioner; KNMP Medicatiebewaking – Koninklijke Nederlandse Maatschappij ter Bevordering der Pharmacie (Medication Surveillance); MBO – "Multidisciplinair Beroepsoverleg" (multidisciplinary consultation); PROMISE (questionnaire) – PROactive MIdication Services; START - Screening Tool to Alert to Right Treatment; STOPP - Screening Tool of Older Person's Prescriptions; STRIP – Systematic Tool to Reduce Inappropriate Prescribing

1.2.5 Switzerland

Category	Switzerland
Included document(s), Year (Reference)	■ Polymedikations-Check in der Apotheke (2024) [61] ■ Medication review in Swiss community pharmacies: Implementation and outcomes (2018) [62] ■ Medication Review Poster – Polymedikations-Check (2011) [63] ■ Tarifverträge LOA (2024) [64] ■ Tarifvertrag Gesamt inkl. Addendum (2024) [65]
Medication review type	■ Polymedication Check (PMC) – intermediate medication review
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Community pharmacies
Process ■ Duration of conversation, frequency	Frequency: ■ Not reported Duration of conversation: ■ Mean ~37 minutes (pilot poster)
Patient selection ■ Usage of selection criteria	■ Patients taking ≥4 prescribed medicines over >3 months (PMC)
Methods ■ Questionnaires or screening tools used	■ Structured assessment form; face-to-face counseling interview (PMC)
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	Clinical components: ■ Identification of drug-related problems; assessment of need for weekly pill organizer Patient-centred components: ■ Focus on adherence; counseling; support with weekly pill organizer System-related components: ■ Not reported
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Pharmacists in community pharmacies Qualifications/additional training: ■ Not reported
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ Not reported Link to electronic health record: ■ Not reported Automated detection of DRPs: ■ Not reported
Costs ■ Costs per intervention, savings potential	Remuneration: ■ Polymedikations-Check (PMC) is NOT reimbursed by mandatory health insurance (KVG/OKP) since 2019; can be offered as a self-pay service. For MTK/UVG/MVG/IVG cases, tariff applies with TPW per contract (e.g., CHF 1.20).

	Costs per intervention: ■ Not reported Savings potential: ■ Not reported
Implementation notes	■ 2018 randomised controlled trial in 54 Swiss community pharmacies showed PMC increased patient knowledge and was well accepted by patients. Under LOA IV/1, the Federal Council excluded the PMC tariff position from the tariff structure (2019); pharmacies may offer PMC as a self-pay service.

Abbreviations: CHF – Confédération Helvétique Franc (Swiss Franc); DRP – drug-related problem; KVG / OKP – Krankenversicherungsgesetz / Obligatorische Krankenpflegeversicherung (Swiss Federal Health Insurance Act / Mandatory Health Insurance); LOA – "Leistungsorientierter Ordnungstarif Apotheke" (Pharmacy tariff agreement); MTK/UVG/MVG/IVG – Swiss social-insurance schemes; PMC – Polymedication Check; TPW – "Taxpoint Wert" (Tax point value)

1.2.6 United Kingdom

Category	United Kingdom
Included document(s), Year (Reference)	■ Structured Medication Reviews (SMR) in Primary Care (2020) [66] ■ SMR Specification Guidance 2020–21 (2020) [67] ■ Network Contract DES SMR and Medicines Optimisation Guidance 2021–22 (2021) [68] ■ Resources to Support Medication Review (2023) [69] ■ Structured Medication Reviews and the Primary Care Network Multidisciplinary Approach – Case Study (2022) [70] ■ PCN Requirements and Entitlements 2025–26 (2025) [71] ■ Network Contract DES Part A – Clinical and Support Services (Section 8) (2024) [72] ■ NG5 Medicines Optimisation (2015) [73] ■ Polypharmacy Guidance 2018 (2018) [74]
Medication review type	■ Structured Medication Review (SMR) under the PCN Network Contract DES (NICE-approved clinical intervention)
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Primary care networks (PCNs) in general practice; may be undertaken face-to-face in the practice, in the patient's home/care home, or remotely as clinically appropriate
Process ■ Duration of conversation, frequency	Frequency: ■ No fixed interval; patients identified and prioritised proactively and reactively based on risk/cohorts and clinical need Duration of conversation: ■ Often 30 minutes or more; exact length varies with patient need
Patient selection ■ Usage of selection criteria	■ PCNs must prioritise: residents in care homes; people with complex/problematic polypharmacy (specifically ≥10 medicines); people on medicines commonly associated with medication errors; people with severe frailty (including isolated/housebound or with recent admissions/falls); and those using potentially addictive pain medicines; others may be offered SMR if likely to benefit
Methods ■ Questionnaires or screening tools used	■ Shared decision-making; use of identification and audit tools; SPS collates tools that can support SMR such as STOPP/START, Beers, MAI, CGA resources, NICE NG5 (Medicines optimisation) and the Scottish Polypharmacy Guidance (7-step approach) are cited resources to support structured review; they can inform SMR conduct alongside local tools (e.g., PINCER, STOPP/START, MAI).
Programme components	Clinical components:

■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	■ Comprehensive clinical review of all medicines to improve safety (reduce ADR risk, errors) and effectiveness; not a repeat-prescription authorisation Patient-centred components: ■ Person-centred, shared decision-making conversation; consider health literacy; agree actions and arrange follow-up as needed System-related components: ■ National MO priorities referenced (e.g., AMR, dependency-forming medicines, lower-carbon inhalers, low-priority items); ■ generic substitution not explicitly stated
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Primarily clinical pharmacists; suitably qualified advanced nurse practitioners and GPs may also undertake SMRs; multidisciplinary support across the PCN Qualifications/additional training: ■ SMRs undertaken only by appropriately trained clinicians with a prescribing qualification and advanced assessment/history-taking skills, or enrolled on a pathway to develop these; pharmacists should have completed or be enrolled on CPPE PCPEP or similar including IP
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ SMRs must be recorded on GP IT systems using the SMR SNOMED code; local templates/tools may be used Link to electronic health record: ■ Recorded directly in GP electronic health record systems; remote consultations permitted with appropriate competence Automated detection of DRPs: ■ PINCER cited as an evidence-based intervention to reduce clinically significant medication errors
Costs ■ Costs per intervention, savings potential	Remuneration: ■ Service delivered under the PCN DES; no per-intervention tariff stated in these documents Costs per intervention: ■ Not reported Savings potential: ■ Potential to reduce hospital admissions and improve value for money noted, but no quantified savings reported
Implementation notes	■ SMR is a structured, holistic and personalised review considering all medicines; invitations to SMRs must explain the purpose of the service to the patient; appointments offered for new and follow-up SMRs; may be undertaken remotely or at home/care home if appropriate; follow-up arranged based on complexity; identification can be proactive (cohorts) and reactive (e.g., post-admission, patient request, monitored dosage system request). PCN DES 2024/25 and 2025/26 specifications (Part A, Section 8) set out ongoing SMR requirements under the Network Contract DES; SMRs must be coded in the GP record and delivered by appropriately trained prescribers within PCNs.

Abbreviations: ADR – Adverse Drug Reaction; AMR – Antimicrobial Resistance; CGA – Comprehensive Geriatric Assessment; CPPE – Centre for Pharmacy Postgraduate Education; DES – Direct Enhanced Service; DRP – Drug-Related Problem; IP – Independent Prescribing; MO – Medicines Optimisation; NICE – National Institute for Health and Care Excellence; PCN – Primary Care Network; PCPEP – Primary Care Pharmacy Education Pathway; PINCER – Pharmacist-led INformation technology intervention for reducing Clinically important Errors; SMR – Structured Medication Review; SNOMED – Systematized Nomenclature of Medicine Clinical Terms; SPS – Specialist Pharmacy Service

1.2.7 Transnational documents

Category	Transnational organisations
Included document(s), Year (Reference)	■ Medication Safety in Polypharmacy – Technical Report (2019) [75] ■ Medication Without Harm – WHO Global Patient Safety Challenge (2017) [76] ■ WHO Technical Series on Safer Primary Care: Medication Safety (2023) [77] ■ The Economics of Medication Safety (2022) [78] ■ Living with Multiple Chronic Conditions (2025) [79] ■ EDQM Guidelines on Medication Review (2024) [80] ■ FIP Global Pharmacy Workforce Review (2025) [81]
Medication review type	■ No specific type reported in transnational documents
Setting ■ Pharmacies, hospitals, doctor's office, home environment	■ Cross-setting applicability; WHO and EDQM emphasise multidisciplinary, person-centred reviews across care transitions
Process ■ Duration of conversation, frequency	Frequency: ■ Not reported Duration of conversation: ■ Not reported
Patient selection ■ Usage of selection criteria	■ WHO technical report provides guidance on prioritising patients at higher risk in polypharmacy for review; ■ EDQM guideline provides structured process and documentation elements for selecting patients
Methods ■ Questionnaires or screening tools used	■ Transnational documents reference structured medication review processes; ■ Specific instruments may be used locally; WHO/EDQM do not mandate a single tool set in these documents
Programme components ■ Clinical components (e.g. analysis of contraindications, interactions, dosages, duration of therapy, identification of drugs without indication) ■ Patient-centred components (e.g. therapy adherence, analysis of administration technique) ■ System-related components (e.g. identification of generic drugs as more cost-effective alternatives)	Clinical components: ■ Transnational guidance highlights systematic identification of drug-related problems (e.g., interactions, duplicate therapy, inappropriate dosing/duration) Patient-centred components: ■ Strong emphasis on person-centred care and shared decision-making; involvement of patients and caregivers System-related components: ■ OECD and WHO documents focus on safety and system-level enablers; generic substitution specifics not reported
Workforce requirements ■ Professional groups involved, qualifications, additional training	Professional groups involved: ■ Multidisciplinary teams recommended (pharmacists, physicians, nurses); EDQM clarifies roles in medication review Qualifications/additional training: ■ FIP global workforce review advocates competency development frameworks; specific transnational training requirements not reported
Digital tools ■ Digital documentation, link to electronic health record, automated detection of drug interactions and other drug-related problems	Digital documentation: ■ Encouragement of standardised documentation/templates (EDQM) and data sharing to support reviews Link to electronic health record: ■ Interoperability and access to accurate medicine lists across settings recommended; no single standard mandated Automated detection of DRPs: ■ Not reported

Costs ■ Costs per intervention, savings potential	Remuneration: ■ Not applicable Costs per intervention: ■ Not applicable Savings potential: ■ OECD reports substantial economic burden from medication-related harm; specific savings from medication review not reported ■ WHO Step-by-step approach to conducting a patient-centred medication review includes the question "Is the therapy cost-effective?" to identify unnecessarily costly medication by considering more cost-effective alternatives (but balance against effectiveness, safety, convenience)
Implementation notes	■ WHO Global Patient Safety Challenge 'Medication Without Harm' aims to reduce severe avoidable medication-related harm by 50%; EDQM 2024 guideline provides detailed process guidance on medication review; OECD 2022 report offers policy recommendations to strengthen medication safety systems; FIP 2025 workforce review presents global workforce capacity indicators

Abbreviations: DRP – Drug-Related Problem; EDQM – European Directorate for the Quality of Medicines & HealthCare; FIP – International Pharmaceutical Federation; OECD – Organisation for Economic Co-operation and Development; WHO – World Health Organization

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