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SYSTEMATIC REVIEW

Medicine Optimisation and Deprescribing Intervention Outcomes for Older People with Dementia or Mild Cognitive Impairment: A Systematic Review

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Abstract

Background Polypharmacy is common amongst older people with dementia or mild cognitive impairment (MCI), increasing the risk of medication-related harm. Medicine optimisation and deprescribing to reduce polypharmacy is considered feasible, safe and can lead to improved health. However, for those living with dementia or MCI, this can be challenging. This systematic review aimed to summarise the evidence on the outcomes of medicine optimisation and deprescribing interventions for older people with dementia or MCI.

Methods Literature was searched using CINAHL, Embase, Medline, PsychINFO, Web of Science and the Cochrane Library from database inception to January 2024. Papers reporting data specific to people with dementia or MCI from medicine optimisation and deprescribing interventional research studies of any design and in any setting were included. A narrative synthesis was conducted owing to heterogeneity of study designs and outcomes. Quality was assessed using the Mixed Methods Appraisal Tool.

Results A total of 32 papers reporting on 28 studies were included, with samples ranging from 29 to 17,933 patients and a mean patient age ranging from 74 to 88 years. Of the studies, 60% were undertaken in long-term care settings. Involvement of patients and/or carers in interventions was limited. Papers were grouped as either incorporating a medication review component ($n = 13$), education component ($n = 5$) or both ($n = 14$). Studies primarily focussed on medication-related outcomes, generally showing a positive effect on decreasing the number and improving appropriateness of medications. Fewer papers reported clinical outcomes (behavioural and psychological symptoms of dementia, falls, quality of life and cognition) with mixed findings. A reduction or no change in mortality or hospital attendance demonstrated safety of the interventions in the few papers reporting these outcomes. The quality of the evidence was mixed.

Conclusions Medicine optimisation and deprescribing interventions generally reduced the number and increased the appropriateness of medications, and although less frequently reported, these interventions seemed to be safe and showed an absence of worsening of clinical outcomes. This review highlights a need for further research, particularly in people with dementia or MCI living at home, with more focus on clinical outcomes and a greater involvement of patients and informal carers.

Protocol Registration The protocol was published in the International Prospective Register of Systematic Reviews (PROSPERO) [Ref: CRD42023398139].

1 Background

In developed countries, most people with dementia or mild cognitive impairment (MCI) have multiple long-term conditions and are prescribed five or more regular medications, which is the most common definition of polypharmacy [1, 2]. Polypharmacy in people living with dementia is associated with increased risk of drug–drug interactions, falls, cognitive decline and serious adverse events such as emergency department attendance, hospitalisation and death [3, 4]. Polypharmacy in this group also increases the risk of potentially inappropriate medication (PIM) [5], a term commonly used to refer to medications for which potential risks outweigh potential benefits and that have a higher risk of adverse drug events [6, 7]. Medication management on a

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Key Points

Medicine optimisation and deprescribing interventions for people with dementia or mild cognitive impairment show a trend towards reducing numbers of medications and improving appropriateness of medication.

There was limited evidence on clinical and safety outcomes and limited involvement of patients and informal carers.

Most studies were conducted on medicine optimisation and deprescribing interventions, focussing on psychotropic medications and people in residential care, with very few studies conducted in primary care settings.

daily basis is a complex and challenging activity involving both older people with dementia and their carers [8, 9].

To reduce the potential harm associated with polypharmacy in this population, medicine optimisation and deprescribing are recommended [10]. Deprescribing is the process of tapering or reducing doses or stopping or switching drugs, with the goal of managing polypharmacy and reducing the risk of adverse outcomes [11]. There is evidence that deprescribing across a wide range of conditions, medications and care settings, and using different deprescribing tools, is feasible, safe and can benefit patients [12–17]. Medication-induced harm is now classified as one of the World Health Organisation's global health priorities and a national priority in many countries, including the UK, Canada, Australia and the USA [18]. Encouraging open and honest conversations about medication is important to reduce and prevent this harm [18, 19]. Optimising medications through deprescribing has the potential to improve outcomes for people living with dementia [20] and may reduce the risk of MCI progressing to dementia [21].

Several systematic reviews have been published to summarise the effectiveness of medicine optimisation and deprescribing interventions in older adults in general, with some focussing on health-related, safety and cost outcomes [12, 17, 22] or on specific clinical settings [15]. One review of the impact of deprescribing among people living with frailty reported that it is feasible, acceptable and can lead to benefits in terms of cognition and medication appropriateness [23]. Reviews report that medicine optimisation and deprescribing could be safe and can benefit patients [12–17]. However, there is limited direct evidence to inform medicine optimisation and deprescribing in older adults with dementia or MCI, specifically. Optimising medications amongst this population is complicated owing to difficulties in comprehension, challenges in communication and involvement of informal carers [24].

A recent survey in the USA of 422 older people with dementia reported that 87% were willing to stop one or more of their medications if advised by their doctors, and 50% were uncomfortable taking five or more medications [25]. Yet, a narrative review published in 2021 found limited evidence of involvement of the person with dementia or their carer in decisions about their medicines [20] and reported that most research concentrated on medication-related outcomes (e.g. discontinuation of high-risk medications) rather than clinical outcomes that have a direct impact on a person's well-being, such as cognition and falls. The authors recommended that more research be conducted on the impact of deprescribing in this population across clinical settings. Reviews in this field have also focussed primarily on identifying barriers and facilitators of deprescribing in this population and less on the effects of deprescribing interventions [24, 26]. Therefore, the aim of this systematic review was to explore the effects of medicine optimisation and deprescribing interventions specific to older people with dementia or MCI.

2 Methods

The methods recommended by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement were used to complete the review [27]. It was registered on the international prospective register of systematic reviews (PROSPERO), ID no. CRD42023398139.

2.1 Data Sources and Searches

The following electronic databases were searched for papers published from database inception to search date (initial search 3 February 2023; updated 26 January 2024): CINAHL, Embase, Medline, PsychINFO, Web of Science and the Cochrane library. The search strategy using keywords, including dementia, mild cognitive impairment, deprescribing, medicines optimisation, polypharmacy and inappropriate prescribing, was developed with a senior librarian (Online Resource 1). Reference lists of included papers were searched for further potentially relevant studies.

2.2 Screening and Study Selection

As the review focussed on interventions, the population, intervention, comparator, outcomes, study design (PICOS) framework was used to develop the inclusion and exclusion criteria, outlined in Table 1. The citations identified from the

searches were screened in three stages using these eligibility criteria.

Firstly, titles were independently double screened using Excel. N.A. screened all titles and B.M., K.A. and K.I. each screened a subset of titles, with citations excluded only where there was agreement between two authors. Abstracts were then independently screened by five authors (N.A., J.A., C.B., S.F. and B.M.) using Rayyan™ software [28], which facilitates and expediates collaborative and blind screening and selection of papers, with any disagreement resolved by discussion. Full text papers of those included at this stage were each independently screened by eight authors (N.A., K.A., C.B., S.F., K.I., E.v.L., R.L. and S.L.), with disagreement resolved by discussion. Consistency of criteria application was then checked by N.A., C.B. and K.I.

2.3 Quality Assessment

The Mixed Methods Appraisal Tool (MMAT) [29], developed for quality appraisal in systematic reviews of mixed studies, was used to assess the quality of the included papers. This allowed the same tool to be used for all the papers, despite heterogeneity in study designs. Quality assessment was completed by two authors independently (M.B. and E.R.), with final ratings agreed by discussion. Each paper was given a score from one to five, with lower scores indicating lower quality studies. Studies were not excluded on the basis of quality; rather, this was used to inform the interpretation of the data.

2.4 Data Extraction

Data from included studies were extracted into a form developed in Microsoft Excel and piloted with two papers. Data extraction was completed independently by N.A. and six other authors (K.A., M.B., C.B., K.I., S.L. or R.L.). Disagreements were resolved through consensus discussion between N.A., C.B. and K.I. Data extracted included: year of publication, country, setting, number and characteristics of participants, description of the deprescribing intervention and any comparator, length of follow-up, medications most frequently deprescribed, deprescribing tools used and involvement of patients and carers in the intervention and outcomes of deprescribing.

2.5 Data Synthesis

Owing to the heterogeneity of study designs and outcome measures, meta-analysis of effect estimates was not possible, and narrative synthesis was conducted using the Synthesis Without Meta-analysis (SWiM) guideline [30]. Studies were grouped according to intervention type, with groupings

Table 1 Inclusion and exclusion criteria for the systematic review

PICOS	Inclusion criteria	Exclusion criteria
Population	Older people with a diagnosis of any type of dementia or mild cognitive impairment or who provide care (formal or informal) to people with a diagnosis of dementia or mild cognitive impairment (determined by study authors) Or Studies with a population that includes older people with a diagnosis of any type of dementia or mild cognitive impairment or those who provide care to this population amongst others, where the data for the target population can be separated from the broader population	People with cognitive impairment but who do not have a diagnosis of dementia or mild cognitive impairment or people who provide care (formal or informal) to people with cognitive impairment owing to other causes
Intervention	Any intervention in any setting that aims to deprescribe medication or involves medicine optimisation or medicine review, including dose reduction/tapering, stopping or switching drugs	Any multi-dimensional interventions that include a deprescribing/medicine optimisation/medicine review element alongside other intervention components, where the data relating to the deprescribing element cannot be separated from the other components
Comparator	Any or no comparator	
Outcomes	Any outcome, including (but not restricted to) safety of deprescribing, clinical outcomes, medication-related outcomes, feasibility of deprescribing, acceptability and cost-related outcomes At least one patient-related outcome, defined as outcomes measured using individual patient data[a]	No patient-related outcomes, defined as outcomes measured using individual patient data[a]
Study design	Interventional research studies with any design and in any setting	Quality improvement, service evaluation or audit[a]
Search limits	Any paper published from database inception to date of search Any language	

[a]Criteria added after initial protocol publication, as per amended PROSPERO record

agreed upon once papers had been identified. Outcome data were categorised into three categories: medication-related outcomes, clinical-related outcomes and safety outcomes. Both medication and clinical outcomes were based on a recent review of outcomes of deprescribing interventions [31]. Safety outcomes included mortality, hospitalisations and emergency department visits as these are the most commonly used outcome measures in deprescribing literature [23, 32].

Outcome data were summarised and then tabulated according to intervention type and direction of effect for comparison.

3 Results

The searches identified 8825 individual citations of which 163 were selected for full text assessment and 29 papers were eligible for inclusion in the review. An additional three eligible papers were identified from the screening of reference lists of included papers, with a total of 32 papers included in this review (Fig. 1). Translation of one potentially eligible non-English paper was unavailable.

3.1 Study Characteristics

The 32 papers included in this review reported findings from 28 unique research studies (Table 2). All included papers were published between 2013 and 2024. Studies were conducted in 12 countries: Canada ($n = 6$), Spain ($n = 6$), the USA ($n = 5$), Australia ($n = 2$), the UK ($n = 2$), France ($n = 1$), Ireland ($n = 1$), Italy ($n = 1$), Japan ($n = 1$), Sweden ($n = 1$), Taiwan ($n = 1$) and the Netherlands ($n = 1$). Over half of the papers reported studies completed in long-term residential care settings ($n = 19$). Papers also reported studies undertaken in primary care or community healthcare services ($n = 6$), hospital inpatient settings ($n = 5$), hospital outpatient settings ($n = 1$) and across multiple settings ($n = 1$). Papers primarily focussed on deprescribing of either psychotropic medications ($n = 16$, all but one in long-term care settings) or PIMs ($n = 9$). Eight papers reported randomised controlled trials (RCTs). The length of follow-up ranged from 11 days (mean length of hospital admission) to 2 years, with most papers reporting follow-up periods of 6 ($n = 12$), 9 ($n = 5$) or 12 months ($n = 5$). Attrition was reported in half of the papers ($n = 16$) and ranged from 8% to 51%, with the main reasons cited being death or a change in the care setting of the participants. The assessed quality of the papers was variable. Quality issues were highlighted with quantitative studies that did not use randomisation to allocate to comparison groups (non-randomised studies) more frequently than with RCTs, quantitative descriptive studies and mixed methods studies. These issues particularly related to confounders and sample representativeness, with non-randomised studies accounting for more than half of the studies ($n = 16$).

In total, 11 of the 32 papers reported interventions that included active involvement of patients and/or informal carers in the medicine optimisation or deprescribing process [32–42]; only one [39], a medication review and education intervention, incorporated shared decision-making. The study protocol reports dialogue between the professionals, person with dementia and their carer during the medication review [43]. In addition, nine papers reported person-centred deprescribing interventions [32–38, 41, 42]; however, it is not possible to determine from the papers whether this involvement implemented shared decision-making principles. Another paper reported an intervention [40] that empowered patients to lead deprescribing decision-making through the use of educational materials.

3.2 Participant Characteristics

Study sample sizes ranged from 29 to 17933 patients. Participants were predominately older people, with the mean patient age ranging from 74 to 88 years. However, this does not preclude a small minority of the study populations from being aged under 65 years; one study explicitly stated that 4% of the participants were under 65 years [44], with an age range of 55 to 99 years (mean of 84 years) provided in one study set in long-term care [45, 46]. Moreover, seven studies explicitly recruited populations aged 65 years and over [32–34, 41, 47–51] and one recruited participants aged 60 years and over [38]. The percentage of female patients ranged from 51% to 79%, except in two outlier studies (one recruited only male patients [52], whilst the other had 22% female patients [47]). In total, 26 papers reported on outcomes for people with dementia, 5 for people with either dementia or MCI and 1 for people with MCI only. Participant dementia type was rarely provided, with this information only provided in five studies [45, 46, 48, 49, 51, 53, 54]. The diagnosis of dementia or MCI was determined by the study authors, mostly using medical records, including documented diagnosis, prescription of anti-dementia medication or other relevant information. Some study authors also used one or more of the following criteria to determine a diagnosis of dementia or MCI: (1) being a resident in a long-term care dementia unit, (2) assessment by specialist professionals and (3) the use of tools to assess disease severity, including the Clinical Dementia Rating Score, Functional Assessment Staging Test, Global Deterioration Scale, Mini Mental State Examination and Montreal Cognitive Assessment.

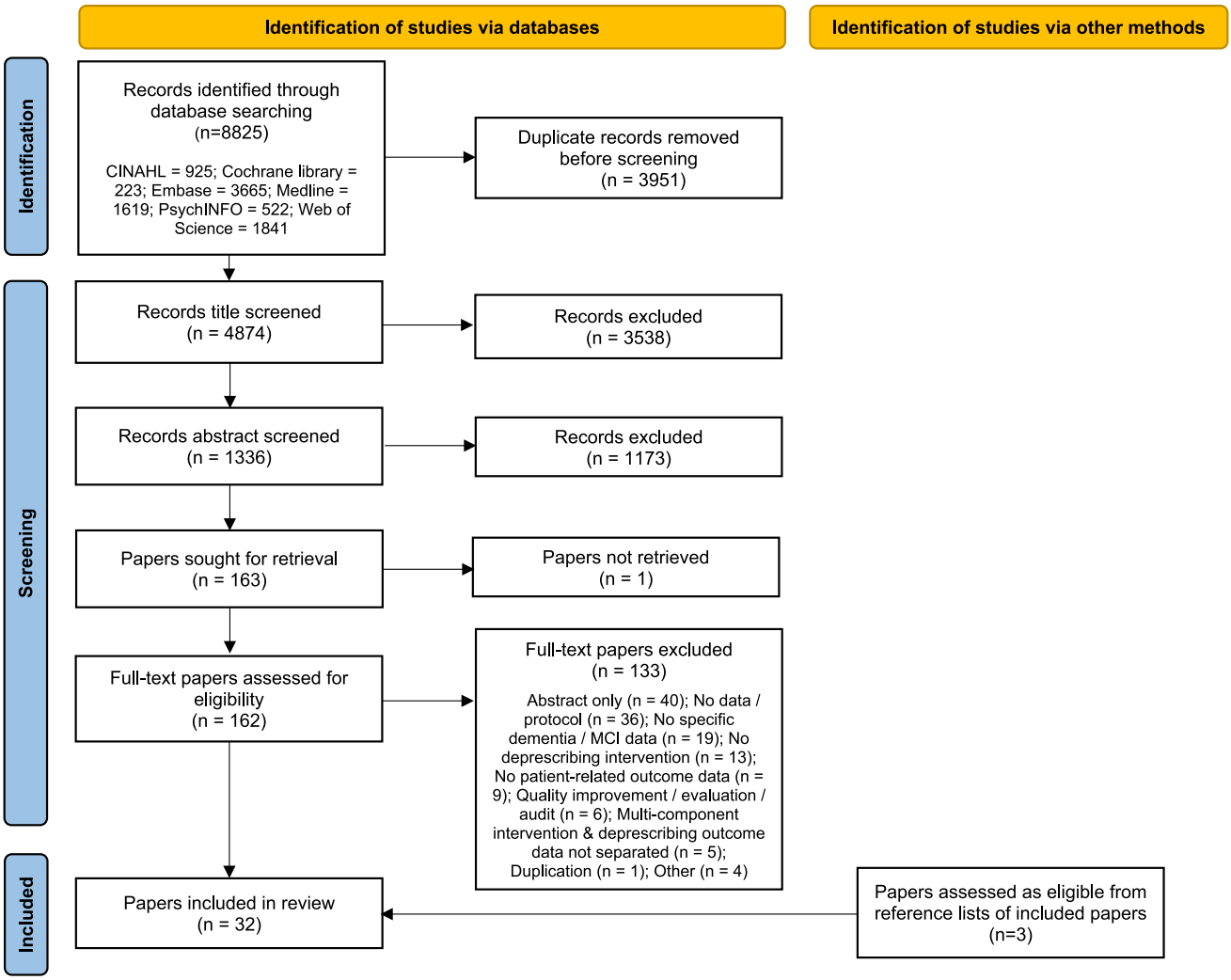

Fig. 1: PRISMA flowchart

3.3 Types of Interventions

Owing to heterogeneity of outcome measures and study designs, papers were grouped according to the intervention investigated as either "medication review and healthcare professional education interventions" (14 papers), "medication review interventions" (13 papers) or "patient, carer and/or healthcare professional education interventions" (5 papers), although there was considerable variation between interventions in each group.

Medication review and healthcare professional education interventions (reported in 14 papers) [35–39, 45, 46, 50, 52, 55–59], all implemented in long-term care settings, involved formal education that included a focus on deprescribing delivered either through taught sessions or by provision of information. The medication review component of the interventions was led by either a doctor, pharmacist or a multi-disciplinary (MDT) team.

Medication review interventions (reported in 13 papers) [34, 41, 42, 44, 47–49, 54, 60–62] were either a standalone intervention ($n = 10/13$) or combined with other components (such as a new model of coordinated primary care or proactive medication monitoring), with data specifically relating to the medication review reported. These were implemented in a range of settings. In total, seven papers reported medication reviews led by pharmacists, four papers reported MDT-led reviews and one paper reported an automated review using a computer algorithm triggering alerts to professionals. There were no details provided of the medication review process in one paper.

Patient, carer and/or healthcare professional education interventions (reported in five papers) all included formal education relating to deprescribing as the only intervention [32, 33, 40, 63, 64]. Two reported studies were completed in long-term care settings and three in primary care or community settings. These involved either educational sessions

Table 2 Characteristics of the papers included in the review

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Medication review and healthcare professional education interventions										
Ballard 2016 [55]; Ballard 2017 [50]	UK Long-term care	Cluster 2 × 2 × 2 factorial randomised controlled trial	277	100% dementia / types not specified	Training of staff in person-centred care and physician-led antipsychotic review.	Multiple comparators	9 mths	Antipsychotics	National or provincial guidelines	4
Brodaty 2018 [56]	Australia Long-term care	Repeated measures, longitudinal, single-arm study	139	98.5 % dementia / types not specified	Education of MDT and pharmacist-developed individualised deprescribing protocol implemented.	Pre-post	12 mths	Antipsychotics	National or provincial guidelines	4
Cossette 2020 (phase 1) [35]	Canada Long-term care	Mixed methods study	464	100 % dementia / types not specified	Knowledge mobilisation strategy and antipsychotic medication review using provincial guidelines.	None	9 mths	Antipsychotics	National or provincial guidelines	3
Cossette 2022 (phase 2) [36]	Canada Long-term care	Prospective, closed cohort, scale-up study	4087	100% dementia / types not specified	As for phase 1 but included a train the trainer approach owing to scale-up.	Phase 1	9 mths	Antipsychotics	National or provincial guidelines	4
Kröger 2023 [38]	Canada Long-term care	Pragmatic, non-randomised controlled study	123	100% dementia / types not specified	MDT knowledge exchange session and leaflet for families plus pharmacist-led medication review.	Usual care	6 mths	Any medication	Intervention specific	4

Table 2 (continued)

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Maidment 2020 [39]	UK Long-term care	Open label (non-blinded), mixed methods feasibility study	29	100% dementia / types not specified	MDT-led medication review involving resident and their carer plus staff training on BPSD treatment.	Meds change vs no meds change	6 mths	Psychotropics	Not specified	3
Massot Mesquida 2019 [57]	Spain Long-term care	Prospective, multi-centre, quasi-experimental, longitudinal, pre-post study	240	100% dementia / types not specified	A GP and pharmacist were trained, who led medication reviews on the basis of BPSD management guidelines.	Pre-post	6 mths	Psychotropics	Intervention specific	3
Muniz 2020 [58]	Spain Long-term care	Observational, longitudinal, prospective validation study	288	71.4% dementia / types not specified	Training of MDT and use of CHROME criteria to guide quality prescribing of psychotropic medicines.	None	2 yrs	Psychotropics	Intervention specific	3
Muniz 2021 [59]	Spain Long-term care	Observational, prospective, two-wave, pilot study	171	84.8% dementia / types not specified; 15.2% MCI	Doctors were trained in the CHROME criteria, using these to reassess diagnoses and deprescribe.	Pre-post	12 mths	Psychotropics	Intervention specific	3
van der Spek 2018 [46]; Smeets 2021 [45]	The Netherlands Long-term care	Cluster randomised controlled pragmatic trial with two parallel groups	380	AD (33%), Vascular (15%), Mixed AD/vascular (11%), other (41%)	Repeated MDT-led medication reviews following national guidelines, after initial education phase.	Usual care	18 mths	Psychotropics	National or provincial guidelines	5

Table 2 (continued)

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Wilchesky 2018 [37]	Canada Long-term care	Quasi-experimental feasibility pilot study	44	100% dementia / types not specified	MDT knowledge exchange session and leaflet for families plus pharmacist-led medication review.	Pre-post	Mean 104 days	Any medication	Intervention specific	4
Yeh 2013 [52]	Taiwan Long-term care	Prospective, open-label, case-control cohort study	67	100% dementia / types not specified	Education materials mailed to GPs, with anticholinergic medications tapered or replaced.	Usual care	3 mths	Anti-cholinergics	CRACHS	3
Medication review interventions										
Andrew 2018 [60]	Canada Long-term care	Observational pre-post study	159 pre 370 post	55.9% pre & 72.8% post with dementia / types not specified	A multi-component intervention including a biannual pharmacist-led medication review.	Pre-post	N/A	PIMs	Beers	5
Bravo-José 2019 [53]	Spain Long-term care	Prospective, single centre, before-after study	35	AD (46%), vascular (14%), non-specific (40%)	Gradual tapering of antipsychotic treatment.	Pre-post	6 mths	Antipsychotics	Intervention specific	3
Coli 2022 [48]	USA Hospital outpatient	Prospective, observational study	180	AD (32%), vascular (7%), Lewy body (2%), Parkinson dementia (2%), other (38%), MCI (28%)	Pharmacist-led medication review, recommendations made prior to the patients' next appointment.	Pre-post	6 mths	PIMs	Beers/STOPP/ Anticholinergic burden scale	4
Gustafsson 2017 [51]; Gustafsson 2018 [49]	Sweden Hospital inpatient	Randomised controlled trial	429	AD (31%), vascular (17%), other or unspecified dementia (52%)	Pharmacist-led medication reconciliation and medication review.	Standard care	6 mths	PIMs	National or provincial guidelines	5

Table 2 (continued)

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Jaidi 2018 [54]	France Hospital inpatient	Prospective, single centre study	125	AD (57%), Mixed AD / vascular (26%), vascular (14%), Lewy body (4%)	Substitution of medications potentially inappropriate owing to anticholinergic burden.	Pre-post	Admission length	Anti-cholinergics	Anticholinergic cognitive burden scale	4
Kable 2023 [61]	Australia Hospital inpatient	Non-randomised experimental study with pre-post design	628	100% dementia or MCI / dementia types not specified	Medication reconciliation and review by hospital pharmacist on admission and prior to discharge.	Pre-post; control	3 mths	PIMs	Beers/modified anticholinergic burden score	4
Liu 2022 [42]	USA Community	Secondary analysis of a multi-centre, single-blind randomised controlled trial	490	100% dementia / types not specified	Protocol-guided, interdisciplinary medication review, with proactive medication monitoring.	Usual care	12 mths	PIMs	Beers	4
Molist Brunet 2014 [34]	Spain Hospital inpatient	Non-experimental pre-post study	73	100% dementia / types not specified	MDT-led systematic evaluation of medication profiles and development of therapeutic plans.	Pre-post	Admission length	Any medication	Beers/STOPP	4
Pearson 2021 [62]	USA Primary care	Retrospective, descriptive analysis of two clinical initiatives *(only one eligible for review)*	40	100% dementia / types not specified	Pharmacist-led medication reconciliation and review, focussed on medications impacting cognition.	Pre-post	6 mths	PIMs	Beers	2

Table 2 (continued)

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Sakakibara 2015 [47]	Japan Community	Non-randomised controlled study	50	100% dementia / types not specified	Prescription drugs were reduced as proposed by a pharmacist.	Usual care	6 mths	Any medication	Not specified	3
Silva-Almodóvar 2020 [44]	USA Cross-settings	Retrospective, observational cohort analysis of a database	17933	100% dementia / types not specified	Computer algorithm-led review of prescription claims data, with alerts sent to prescriber.	None	12 mths	PIMs	Beers	3
Weeks 2019 [41]	Spain Long-term care	Quasi-experimental, retrospective, match-controlled, observational analysis	1653	100% dementia / types not specified	MDT-led medication review OR Use of STOPP/START criteria OR patient "Decision Aid" use.	Matched controls	4 wks	Psychotropics	Intervention specific	4
Patient, carer, and/or healthcare professional education interventions										
Bayliss 2022 [33]; Boyd 2024 [32]	USA Primary care	Pragmatic cluster randomised controlled trial	1433	88.1% dementia / types not specified; 21.9% MCI	Educational brochure mailed to patients before appointment; tip sheets provided to clinicians.	Usual care	6 mths	PIMs	Beers	4
Martin 2017 [40]	Canada Community	Post-hoc analysis of randomised, double-blind, wait-list controlled trial	261	46.7% MCI	Educational brochure including a deprescribing tool mailed to patients.	MCI vs no MCI	6 mths	Benzo-diazepines	Intervention specific	5

Table 2 (continued)

First author and year of publication	Country and setting	Study design	Sample size	% dementia or MCI and type of dementia	Intervention	Comparator	Follow-up	Medication class	Deprescribing tool	Quality score[a]
Pasina 2016 [63]	Italy Long-term care	Quantitative, multi-centre, prospective pilot study	295	66.2% dementia / types not specified	MDT-led educational interventions and training on use of a digital prescription support system.	Pre-post	9 mths	Psychotropics	Beers/STOPP/ Anticholinergic cognitive burden scale	3
Walsh 2022 [64]	Ireland Long-term care	Mixed methods feasibility study	43	57% dementia / types not specified	Education of nursing home staff (direct or via 'opinion leaders'); academic detailing with GPs.	None	3 mths	Antipsychotics	Intervention specific	4

AD Alzheimer's disease, *BPSD* behavioural and psychological symptoms of dementia, *CHROME* CHemical Restraints avOidance MEthodology, *CRACHS* clinician-rated anticholinergic score, *MCI* mild cognitive impairment, *MDT* multidisciplinary team, *Mths* months, *PIMs* potentially inappropriate medications, *START* Screening Tool to Alert to Right Treatment, *STOPP* Screening Tool of Older Person's potentially inappropriate Prescriptions, *Wks* Weeks, *Yrs* Years

[a]Score calculated using 'yes' responses to the five quality appraisal questions for the appropriate study type of the Mixed Methods Appraisal Tool [29]

or the provision of educational materials: two interventions were solely for professionals, one intervention was solely for patients and two interventions involved patients, informal carers and professionals.

Variation in intervention characteristics within these groups are explored in the synthesis narrative and more details about each individual intervention is provided in Online Resource 2. A range of deprescribing tools was used across all intervention group types, including Beers criteria [65], the Screening Tool of Older Person's Prescriptions (STOPP) [66], anticholinergic burden scores, national or provincial guidelines, and intervention specific tools (Table 2). These were used either to inform the intervention, such as medication review or educational content, or to identify inappropriate medications for the purposes of measuring study outcomes.

3.4 Outcomes of Interventions

To assess effects of the interventions, the outcomes have been grouped into medication-related outcomes (reported in 28/32 papers), clinical-related outcomes (reported in 19/32 papers), and safety-related outcomes (defined as reported adverse events, hospital admission and/or mortality; reported in 10/32 papers) and are outlined in Sections 3.4.1–3.4.3. Less than four papers reported outcomes related to feasibility and/or costs, and measurements were too varied to usefully synthesise.

The direction of effect of the interventions on each outcome is summarised in Table 3 (full details are provided in Online Resource 3).

3.4.1 Medication-Related Outcomes

3.4.1.1 Psychotropic Medication In total, 17 papers reported impact on psychotropic prescribing in general (n = 6) or specific medication classes [such as antipsychotics (n = 6) or benzodiazepines (n = 1)] from across all intervention groups. The studies were primarily completed in long-term care settings (n = 14) [35–38, 41, 45, 53, 55–59, 63, 64], with two in community settings [40, 42] and one in an inpatient setting [61]. Effects were not measured in the same way across the studies. The most common measures used were the percentage of participants for whom psychotropic medications were stopped or reduced (n = 7) and the change in the mean number of psychotropic medications per participant (n = 5).

A decrease in at least one class of psychotropic medication was reported in 12 out of the 17 papers [35, 36, 40–42, 53, 55–59, 63], with no obvious correlation between the type of intervention and effect on psychotropics. Moreover, 5 out of the 17 papers reported either no effect (n = 3) or an increase in the number of prescribed psychotropic drugs (n = 2), although a second paper from one study showed a reported improvement in psychotropic appropriateness [46].

3.4.1.2 Potentially Inappropriate Medications Nine papers reported outcomes related to PIMs [33, 37, 38, 42, 44, 48, 49, 61, 62], with the majority of interventions incorporating a medication review component (n = 8). Six papers defined PIMs on the basis of the Beers criteria [65] either on its own [33, 42, 44, 62] or in combination with anticholinergic burden scoring [61] or anticholinergic burden scoring and STOPP [49]. One paper used Swedish national quality indicators [49], and the other two used criteria developed with clinical experts, specifically for older adults with severe dementia [37, 38]. Outcome measures varied, including changes to total numbers of PIMs, changes to numbers of patients taking one or more PIMs, and discontinuation rates. Six out of nine papers reported a significant reduction in the number of PIMs post intervention [37, 42, 44, 48, 49, 62], primarily medication review interventions (n = 5). No effect was reported in three papers [33, 38, 61]. The interventions were implemented across all three intervention groups and the full range of settings, with no association between intervention type or setting and effect on outcome measure.

3.4.1.3 Total Number of Medications Seven papers reported on changes to total number of medications prescribed [33, 34, 37, 38, 42, 47, 60]. Four out of the seven papers (three combination medication review and education interventions and one medication review intervention) [34, 37, 47, 60] reported a decrease in the total number of medications post-intervention. The decrease in total medications ranged from a mean of 1.05 to 2.6 per participant across these studies. Three papers (one of each type of intervention) did not report a significant decrease in the number of medications [33, 38, 42]. Of note, the types of medications included in the total medication counts were not consistent across the seven studies. For example, one included just regular medications [37], another included both regular and pro re nata (PRN) medications [60], and one included any medication prescribed for at least 28 days [33].

3.4.1.4 Anticholinergic Burden Five papers measured changes in anticholinergic burden (ACB), and all interventions involved medication review, either with or without education [42, 48, 52, 54, 61]. Four studies assessed anticholinergic burden using the Anticholinergic Cognitive Burden Scale, with one using a version modified for use in Australia [61]. The other study [52] used the Clinician-Rated Anticholinergic Score (CRACHS). Three studies showed a reduced ACB, whilst two studies [42, 61] showed no effect, with no association with the ACB assessment tool used.

3.4.2 Clinical-Related Outcomes

3.4.2.1 Behavioural and Psychological Symptoms of Dementia (BPSD) Outcomes related to BPSD were measured in 12 papers, across all three intervention groupings, primarily in long-term care settings [35–39, 45, 53, 55, 56, 59, 64], except one undertaken in an inpatient environment [54]. All studies measured changes in BPSD using the Neuropsychiatric Inventory (NPI) and/or the Cohen–Mansfield Agitation Inventory (CMAI), with mixed findings across those assessed with each tool. Most of the studies focussed on optimising psychotropic medication ($n = 9$) [35, 36, 39, 45, 53, 55, 56, 59, 64]. Follow-up ranged from 3 to 12 months, except in two studies, which had variable follow-up periods: one reporting a mean follow-up period of 104 days [37] and the other being the length of hospital inpatient admission [54].

Half of the papers (6/12) reported that the intervention had no effect on BPSD [37, 39, 45, 53, 56, 64]. Although one of these interventions, a combined medication review and education intervention focussed on any medication, showed no effects in the pilot study [37], a subsequent larger study reported improvements in BPSD [38]. Four other papers reported improvements post-intervention that included a medication review either alone or in combination with education [35, 36, 38, 54, 59]. Of these, three focussed on optimising psychotropic medication and one focussed on optimising anticholinergic medication [54]. The last paper reported mixed effects, finding that antipsychotic medication review combined with education led to no effect on agitation assessed using CMAI but a worse outcome on overall neuropsychiatric symptoms measured using NPI [55]. There was no association between follow-up length and effect on outcome measure.

3.4.2.2 Falls Impact on falls was assessed in six papers, across all intervention groups, with most showing no significant change in either number of falls or fall risk. Five of the papers focussed on optimising psychotropic medication in long-term care settings [35, 36, 41, 56, 64] and one focussed on PIMs in a hospital outpatient setting [48]. One paper combined medication review and education intervention which showed little impact on falls in an initial study involving 24 long-term care wards [35] but a significant reduction in falls when scaled up to 329 wards [36]; both studies had a follow-up period of 9 months.

There was variation in how falls were assessed, with most using number of actual falls in either the previous month ($n = 3$) or 6 months ($n = 1$). One paper measured risk of falls, which was determined using patient self-reported feelings of unsteadiness documented in medical records, and another reported the odds ratio for patient falls. Length of follow-up also varied significantly, ranging from 4 weeks [41] to 12 months [56].

3.4.2.3 Quality of Life Three papers measured the impact on health-related quality of life (HRQOL) by using a validated proxy measure, with mixed results. Two papers

Table 3 Direction of effect of intervention on study outcomes for each included paper

First author and year of publication (Intervention name)	Medication-related outcomes				Clinical-related outcomes				Safety-related outcomes	
	Psychotropic drugs (Effect on amount of psychotropic medication)	PIMs (Effect on number of PIMs)	Total medication (Effect on total number of medications)	Anti-cholinergic Burden (Effect on anticholinergic burden score)	BPSD (Effect on NPI or CMAI scores, decrease indicating improvement in BPSD)	Falls (Effect on number of falls or falls risk)	HRQoL (Effect on HRQoL measure score; increase indicating improvement)	Cognition (Effect on cognitive assessment score; increase indicating improved cognition)	Mortality (Effect on mortality rate or deaths attributable to intervention)	Hospital attendance (Effect on emergency department attendances or hospitalisations)
MEDICATION REVIEW AND HEALTHCARE PROFESSIONAL EDUCATION INTERVENTIONS										
Ballard 2016 (WHELD) [55]	Decrease				Increase (NPI) / No effect (CMAI)				No effect	
Ballard 2017 (WHELD) [50]							Decrease			
Brodaty 2018 [56]	Decrease				No effect (NPI & CMAI)	No effect		No effect		No effect
Cossette 2020 (OPUS-AP) [35]	Decrease				Decrease (CMAI)	No effect			Decrease	
Cossette 2022 (OPUS-AP) [36]	Decrease				Decrease (CMAI)	Decrease				
Kröger 2023 (OptimaMed) [38]	Increase	No effect	No effect		Decrease (CMAI)					
Maidment 2020 [39]					No effect (NPI)					
Massot Mesquida 2019 [57]	Decrease									
Muniz 2020 (CHROME) [58]	Decrease									
Muniz 2021 (CHROME) [59]	Decrease				Decrease (NPI)		No effect			
Smeets 2021 (PROPER) [45]	Increase				No effect (NPI & CMAI)					
van der Spek 2018 (PROPER) [46]										
Wilchesky 2018 (OptimaMed) [37]	No effect	Decrease	Decrease		No effect (CMAI)					
Yeh et al 2013 [52]				Decrease				No effect		No effect
MEDICATION REVIEW INTERVENTIONS										
Andrew 2018 [60]			Decrease							
Bravo-José 2019 [53]	Decrease				No effect (NPI)					
Coli 2022 [48]		Decrease		Decrease		No effect		Decrease		

Table 3 (continued)

	Medication-related outcomes				Clinical-related outcomes				Safety-related outcomes	
Gustafsson 2017 [51]										No effect / Decrease[a]
Gustafsson 2018 [49]		Decrease								No effect
Jaidi 2018 [54]				Decrease	Decrease (NPI)					
Kable 2023 [61]	No effect	No effect		No effect						
Liu 2022 [42]	No effect / Decrease[b]	Decrease	No effect	No effect						
Molist Brunet 2014 [34]			Decrease							
Pearson 2021 [62]		Decrease								
Sakakibara 2015 [47]			Decrease				No effect / Increase			
Silva-Almodóvar 2020 [44]		Decrease								
Weeks 2019 [41]	Decrease					No effect			No effect	
PATIENT, CARER, AND/OR HEALTHCARE PROFESSIONAL EDUCATION INTERVENTIONS										
Bayliss 2022 (OPTIMIZE) [33]		No effect	No effect						No effect	No effect
Boyd 2024 (OPTIMIZE) [32]									No effect	No effect
Martin 2017 [40]	Decrease									
Pasina 2016 [63]	Decrease									
Walsh 2022 [64]	No effect				No effect (NPI)	No effect				

[a] No effect on drug-related readmission or time to drug-related readmission; significant reductions were found after adjustment for heart failure.
[b] No effect overall, positive effect for subgroup who had benzodiazepines deprescribed.
BPSD Behavioural and Psychological Symptoms of Dementia
CMAI Cohen-Mansfield Agitation Inventory
HRQoL Health-Related Quality of Life
NPI Neuropsychiatric Inventory
PIMs Potentially Inappropriate Medications

BPSD behavioural and psychological symptoms of dementia, *CMAI* Cohen-Mansfield Agitation Inventory, *HRQoL* health-related quality of life, *NPI* neuropsychiatric inventory, *PIMs* potentially inappropriate medications

[a]No effect on drug-related readmission or time to drug-related readmission; significant reductions were found after adjustment for heart failure

[b]No effect overall, positive effect for subgroup who had benzodiazepines deprescribed

found no effect, one found a combined medication review and education intervention focussed on optimising psychotropics [59] and one found a medication review intervention focussed on any medication [47]; study follow-up periods were 12 months and 6 months, respectively. However, although Sakakibara et al. [47] found no effect overall, sub-analysis showed there was a significant improvement in HRQOL scores for those who underwent benzodiazepine deprescribing. The third paper, reporting a combined medication review and education intervention with a 9-month follow-up period, found that deprescribing antipsychotics had a negative impact on quality of life [50].

3.4.2.4 Cognition Three papers assessed the impact on cognition. Two of the papers found that the interventions, both combined medication review and education, had no impact on cognition, one paper focussed on anticholinergics over 3 months [52] and the other focussed on antipsychotics over 12 months [56]. One paper reporting a medication review intervention focussed on PIMs over 6 months found a statistically significant decline in cognition, although the authors considered this to be owing to the natural progression of dementia or MCI rather than to the intervention. Limitations in cognitive assessment were also acknowledged [48].

3.4.3 Safety-Related Outcomes

3.4.3.1 Mortality Five papers across all three intervention groups reported mortality [32, 33, 35, 41, 55], either measuring mortality rates or deaths during the study that were considered likely due to the intervention. Three papers reported studies in long-term care settings and two papers reported a study in primary care. All showed no effect [32, 33, 41, 55] or decreased mortality [35], indicating safety of the interventions.

3.4.3.2 Hospital Attendance Six papers outlined the impact of the intervention on hospital attendances and all of them were shown to be safe in so far as they had no effect or led to a non-significant decrease in hospital attendance. One paper [51] found a significant decrease in sub-group analyses that excluded patients with heart failure. The interventions were from across all three groups of interventions, in a range of settings, and focussed on various medication types.

4 Discussion

This systematic review identified 32 papers reporting interventional studies that explored outcomes of interventions to reduce polypharmacy in older people with dementia or MCI. The included papers reported interventions that incorporated either a medication review component, an education

component or both, mainly implemented in long-term care settings. The interventions had mixed effects. In line with previous reviews, medication-related outcomes were the most frequently reported outcome measure [20, 67]. There was a trend towards interventions having a positive effect on reducing the number and improving the appropriateness of medications and psychotropic prescriptions. Some interventions were considered to be safe, with either no effect or a slight improvement in mortality and hospital attendance observed. However, the effects of the interventions on BPSD, falls, quality of life and cognition were inconsistent. There was no indication that any one type of intervention worked best. In addition, none of the included studies reported the frailty status of participants and, with the exception of four studies, potentially included participants with limited life expectancy, both factors that could influence outcomes.

Most interventions focussed on medicine optimisation and deprescribing in long-term care settings or inpatient settings, with less than 20% of the papers reporting studies undertaken in primary care or community healthcare service settings. Yet, in the UK, it is estimated that 61% of people with dementia live at home, where medication is a part of daily living [68]. This limits the generalisability of the findings to community-dwelling older adults being cared for by family members, despite reports of widespread exposure to potentially inappropriate medications amongst this cohort [69, 70]. Deprescribing interventions implemented in primary and community settings have, to date, primarily focussed on older people in general and have not been specific to people with dementia or MCI [71–73].

Psychotropic medications and PIMs were the main types of medications investigated, with more than two thirds of papers reporting studies aiming to reduce prescriptions of these medications. This is in line with a recent systematic review of outcomes reported in deprescribing studies which found that the majority of studies targeted PIMs [31]. A focus on PIMs, which include many psychotropic medications, is unsurprising given that many have side effects that pose a risk for people living with dementia, such as exacerbating confusion and increasing the risk of falls [61]. Multiple tools for identifying PIMs were used, the most frequent being the internationally recognised Beers criteria [46], likely reflecting that this includes medications inappropriate for individuals with dementia or cognitive impairment, unlike other commonly used criteria such as STOPP [66].

Few papers in the review reported clinical outcomes such as BPSD, falls, cognition and quality of life. This lack of clinical outcome data has also been highlighted as a limitation in deprescribing studies to date. A 2022 review of deprescribing interventional studies amongst older people in general reported the outcome measures most commonly used were number of medications or PIMs stopped, healthcare use and adverse events [67], with patient-reported outcomes or geriatric syndromes (e.g. falls, fractures, gait speed, depression and delirium) infrequently reported. The US Deprescribing Research Network (USDeN) recommendations state that clinical outcomes should be the primary outcome assessed in deprescribing trials [67], but a recent review showed the choice of outcome was rarely justified or applied, as was the method of measurement [31]. Similarly, there is no consensus amongst researchers and clinicians on appropriate outcomes of deprescribing in people with dementia and more research is needed in this area. A recent review of 231 deprescribing RCTs found that deprescribing is a promising intervention across different settings and situations, but there is a notable gap in literature concerning its effects on health- and clinical-related outcomes [74].

The review identified limited evidence regarding the effect of deprescribing on clinical outcomes. This reflects findings from other systematic reviews of deprescribing in older adults which have shown, for example, little or inconsistent effect on cognition [75] and falls [72, 76]. Short follow-up periods may have an impact as many months may be required for certain changes, such as slowing of cognitive decline, to become clinically detectable [67]. Yet, in both this review and other reviews [72, 75, 76], many studies measured clinical outcomes for 6 months or less.

The most frequently measured clinical-related outcome was BPSD, assessed primarily in long-term care settings. This reflects both the focus on psychotropic medications and concern about overuse of antipsychotics for BPSD [77], with current guidelines suggesting that antipsychotics should not be prescribed for BPSD unless a person is severely distressed or at risk of harming themselves or others and should be reviewed at least every six weeks [78]. Indeed, the findings of this review highlight that a decrease in psychotropic medication mostly had either no effect or led to an improvement in BPSD, with only one study showing a worsening of BPSD assessed using NPI, although there was no effect on CMAI scores.

Amongst older people with dementia or MCI, a few of the included papers in this review reported safety outcomes and found that medicine optimisation and deprescribing did not adversely impact hospital attendance or mortality. A number of systematic reviews have investigated the impact of deprescribing on mortality amongst the general population of older people. One reported that deprescribing reduced mortality in non-randomised studies but no changes were observed in RCTs [12]. Other reviews suggested a reduction in all-cause mortality with deprescribing interventions in long-term care residents [79, 80] or no change in people living with frailty [23]. Overall, research therefore suggests that deprescribing is safe amongst older people, including those with dementia or MCI.

Mixed effects of medicine optimisation and deprescribing on the HRQOL amongst older people with dementia or MCI were reported in our review. These findings are consistent with literature published on older people in general [81, 82]. Possible explanations for this might be that the impact of deprescribing on HRQOL may depend on the specific combination of medication(s), setting, timing of the HRQOL measurement or the HRQOL measurement tools used. A recent scoping review included 52 papers which reported that the measurement properties of scales for capturing changes in quality of life (QoL) from deprescribing were uncertain and that because medication specific QoL scales have not been employed in deprescribing clinical trials, their performance in this context is also not clear [83]. QoL in older people is complex and might be difficult to improve with a single intervention targeting the number of prescribed medicines.

There was a general absence of measurement of cost implications of interventions, reflecting previous findings relating to deprescribing interventional research amongst older people [67]. However, although overall the review shows an absence of improvement in clinical outcomes, the lack of a worsening of outcomes and evidence that deprescribing is safe can be considered positive in respect of potential cost savings. Given the significant cost of medications and other costs relating to the prescription and dispensing of medication [84], the reduction in medications, evidenced by many of the interventions, would represent cost savings.

The number of interventions in which patients and carers were involved was limited. Only two of the interventions involving education included direct education of patients and/or carers. One of these interventions involving direct patient education showed similar levels of deprescribing for people with MCI as for those with normal cognition. However, in both the education interventions and other interventions, the views and experiences of patients and carers in relation to the intervention and the impact of the intervention on their medicine optimisation was lacking. From the patient and carer perspective, considerations such as treatment burden and optimising quality of life are likely to be important, yet HRQOL was only reported in three papers. Further research is required on how shared decision-making can be achieved and its impact on outcomes, especially for those individuals living in their own home. There is a need, therefore, to integrate person-centred and contextual factors (such as an individual's condition and circumstances) into deprescribing decision-making models [85]. This requires tools to support tailored deprescribing for people with dementia and MCI, although the evidence base needed to underpin these has previously been reported to be of generally low or moderate quality [20].

4.1 Strengths and Limitations

This is the first systematic review to bring together the evidence on this important topic. The review used robust methodology, following a protocol using the PRISMA statement methods and being registered on PROSPERO. A comprehensive search strategy allowed inclusion of all relevant studies from database inception to January 2024 and identified a large number of interventional studies in this population. However, there is the potential that some papers were missed owing to searching the Medline database rather than PubMed. The heterogeneity of the included studies, with a wide variation of study designs, settings and outcome measurements meant robust quantitative synthesis was not possible. Although the interventions were grouped to manage the data, each group included a range of interventional approaches. This review also confirms a continued lack of robust evidence, particularly for deprescribing in primary and community care services. The focus on long-term care, PIMs and psychotropic medications in the included papers limits the generalisability of the findings to settings such as primary and community services. The assessed quality of the included papers varied from quite low to high, with only four RCTs (eight papers) included in the review.

4.2 Future Research

Given the complex and context-specific nature of deprescribing for people with dementia and MCI, this review highlights the fact that further research is needed, particularly in settings other than long-term care. Future RCTs should focus on reporting the impact of deprescribing on clinical outcomes where longer follow-up periods are included. Further research is also required to understand how a shared decision approach to deprescribing involving patients, carers and healthcare professionals can be achieved and assessed for its impact. Healthcare professionals may benefit from tools to support SDM [86] and to help them balance the benefits and risks, but these tools require more robust evidence to inform them.

5 Conclusions

This review provides the first systematic assessment of the effects of medicine optimisation and deprescribing interventions for older people with dementia or MCI. The findings show that many interventions were effective in reducing numbers of medications and PIMs. However, evidence on safety and clinical outcomes was more limited, although studies measuring safety outcomes demonstrated that deprescribing was safe. An absence of worsening of clinical

outcomes is indicative of potential cost savings. There was a paucity of research outside of institutional settings and no evidence that any one type of intervention worked best. Future designs of deprescribing interventions need to involve patients and carers and tailored, evidence-based deprescribing tools to ensure their needs are met, as well as those of healthcare professionals. Given an aging population and associated increase in the prevalence of dementia, and the potential harms of over-prescribing and inappropriate polypharmacy in this vulnerable group, there is an urgent need for further high-quality research, particularly in primary care and community service settings.

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