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Pharmacist-led primary care interventions to promote medicines optimisation and reduce overprescribing: a systematic review of UK studies and initiatives

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Abstract

Objectives: To systematically review and synthesise evidence on the effectiveness and implementation of pharmacist-led interventions to promote medicines optimisation and reduce overprescribing in UK primary care.

Design: Systematic review

Setting: UK primary care

Methods: We searched MEDLINE, Embase, CINAHL and The Cochrane Library for UK-based studies published between January 2013 and February 2023. Targeted searches for grey literature were conducted in May 2023. Quantitative and qualitative studies (including conference abstracts and grey literature) that addressed a relevant intervention and reported a primary outcome related to changes in prescribing were eligible for inclusion. Quality of included studies was assessed using the Multiple Methods Appraisal Tool (MMAT). We performed a narrative synthesis, grouping studies by publication status, setting and type of data reported (effectiveness or implementation).

Results: We included 14 peer reviewed journal articles and 11 conference abstracts, together with four case study reports. The journal articles reported 10 different interventions, five delivered in general practice, four in care homes and one in community pharmacy. The quality of evidence was higher in general practice than in care home settings. It was consistently reported that the intervention improved outcomes related to prescribing, although the limited number of studies and wide range of outcomes reported made it difficult to estimate the size of any effect.

Implementation was strongly influenced by relationships between pharmacists and other health and care professionals, especially GPs. Implementation in care homes appeared to be more complex than in general practice because of differences in systems and 'culture' between health and social care.

Conclusions: Pharmacist-led interventions have been shown to reduce overprescribing in primary care settings in the UK. More research is needed in community pharmacy settings; to assess intervention effects on patient outcomes other than prescribing; and to investigate how reducing overprescribing can impact on health inequalities.

Registration: PROSPERO [CRD42023396366].

Strengths and limitations of this study

- We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness.

- Many of the studies lacked a control group and the research took place in a highly complex and evolving system, meaning that results could have been influenced by confounding factors such as other interventions in the health and social care system.
- Some review processes were performed by a single reviewer and meta-analysis was not feasible.

Introduction

Overprescribing has been defined as 'the use of a medicine where there is a better non-medicine alternative, or the use is inappropriate for that patients' circumstances and wishes'[1]. Overprescribing is often related to the concept of problematic polypharmacy, where harmful effects result from the prescription of multiple medications. However, there is no agreed definition of polypharmacy and patients with complex health conditions may require multiple medications.

Medicines optimisation is an umbrella term for interventions designed to ensure that medicines are used safely and effectively, producing the best possible outcomes for patients. In this context, deprescribing refers to the process of stopping medications that are no longer appropriate to a patient's needs. Deprescribing is a response to overprescribing and problematic polypharmacy and involves collaboration between health professionals and patients and/or carers to ensure shared decision-making. Another related term, medicines reconciliation, is a more technical process to ensure consistency between prescription records and the medications the patient is actually receiving and taking. The terminology around overprescribing and other forms of medicines misuse was recently reviewed by Singier et al[2]. Medication review involves examining a patient's prescriptions as a whole and is separate from measures to reduce inappropriate prescribing of specific medications or types of medication such as antibiotics or proton pump inhibitors.

Overprescribing can cause direct harm to patients in a variety of ways. It has been estimated that about 6.5% of hospital admissions are caused by harmful effects of medication, rising to 20% for people aged over 65[1]. In addition to physiological harms, long-term use of some medications can lead to dependency and problems when attempting to withdraw the medication.

Issues relating to prescribed medication can arise from a whole range of causes, including patients requiring treatment for multiple conditions, lack of co-ordination between different health professionals or organisations and failures of communication between health professionals and patients (for example failing to gather information because of time constraints on appointments). Availability of new medications and increasing numbers of people living with long-term conditions such as arthritis and diabetes have resulted in patients being prescribed more medications and continuing to take them for long periods of time, often for life. The average number of prescription items per head of population doubled between 1996 and 2016, and over 75% of prescriptions are repeat prescriptions[1].

In addition to their fundamental role in preparing and dispensing medicines, pharmacists are trained to provide advice and support to patients and other health professionals. While most prescriptions are ordered by doctors, pharmacist independent prescribers (PIPs) have existed since 2006 and patients are increasingly asked to consider the community pharmacy as a first source of support for minor health conditions. Alongside community pharmacies, many general practices have pharmacists as members of the practice team.

Pharmacists are thus well placed to support processes of medicines optimisation, which involve them working closely with medical professionals (particularly GPs), commissioners of health care and patients. The report of the National Overprescribing Review for England, published in 2021, provides numerous examples and case studies[1]. Shared decision-making with patients and/or carers is fundamental to successful medicines optimisation[3] but the need for time and resources to ensure that this takes place can create barriers to service delivery.

The National Overprescribing Review (NOR) for England was set up in 2018 to evaluate the extent of overprescribing in the NHS and recommend measures to reduce it, particularly in primary care. A review of existing research (overview of systematic reviews) was commissioned to support the national review[4]. The NOR identified a need for a more consistent and effective approach to medication review, which requires both the identification of effective interventions and an understanding of the factors that need to be addressed in terms of organisational and cultural barriers to implementation. The national review's recommendations included changes to systems (patient records, transfers of care and clinical guidance) and culture (reduced dependence on medication and support for shared decision-making), as well as the appointment of a National Clinical Director for Prescribing[1].

This evidence review was commissioned to support implementation of the NOR recommendations by examining research on pharmacist overprescribing interventions in UK primary care settings. We aimed to assess the effects of relevant interventions on outcomes related to prescribing, identify key characteristics of the interventions and examine barriers and facilitators to implementation in routine practice. A further aim was to assess the quality of the evidence base and identify priorities for further research. In addition to this UK-focused paper, outputs from the project include a broader scoping review of reviews of interventions for overprescribing in primary care (Preston et al. in preparation) and an evidence-based analysis of factors for service commissioners and providers to consider in developing and delivering services to reduce overprescribing and optimise medication use.

Methods

Review aims and objectives

We aimed to perform a systematic review of published literature and published or informally published evaluations reporting UK-based, pharmacist-led interventions for overprescribing, including the following components:

i. A review and synthesis of outcomes of effective interventions

ii. A review of the characteristics of effective interventions using the TIDieR framework

iii. Evaluation of the UK evidence base in terms of quality and risk of bias

iv. Identification of case study examples of effectively implemented interventions in the UK

Inclusion and exclusion criteria

Inclusion criteria for the review were as follows

- Population/setting: UK primary care
- Intervention: Pharmacist-led interventions aimed at review and optimisation of prescribed medications
- Comparator: Not required
- Outcomes: Studies had to report a primary outcome related to changes in prescribing. Secondary outcomes were other patient and health service outcomes, including but not limited to changes to type of medicines prescribed, quality of life, hospital admissions and deaths.
- Study design: Quantitative and qualitative studies were eligible for inclusion, with no exclusions based on study design or quality. Reports of local initiatives published as grey literature reports or conference abstracts were included to give a fuller picture of activity across the NHS.
- Other: Studies published in English between January 2013 and February 2023

We excluded interventions aimed at reducing overprescribing of specific medications or types of medication, e.g. antibiotics or proton pump inhibitors. Studies of children and young people were also excluded.

Search methods

A common literature search was performed for this review and the associated scoping review of reviews (Preston et al. in preparation). Searches were conducted by an information specialist (MC) in order to identify published and unpublished evidence on primary care interventions to reduce overprescribing.

Phase 1: peer reviewed literature

A first phase of database searches was run in February 2023 to retrieve relevant peer-reviewed literature. Searches were designed around the following concepts:

PROBLEM	INTERVENTION	SETTING
Overprescribing; Inappropriate prescribing; polypharmacy	Deprescribing; Structured medication review; medication reconciliation; medicines optimisation; shared decision making; personalised care	Primary Care (including international terms for primary care where relevant)

While we are aware of the Morel filter (2022) for identifying studies of deprescribing[5], our focus was specifically on a primary care setting. Search strategies are provided in Appendix 1 (see supplementary files).

Searches covered the databases MEDLINE, Embase, CINAHL and The Cochrane Library and were limited to studies published since 2013 and in OECD countries with healthcare systems similar to the UK.

Phase 2: grey literature

A further phase of targeted searches was conducted in May 2023 to identify unpublished or "grey" literature. This involved searching for the case studies identified by the National Overprescribing Review (to identify any which had produced a report or evaluation), and then searching the Overton.io platform for pharmacist-led deprescribing/overprescribing and medicines optimisation.

Searches were complemented by input from stakeholders (internal and external topic advisers) to minimise the risk of missing any other relevant evidence.

Study selection

Records retrieved by the literature search were stored in a shared EndNote library and de-duplicated. Screening for inclusion at the title level was performed by single reviewers after piloting of a test set. Reviewers could refer records to another team member in the event of uncertainty and a 20% sample of records was screened by a second reviewer to validate title level inclusion decisions.

Screening for inclusion at the abstract and full text level was performed by pairs of reviewers acting independently. Disagreements were resolved by discussion among the reviewers involved (AC, DC and LP). Reasons for exclusion at the full text stage were recorded.

Data extraction

Data extraction tables and summary tables were developed in Microsoft Word. Extraction was performed by a single reviewer, with a 10% sample being checked for consistency and accuracy. In addition to standard data extraction fields (study design/sample size, setting, intervention, key findings and strengths/limitations) , we used the TIDieR Lite framework to collect information on the features of interventions reported as 'successful' to determine whether service commissioners and providers should consider specific factors when commissioning/delivering services. TIDieR Lite is a simplified version of the TIDieR (Template for Intervention Description and Replication) checklist [6].

Quality assessment

Methodological quality of peer reviewed journal articles was assessed using the Mixed Methods Appraisal Tool (MMAT) version 2018[7]. The tool includes screening questions and methodological quality questions for different study designs (qualitative, randomised trials, non-randomised quantitative studies, descriptive studies and mixed methods). Quality assessment results were combined with identified strengths and limitations (including those reported by study authors) to characterise the contribution of individual studies and groups of studies to the overall evidence base.

Data synthesis

We performed a narrative synthesis of the included studies using text and tables to describe study and intervention characteristics in line with methodological and reporting guidelines[8, 9]. We initially grouped studies by publication status, considering peer-reviewed journal articles (regardless of study design and quality) separately from conference abstracts and case studies. Within these three categories, we grouped studies by setting (general practice, care homes or community settings). We also distinguished between studies reporting effectiveness of interventions and those reporting implementation of interventions (e.g. qualitative studies and process evaluations). In view of study heterogeneity and reporting limitations, effectively implemented interventions were defined as those where the study authors' conclusions indicated that the service was regarded as a success and was planned to continue or be expanded.

Studies reported a wide variety of outcomes using diverse effect measures. For this reason we did not attempt to calculate a standardised metric to compare effect sizes across outcomes. The synthesis used a 'vote-counting' method (number and proportion of studies reporting positive, negative or neutral outcomes), prioritising prescribing-related outcomes over patient and other outcomes. Reported effect measures and associated 95% CIs were recorded in the text and tables. Tables of study characteristics and findings were presented alphabetically by author for consistency. While reporting results from all study designs we prioritised stronger study designs (experimental and quasi-experimental) over those of uncontrolled observational studies. In terms of exploring heterogeneity, the structure of the synthesis allowed consideration of potential modifiers including study design, study quality and setting. Intervention components and aspects of implementation were examined using modifications of existing frameworks, the component analysis was pre-specified in the review protocol.

We did not use the GRADE approach to assess certainty of evidence because of its emphasis on randomised trials and downgrading of other study designs. Instead we distinguished between controlled and uncontrolled studies, identified areas of consistency and inconsistency and highlighted areas of particularly limited evidence (e.g. settings or outcomes represented by single studies). A similar approach has been used by team members in previous reviews[10].

Public involvement

The review was supported by a public panel who provided feedback on public perceptions that informed the review and are reflected in the Discussion.

Variations from protocol

We used Tidier Lite instead of the full TIDieR framework. This was because the full framework is designed to allow the replication of interventions and therefore goes beyond the degree of detail required for evidence synthesis.

Results

Results of literature search

The PRISMA flow diagram (Figure 1) summarises the study selection process. After screening 1774 records at the title and abstract stage and 215 full-text articles, we included 14 published articles, 11 conference abstracts and four case study reports. The majority of exclusions were of studies conducted outside the UK, with a smaller number excluded because the intervention was not pharmacist–led or the article did not report empirical data. Characteristics of the included studies are reported in the following sections.

Research studies

Study characteristics

Study characteristics are summarised in Table 1, with full data extraction tables in Appendix 3 (see supplementary files). The 14 publications reported on ten interventions, of which five were delivered in general practice (seven publications[11-17]), three in care homes for older people (five publications[18-22]), one in care homes for people with intellectual disabilities (ID) [23] and one in community pharmacies[24].

All the interventions involved medication review in some form. Distinctive features of interventions included use of IT to identify patients for review[11-13, 15, 16]; a key role for pharmacist independent prescribers in medication management in care homes[21, 22]; and employment of pharmacists by groups of general practices (primary care networks, PCNs) to provide a holistic patient-centred service specified by NHS England[14]. Intervention characteristics are considered in more detail below.

Study designs used included one individual RCT[17] and two cluster RCTs (CHIPPS[18, 21] and PINCER[11]), although the primary publications of the latter two trials fell outside the time period covered by this review. Two studies used an interrupted time series (ITS) design[15, 16] and five used qualitative approaches[12-14, 18, 22]. One study was a mixed methods process evaluation[21]. The remaining studies were described as service evaluations or quality improvement reports with an uncontrolled before vs. after design [19, 20, 23, 24].

Included studies reported a wide range of outcomes (Table 1). For further analysis, see below under ‘effects of interventions’ and ‘Implementation/system issues, respectively. None of the studies reported details of participants other than age and sex, making it difficult to assess equity, diversity and inclusion across the evidence base.

Table 1: Summary of research study characteristics

Reference	Population	Intervention	Study design	Outcome measures
Alharthi 2023[18]	Care home residents	Deprescribing by pharmacist independent prescriber	Qualitative interviews with participants in a cluster RCT (CHIPPS study)	Barriers and facilitators to deprescribing
Alves 2019[19]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (5 year uncontrolled study)	Interventions by pharmacist (including deprescribing and changes to prescriptions)
Baqir 2017[20]	Care home residents	Medication review by pharmacist with or without GP	Retrospective analysis of data from QI programme	Number and type of medications stopped
Birt 2021;[21]	Care home residents	Pharmacist independent prescribers responsible for medicines management (CHIPPS)	Mixed methods process evaluation	PI activities, perceived benefits and barriers to implementation
Howard 2014[11]	Pharmacists delivering intervention	IT-enabled pharmacist-led review to reduce medication errors	Cluster RCT (PINCER trial)	Time taken to complete reviews; recommended interventions and whether they were implemented
Jeffries 2018[12]	Pharmacists delivering intervention, GPs and CCG staff	Pharmacist-led intervention involving the use of an electronic audit and feedback surveillance dashboard to identify patients potentially at risk of hazardous prescribing or monitoring of medicines in general practice	Qualitative interviews	Themes related to implementation of the intervention and role of practice pharmacists and others
Jeffries 2017[13]	Stakeholders in general practice and CCG	Electronic medicines optimisation system	Qualitative realist evaluation	Suggestions to support implementation of the system
Lane 2020[22]	Doctors, pharmacists, care-home managers and	Pharmacist independent prescriber service	Qualitative focus groups and interviews	Perceived benefits of the service and barriers and facilitators to implementation

	staff, residents and relatives			
Madden 2022[14]	Pharmacists working in general practice within PCNs	Structured medication review service within Primary Care Networks	Qualitative interview study	Themes related to early implementation of SMR service
Peek 2020[15]	General practice patients with one or more risk factors for hazardous prescribing or inadequate blood test monitoring	Pharmacist-led Safety Medication dASHboard (SMASH) intervention	Interrupted time series analysis	Rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring
Rodgers 2022[16]	General practices in the East Midlands	Pharmacist-led IT intervention (PINCER)	Multiple interrupted time series	Indicators of potentially hazardous prescribing
Syafhan 2021[17]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness plus clinical outcomes and costs
Thayer 2021[23]	Care home residents with intellectual disabilities	Collaborative service initiative involving community pharmacists and a specialist mental health pharmacist providing review of medicines and lifestyle risk factors	Service evaluation	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists
Twigg 2015[24]	Patients over 65 prescribed four or more medications	Community pharmacist consultation including medication review using STOPP/START rules	Service evaluation	Number of recommendations; falls, medication adherence, quality of life and costs at 6 months

Table 2: Summary of studies reporting effects of interventions

Reference	Intervention	Setting	Study design and sample size	Outcome measure and effect size
Alves 2019[19]	Medication review	Care homes	Service evaluation 10,405 patient reviews over 5 years	Interventions by pharmacis
Baqir 2017[20]	Medication review	Care homes	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Number and type of medicines stopped 19.5% reduction in number of medicines being prescribed relative to baseline
Peek 2020[15]	Safety medication dashboard	General practice	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	Potentially hazardous prescribing (composite of 10 indicators) Potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p < 0.001$) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p < 0.001$) at 12 months
Rodgers 2022[16]	Pharmacist-led IT-assisted intervention (PINCER)	General practice	Multiple interrupted time series 393 general practices covering approximately 3 million patients	Indicators of potentially hazardous prescribing The PINCER intervention was associated with a decrease in the rate of hazardous prescribing of 16.1% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6 months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention
Syafhan 2021[17]	Pharmacist-led medicines optimisation	General practice	Individual RCT 356 patients at risk of medication-related	Medication-related problems (MRP); Medicines Appropriateness Index (MAI) Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p < 0.00$ in patients who received the full

			problems (MRPs) from 8 GP practices	intervention schedule. MAI scores were reduced (medications more appropriate) for the intervention group, but not for control group.
Thayer 2021[23]	Review of medicines and lifestyle risk factors	Care homes for adults with intellectual disabilities (ID)	Service evaluation 160 care home residents with ID	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists
Twigg 2015[24]	Community pharmacist consultation including medication review	Community pharmacies	Service evaluation 620 patients (aged over 65 years and prescribed ≥ 4 medications	Number of recommendations, falls, medication adherence, quality of life and costs at 6 months

Intervention characteristics

Appendix 3 Table 1 (see supplementary files) summarises characteristics of the included interventions using the TIDieR Lite checklist. The table includes limited data extracted from studies cited by included studies but not themselves included in the review [25-27].

The pharmacists involved in delivering the interventions were variously described as pharmacist independent prescribers[21]; trained pharmacists and pharmacy technicians[11, 16]; primary care pharmacists[19]; clinical pharmacists working in general practice[13-15]; GP practice-based pharmacists working as part of a wider primary care team[17]; community and specialist mental health pharmacists[23]; and community pharmacists and pharmacy team members[24]. One study simply referred to 'pharmacists'[13].

Four interventions were explicitly stated to require training of pharmacists to deliver them[11, 17, 21, 24]; the extent of training was described for three of these[17, 21, 24]. Training pharmacists to deliver the PINCER intervention was described in a separate paper[11]. Interventions were delivered with other primary care team members depending on the setting of the study and in some cases with staff employed by clinical commissioning groups (CCGs). In particular, only the CHIPPS study involved pharmacists with the power to prescribe medication independently; in other studies recommendations were passed to the patient's GP or another medically qualified professional for implementation. Shared decision-making with patients and/or families was specifically reported for three interventions[14, 17, 20].

Reporting of interventions varied between studies. Most studies reported the process of medication review including patient selection for review and the review itself in more detail than resulting follow-up actions. Two qualitative studies reported limited details of the review process[12, 14], although a service specification was available for the NHS England SMR investigated by Madden et al.[14]. For studies where the intervention was primarily directed at improving medication review processes using general practice data[11-13], it was unclear whether there was a standard process to discuss findings with the patient and make changes to their prescriptions. All studies reporting on effectiveness of medication reviews stated that the person undertaking the review had access to relevant patient records[15-17, 19, 20, 23, 24].

Intensity of interventions was also variably reported. In the CHIPPS study, PIPs committed a minimum of 16 hours/month to deliver care to approximately 20 care home residents[25]. Madden et al. reported that SMR appointments were recommended to allow at least 30 minutes for review and shared decision-making[14]. The medicines optimisation intervention evaluated by Syafhan et al. involved up to three meetings between patient and pharmacist[17], while the FOMM study in community pharmacies estimated times of 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review[24]. Other studies reported that time and level of support allocated to interventions varied between and within CCG areas depending on local resources and priorities[16, 19]. Another measure of intervention intensity was the number of recommended actions, averaging 3.3/resident in care home residents with IDs[23].

Most included studies reported on a single round of medication reviews with variable periods of follow-up. As noted above, some interventions required multiple interactions between pharmacists and patients.

Effects of interventions

Seven studies reported on effects of pharmacist-led interventions in some form (Table 2): three in general practice[15-17], three in care homes[19, 20, 23] (including one in a care home for people with ID[23]) and one in community pharmacies[24].

The strongest evidence for the effectiveness of interventionscame from the studies in general practice. The interrupted time series (ITS) studies of Peek et al.[15] and Rodgers et al.[16], which used indicators of inappropriate prescribing to identify patients for intervention, reported significant decreases in inappropriate prescribing at 6 and 12 months after intervention (Table 2). Estimated reductions were larger in Peek et al. (27.9% and 40.7%) compared with Rodgers et al. (16.7% and 15.3%)[15, 16]. The 95% confidence intervals of the two studies at 12 months did not overlap, suggesting some uncertainty about the magnitude of the effect. The randomised trial by Syafhan et al.[17] preferentially recruited patients based on prescription of six or more medications and a history of recent unplanned hospital admission. The intervention was associated with a reduction in medication-related problems in those who completed the full programme (up to three appointments) and an improvement in MAI scores.

Of the three studies set in care homes, only Baqir et al. reported a direct effect on prescribing associated with medication review, a 19.5% reduction in number of prescribed medicines[20]. Alves et al.[28] reported on pharmacist interventions and potential financial savings over 5 years. In the one year reported in detail, 24.5% of interventions involved deprescribing. Potential drug cost savings were estimated at £812,441 annually, of which £431, 493 (55%) was attributed to deprescribing. The study of Thayer et al.[23] differed from the others in involving care home residents with ID. There was a high level of polypharmacy at baseline and pharmacists made an average of 3.3 interventions/recommendations per resident, of which 12.8% involved deprescribing. A large majority of pharmacist recommendations were accepted by GPs/psychiatrists caring for the residents.

The one study in a community pharmacy setting recruited patients aged 65 or older who were prescribed four or more medications[24]. Of 620 patients recruited, 441 (71.1%) completed the 6-month study. Pharmacists made 142 recommendations related to 110 patients, largely dealing with potentially inappropriate prescribing of NSAIDs and PPIs or duplication of therapy. The study also reported a significant decrease in falls and improvements in medication adherence and quality of life at follow-up.

The review included two publications from the CHIPPS Care Homes Independent Pharmacist Prescriber Study) trial[18, 21] but the paper reporting effectiveness and safety results from this cluster RCT[29] was published too late for formal consideration for inclusion in our review. The primary outcome was rate of falls, with Drug Burden Index (DBI) being one of the secondary outcomes. Fall rate at 6 months did not differ significantly between intervention and control groups

but DBI was lower in the intervention group (mean 0.66 vs. 0.73; adjusted rate ratio 0.83, 95% CI 0.74 to 0.92).

Implementation/system issues

Seven studies provided quantitative and/or qualitative evidence on factors affecting implementation of pharmacist-led interventions, of which four were performed in general practice[11-14] and three in care homes[18, 21, 22].

The general practice studies focused on different parts of the implementation pathway. Two dealt with implementation of IT systems to support detection of potentially hazardous prescribing[12, 13]; one was a process evaluation of the PINCER trial[11]; and one focused on implementation of structured medication reviews as recommended by NHS England in routine practice[14]. The studies of IT-supported interventions were broadly positive about the potential for implementation and sustainability, but the study of NHS England's SMR programme concluded that its early implementation failed to deliver the planned holistic and patient-centred approach.

Other evidence

Conference abstracts

We included 11 conference abstracts (Table 4), of which two were earlier reports of studies subsequently published as full papers[28, 30]. All of the included abstracts focused on intervention effects on prescribing and related outcomes.

Five abstracts reported research in general practice, of which three involved patients with polypharmacy identified from the overall practice population[31-33]. As a group, these three abstracts provided weak evidence of associations between pharmacist-led medication reviews and changes in medication and cost savings together with high levels of patient satisfaction (Table 3),

Two abstracts reported on selected general practice populations. The only comparative study in this group reported that patients living with frailty who were reviewed by a pharmacist as part of a multi-disciplinary team review had a reduction in total medications compared with a control cohort[34]. When patients recently discharged from hospital were reviewed by a pharmacist working in their general practice, 16 out of 35 had changes made to their medication, with 74% of changes involving deprescribing[35].

Turning to studies performed in care homes, two abstracts by Doherty et al. (2020)[36, 37] evaluated an intervention entitled Medicines Optimisation in Older People (MOOP) which involved case management by pharmacists. The authors reported that inappropriate prescribing (based on the MAI) was highly prevalent at baseline *84%) but declined significantly following the intervention. Swift et al. reported that a team comprising pharmacists and pharmacy technicians who both performed medication reviews and supported care home staff significantly reduced inappropriate polypharmacy (measured by prescribing quality indicators) between 2024 and 2017[38]. For care home residents receiving palliative care, structured medication reviews involving shared decision-

making were associated with high rates of changes to medication (1787 suggested changes from 574 reviews, 76% of which were implemented) and associated cost savings[39].

Grey literature case studies

We included reports of four case studies reporting on local initiatives in three areas of England (see Table 4).Details of all case studies may be found in Annex C of the National Overprescribing Review report[1]. Case studies were submitted by NHS organisations (mainly CCGs) and included varying amounts of data on intervention characteristics, support for implementation and outcome measures. Three interventions were delivered in general practice and one in care homes. The initiative developed by Swale CCG was distinctive in using pharmacy technicians to review less complex cases, although the initiative was targeted at patients considered high-risk for ADRs. Although not classified as research, such case studies can provide useful data on implementation of interventions and outcomes achieved in routine practice

Table 3: Summary of studies published as conference abstracts

Reference	Population	Intervention	Study design	Outcome measures and key findings
Alves 2016[28]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (retrospective analysis and interviews)	Interventions by pharmacist; barriers and facilitators A total of 2916 interventions were made in 1047 patients, of which deprescribing represented 22%
Bryant 2019[31]	Primary care patients taking ten or more medications	Polypharmacy clinics in GP surgeries	Service evaluation (retrospective data analysis)	Reductions in prescribing; cost savings; hospital admissions avoided April 2017 to March 2018, 370 patients reviewed and £50,766.63 saved. Figures for April to December 2018 were 209 and £14,912, respectively
Chauhan 2022[35]	Patients recently discharged from hospital	Post-discharge medication review by clinical pharmacist linked to GP practice	Formative service evaluation (uncontrolled)	Medication changes following review 16/35 patients had medications changed; 74% (25/34) of changes were medications stopped
Din 2020[32]	Patients referred by GPs	Polypharmacy review clinics led by pharmacist independent prescriber with shared decision-making	Service evaluation (uncontrolled)	Changes to medication, feedback from patients and MDT Pharmacist medication reviews were effective, with positive feedback received from patients and members of the MDT. Deprescribing and inhaler counselling were the most common interventions.
Din 2022[34]	Primary care patients living with frailty	Frailty review involving pharmacist as part of MDT	Comparative cohort	Changes in medication (including cholinergic burden), practice contacts and falls Intervention group had a reduction in total number of medications when compared with non-intervention cohort. Anti-cholinergic burden scores were reduced by a mean of 26%

Doherty 2020a[36], 2020b[37]	Care home residents	Medicines Optimisation in Older People (MOOP) involving case management by pharmacists	Uncontrolled before/after	Inappropriate prescribing; unplanned hospital admissions; GP visits; clinical interventions Inappropriate prescribing was highly prevalent at baseline (84.1%) but improved significantly from baseline (M = 14.87, SD = 13.11) to post-intervention (M = 0.70, SD = 2.04, Z = 25.97, p<.001).
Donyai 2017[33]	Patients aged at least 75 years and prescribed 15 or more medication	Pharmacist-led polypharmacy review clinic in primary care	Survey	Patient satisfaction and related outcomes Of the 166 patients who returned a satisfaction questionnaire (40% response rate), 83% found the service helpful, 13% did not, 2% did not know and 2% did not respond
Kolovetsios 2018[39]	Care home residents needing palliative care	Structured medication reviews carried out in agreement with patient, nurse, family/carer and GP	Service evaluation	Changes to medication, estimated cost savings From January 2017 to January 2018, 574 medication reviews took place resulting in 1787 suggested medication changes. Approximately 76% of these changes were agreed and actioned by patients' GPs, with estimated savings of £169,986.96.
Swift 2018[38]	Care home residents	Care home team (pharmacists and pharmacy technicians) delivering medication reviews and supporting care home staff	Service evaluation	Prescribing quality indicators (including reduced inappropriate polypharmacy); CQC ratings Medication reviews were completed for 749 care home residents between August 2014 and March 2017. Of the recommendations made to prescribers, 85% were accepted and resulted in a reduction in inappropriate polypharmacy
Syafhan 2019[30]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness A total of 356 adult patients (175 control and 181 intervention) were recruited. Among 108 intervention patients who had three pharmacist face-to- face contacts, 346 MRPs were identified at baseline and 83 MRPs at 6 months. Median values were 3 MRPs at baseline and 1 at 6 months (p<0.001).

Table 4: Summary of selected grey literature case studies

Setting	Name of initiative	Key findings	Comments
Brighton and Hove CCG	An evaluation of a clinical pharmacist medication review service in primary care	A total of 1,300 patients were referred into the service and reviewed between April 2017 and March 2018; 9% of patients were deprescribed high-risk medicines	The target patient cohort of frail or older persons prescribed polypharmacy was identified from searches within GP clinical systems and through referrals from clinical practitioners, voluntary and social care services
Swale CCG	Medicines Optimisation Review Programme	In 2018/19, pharmacists and pharmacy technicians reviewed 5281 patients and made 3859 interventions, 37% for adverse drug reactions (ADRs). Estimated in-year cost savings were £239,546	Targeted 'high-risk' patients Key feature is use of technicians for less complex cases
NE Hampshire and Farnham CCG	Care homes pharmacist	Pharmacist accompanying GPs visiting care homes carried out over 250 medication reviews and 800 interventions. Average number of medicines per resident fell from 9.4 to 7.6	Limited data reported
NE Hampshire and Farnham CCG	Polypharmacy prescribing comparators	Tool developed by Wessex AHSN was used to identify patients at risk of harm, resulting in significant reductions in percentage of patients aged over 75 prescribed 15 or more medications and percentage with an anticholinergic burden score of 6 or more	Limited data reported

Study quality

Quality assessment results using the MMAT are presented in Appendix Table 3 (see supplementary files). The results should be read in conjunction with the study strengths and limitations (see Appendix Table 1 (see supplementary files).

Five different checklists within the MMAT were used to assess the 14 studies. The sample included one RCT[17]; six studies were classified as quantitative non-randomised[15, 16, 19, 20, 23, 24]; one as quantitative descriptive[11]; one as mixed methods[21]; and five as qualitative[12-14, 18, 22]. All studies passed the screening questions (are there clear research questions? and do the collected data allow to address the research questions?)

The RCT by Syafhan et al. was described as a pragmatic trial and was at relatively high risk of bias for this type of design. The trial did not achieve the planned number of participants and there was a high rate of attrition (about 30%), meaning that many participants did not receive the full intervention or provide outcome data. The trial also suffered from unclear reporting: method of randomisation and whether outcome assessors were blinded was not reported, making it difficult to assess overall risk of bias.

The quantitative non-randomised studies comprised four observational studies at high risk of bias because of the absence of a control group[19, 20, 23, 24] and two large ITS studies[15, 16]. The MMAT tool identified some limitations of these studies, including some risk of confounding and incomplete outcome data in one study[16]. However, these were large studies conducted in routine practice and providing evidence of a statistically significant effect at 12 months post-intervention. The process evaluations of the CHIPPS[21] and PINCER[11] studies both scored highly on the MMAT assessment.

The qualitative studies were generally of good quality, with sufficient data presented in support of conclusions and appropriate use of frameworks and thematic analysis to organise presentation of the findings. The study by Alharthi et al.[18] was a secondary analysis of data collected for another purpose, making it unclear whether qualitative data collection methods were adequate.

Using the system applied by the authors in previous studies of complex health service interventions[10], the overall strength of evidence was classified as borderline 'stronger' (generally consistent findings in multiple studies with a comparator group) for general practice, 'weaker' (generally consistent findings in one study with a comparator group design and several non-comparator studies or multiple non-comparator studies) for care homes and 'very limited' (single study) for community pharmacies.

Effectively implemented interventions

Three research studies met the criteria for 'effectively implemented' interventions: the closely related PINCER[16] and SMASH[15] interventions in general practice and the Somerset model of medication review in care homes[19]. Further examples of effectively implemented medication review in care homes were identified among the included conference abstracts[36-39]. Case studies from Brighton and Hove and Swale CCGs appeared to report effectively implemented interventions

targeted at high-risk patients in general practice (Table 5). An evaluation of the early implementation of SMRs in primary care networks indicated that the service as provided did not match the vision of a patient-centred holistic review with an emphasis on shared decision-making[14].

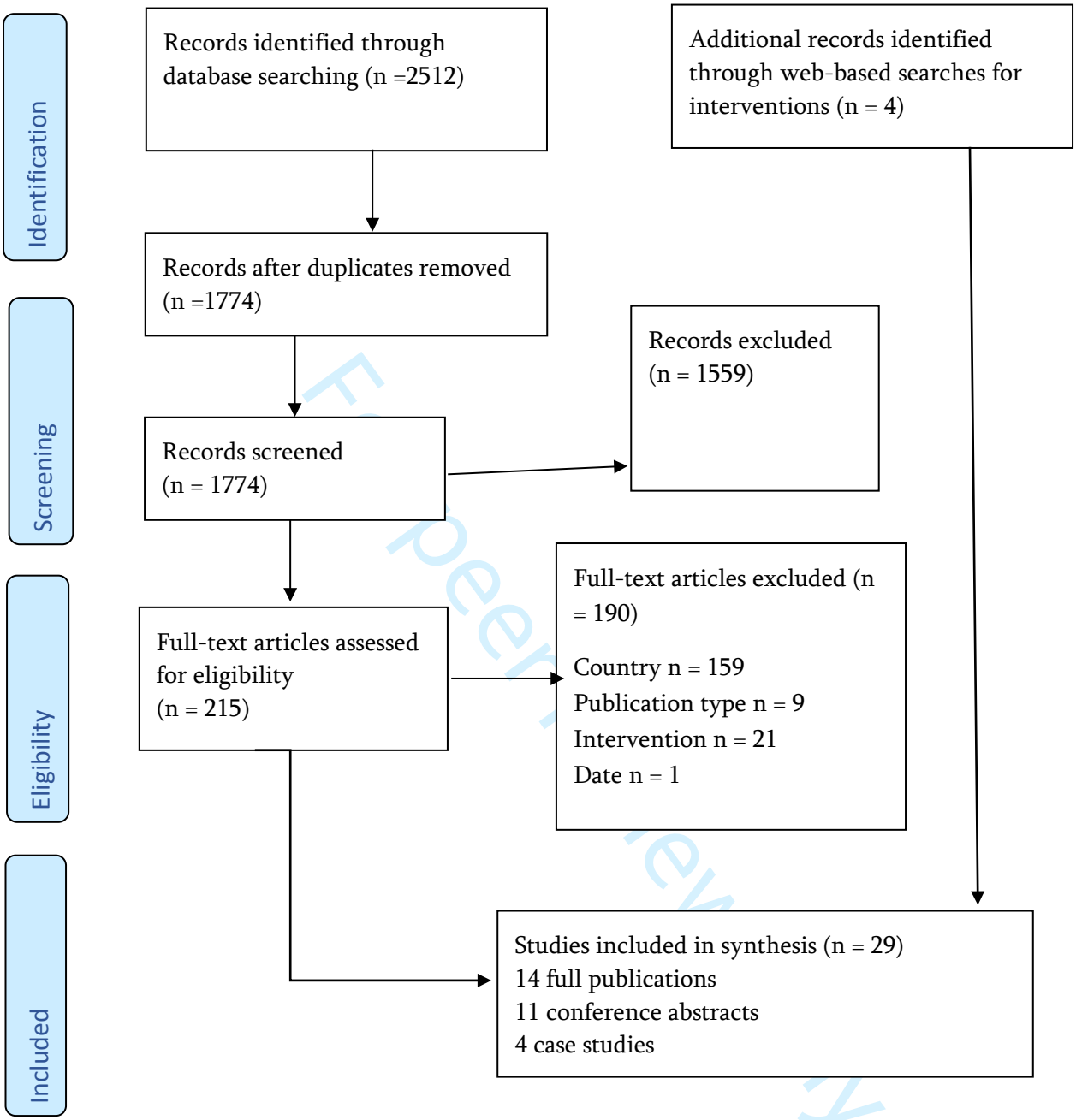

Figure 1 PRISMA Flowchart

.Discussion

Summary of findings

In spite of its broad inclusion criteria, this review identified a relatively small number of studies of pharmacist-led interventions in UK primary care (14 peer reviewed journal articles, 11 conference abstracts and four case studies). Overall, the bulk of evidence came from the care home sector but most of the better quality evidence was derived from studies conducted in general practice. The majority (8/14) of peer reviewed papers were published in 2020 or later, suggesting that this is a developing area of research and practice in the context of encouraging patients to consult pharmacists initially for minor conditions and to increase pharmacists' prescribing rights. It was encouraging that we identified a number of effectively implemented interventions and initiatives in both care homes and general practice.

Outcomes of effective interventions

This systematic review suggests that pharmacist-led interventions may reduce overprescribing in primary care settings in the UK. The evidence is strongest for interventions implemented in general practice, where we identified a small randomised trial[17] as well as two large quasi-experimental studies (interrupted time series)[15, 16] and various uncontrolled studies and service evaluations. Evidence from care home settings was of lower quality with the exception of the CHIPPS study involving pharmacist independent prescribers working in care homes[21]. We located only one uncontrolled study based in UK community pharmacies[24].

Although the direction of reported effects was clear, the limited number of studies combined with the wide range of outcomes reported makes it difficult to estimate the size of any effect. For example, the two ITS studies using similar interventions reported markedly different reductions in measures of inappropriate prescribing at 6 and 12 months after implementation of the intervention[15, 16]. Uncertainty about effect sizes is increased because many of the studies lacked a control group and the results could have been influenced by other interventions in the health and social care system, for example the Enhanced Health in Care Homes programme implemented in England. While our review focused primarily on outcomes related to prescribing, data on cost savings were also widely reported but the evidence was generally of low quality. We also found limited evidence of a link between reductions in measures of overprescribing and clinical outcomes, mainly because of lack of reporting. The CHIPPS study found no significant difference in its primary outcome of fall rate, although there was a reduction in Drug Burden Index (a secondary outcome) in the intervention group at 6 months[29].

Characteristics of effective interventions

The TIDieR Lite checklist provided a suitable structure for describing intervention characteristics for evidence synthesis purposes and this discussion follows its structure. Lack of reporting (especially of intervention intensity/frequency) was a limiting factor, as was reporting of varying intervention information across multiple publications.

Medication reviews were undertaken by pharmacists acting independently or in conjunction with GPs or care home staff. In a study in care homes for people with intellectual disabilities, psychiatrists were also involved in review where appropriate[23]. Pharmacy technicians were also involved in the PINCER study and could potentially have a greater role in relatively straightforward medication reviews[11, 16]. The included studies reported a variety of models of employment of pharmacists, including direct employment by GP practices, CCG Medicines Optimisation Teams, PIPs and community pharmacists. PCNs support employment of pharmacists by general practices and are the route chosen by NHS England to implement its model of SMR.

A major difference between settings is the need to identify patients requiring medication review in general practice, whereas most care home residents take multiple medications and could be considered candidates for review as part of their routine health care. A key element of the PINCER[11, 16] and SMASH[15] interventions is the use of information technology to search electronic patient records efficiently across large numbers of general practices. Effective interventions were also characterised by attention to training and tools to support and sustain change in practice, e.g. an 'audit and feedback' dashboard[15].

Training of pharmacists and other staff to deliver interventions was reported to varying degrees, reflecting in part the publication channel of the research. For example, in the CHIPPS study PIPS had comprised 2 days of face-to-face instruction plus time in practice to develop relationships with the GP and care home staff.[21] Specification and provision of appropriate training will be important for future development of pharmacist-led interventions, as also highlighted by the evaluation of NHS England's SMR programme[14].

Intervention intensity is another important factor in developing and delivering interventions. For the CHIPPS study, participating PIPs committed a minimum of 16 hours/month to the service. [21] In general practice settings, NHS England recommended allowing 30 minutes for an SMR to give time for shared decision-making; this was interpreted to include time for preparation and writing-up[14]. This level of time requirement was also reported in the one study from a community setting, which estimated pharmacist time at 25 minutes for an initial consultation[24].

In terms of intensity more generally, resourcing of interventions was reported to vary between commissioning groups (CCGs) depending on staff availability and other priorities[11, 16, 19]. General practices varied in their use of a medication safety dashboard[26]. Frequency of intervention was rarely reported, reflecting the short time frame of most included studies but it seems possible that there could be an ongoing need for review as patients get older and/or their health state changes.

Quality and risk of bias

The MMAT provided a good alternative to the use of multiple tools to assess risk of bias across diverse study designs. The only randomised trial assessed was designed as a pragmatic trial[17] and the assessment confirmed a relatively high risk of bias. Publications from the CHIPPS study were included but the trial *per se* was not assessed for risk of bias because of the publication date of the main study report. Similarly, the PINCER intervention was supported by a randomised trial published in 2012, before the cut-off date for our review [40]). Well-conducted studies included in the review included large ITS studies[15, 16], process evaluations[11, 12, 21] and qualitative studies[13, 14]. Service evaluations and other lower quality evidence tended to support higher quality studies by highlighting implementation and results achieved in routine practice, although a causal relationship between intervention and outcome remains uncertain in studies without a parallel control group.

Implementation barriers and facilitators

Implementation of pharmacist-led interventions was strongly influenced by factors affecting relationships between pharmacists and other health and care professionals, especially GPs. Given that most pharmacists are not prescribers, their recommendations around (de)prescribing need to be seen as 'legitimate' by GPs who are generally responsible for acting on the recommendations. This is facilitated by continuity at the system level, including existing links between pharmacists and GPs[21] and good access to data[12]. Jeffries et al. reported that pharmacists took the lead in developing relationships with GPs, enabling a 'learning health system'[12]. The benefits of continuity at the system level could help to explain why early implementation of the SMR programme through the relatively new medium of PCNs was reported to be less successful than initially hoped[14].

Implementation in care homes may be more complex than in general practice because of differences in systems and 'culture' between health and social care[22]. Patients and their families may be supportive of medication review or oppose it based on real or perceived benefits of medication[18].

The main message regarding implementation of pharmacist-led interventions across all settings is the need for involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers[22].

Identification of effectively implemented interventions/initiatives:

Our simple criteria for 'effectively implemented' interventions/initiatives identified a number of examples published as research papers, conference abstracts or case studies (see 'Effectively implemented interventions' above). Despite limitations as research, some of the abstracts and case studies provided valuable information about how commissioners and providers had supported interventions and their commitment to continue the programme[36-39]. In other studies, despite promising results, it was unclear whether the intervention would be implemented more widely[17].

Relationship to previous research

To our knowledge, this is the first systematic review of pharmacist-led interventions and initiatives specifically in UK settings. A scoping review of reviews by the same authors (Preston et al., in preparation) included 20 systematic reviews published between 2014 and 2023. The most recent review covered pharmacist integration into general practice to optimise prescribing and outcomes for patients with polypharmacy[41]. The review included 23 studies, of which just three were from the UK. The conclusion that pharmacist integration probably reduced PIP and number of medicines (moderate certainty evidence) was in line with the findings of the present review.

Strengths and limitations

The UK focus is both a strength and limitation of this review. We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness. The dual focus reflects the fact that pharmacist-led medicines optimisation and deprescribing in primary care is both an area of active research and of implementation within the health care system. Nevertheless, some of the evidence is not of high quality and we have tried to be appropriately cautious in our conclusions and identified implications.

Our broad review questions and UK focus resulted in a heterogeneous group of included studies. Meta-analysis was not possible so we performed a narrative synthesis in line with appropriate guidelines[8, 9]. The review was undertaken by a small but experienced team with expertise in systematic review methods and prescribing.

Implications for service delivery

Several studies indicate that barriers to successful service delivery often arise from 'system' issues and differences in 'culture'[14, 22]. Commissioners and providers engaged in developing new pharmacist-led services should ensure equitable access to data and information to avoid perceptions of 'ownership' by certain groups at the expense of others[13]. In care homes, where medication review is an important component of health care for residents[19], implementation requires health and social care professionals to work together and 'understand each other's systems'[22]. The holistic patient-centred SMR envisaged by NHS England may require culture change/training to foster an emphasis on direct patient contact and shared decision-making. Removal of financial incentives for PCNs to carry out SMRs as reported recently (https://pharmaceutical-journal.com/article/news/nhs-england-removes-financial-incentives-for-structured-medication-reviews-in-2023-2024) may complicate delivery, although the service remains a contractual requirement.

Services have been delivered successfully through CCGs Medicines Optimisation Teams with suitable training[11, 16]. The review also found evidence that services provided by PIPs appear to be a valid alternative to approaches requiring action by GPs or other medical professionals[21].

Implications for research

A major priority for research is to further evaluate the effectiveness of medication review in community pharmacy settings and how pharmacies might be best supported to deliver the service. A related need is for research to better understand public perceptions of community pharmacies as a setting for medication review and their pros and cons compared with alternative settings such as GP surgeries. Research is needed to support the development of the PIP role and how PIPs might best be used in combination with GPs and other professionals to support optimal prescribing across the health and care system.

Shared decision-making is key to the success of pharmacist-led interventions. Qualitative research is needed to better understand patient and family attitudes to shared decision-making in the context

of deprescribing and the barriers and facilitators operating in different settings and with different professionals.

The present review focused on outcomes related to prescribing and a review of effects on patient and health system outcomes would be a logical follow-up, as would further review work to address any gaps identified by the accompanying review of reviews (Preston et al. in preparation). Finally, further research is needed to understand the effects of implementing pharmacist-led medication review in general practice on health inequalities and how to reduce unwarranted variations in service delivery between different practices or regions.

Conclusions

Pharmacist-led interventions have demonstrated the potential to reduce overprescribing in primary care settings in the UK. The evidence base varies widely in terms of quality but studies have consistently reported improvements relative to a comparator group or baseline. The diversity of interventions and outcomes reported makes it difficult to generalise about effect sizes but given the reported extent of the problem, even small relative reductions could be highly beneficial for patients and the health and care system.

The existing evidence base requires cautious interpretation because of a shortage of controlled studies and this is particularly the case for studies in community pharmacy settings. Further rigorous evaluation of interventions, particularly those delivered in community pharmacies, is required. Although not a focus of this review, there appears to be a shortage of high-quality economic evidence to guide decision-making.

The problems encountered in the early implementation of NHS England's SMR programme[14] suggest a need for further research on the implementation of pharmacist-led interventions. Implementation of this type of interventions requires the involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers.

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Conflict of interest

The authors have no conflicts of interest to declare.

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and Social Care.

Contribution of authors

Duncan Chambers contributed to all review processes and wrote the first draft of the paper. Louise Preston managed the review team, and contributed to all review processes and to writing the paper. Mark Clowes developed search strategies, performed literature searches and contributed to writing the paper. Anna Cantrell contributed to all review processes and to writing the paper. Elizabeth Goyder provided topic expertise and contributed to writing the paper. All authors have approved the version to be submitted.

Data sharing

Any additional data not included in this report and its appendices are available on request. All queries should be submitted to the corresponding author.

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Data extraction tables

Table 1: Study characteristics of included research studies (full data extraction table)

Study ID	Study design/sample size	Setting	Intervention	Key findings	Authors' conclusions	Study strengths/limitations
Alharthi 2023[18]	Secondary analysis of qualitative interview data 11 pharmacist independent prescribers (PIPs) who participated in a cluster randomised trial	Care homes in England and Scotland	Integration of PIPs into care homes to improve medication management	Factors that acted as both enablers and barriers were PIP relationship with General Practitioner (GP), care home staff and residents/families, awareness of the PIP role and family trust in PIPs' deprescribing activities *(social influences)*; PIPs' independent prescribing confidence, previous experience and ability dealing with residents' medications *(beliefs about capabilities)*; understanding of PIP role and PIP confidence in their role as an independent prescriber *(social/professional role and identity)*; access to residents' records, deprescribing decision support, regular follow-up from care home staff, resident	PiPs' involvement in care homes is influenced by numerous barriers and enablers that can be addressed to improve intervention effectiveness	Strengths: Diverse PIP contexts and perspectives on deprescribing; theory-informed analysis using Theoretical Domains Framework to identify barriers and enablers Limitations: Only PIP perspective considered; analysis used data from interviews focused on the whole intervention process rather than exclusively on deprescribing

				difficulties with medications, teamwork, and time restraints *(environmental context and resources)*. Belief that the negatives of deprescribing outweigh benefits regarding certain medications *(beliefs about consequences) acted as a barrier.*		
Alves 2019[19]	Service evaluation 10,405 patient reviews over 5 years	Care homes in Somerset	Medication review by primary care pharmacists linked to GP practices	Pharmacists made 23,955 interventions (mean 2.3 per patient) from the 10,405 patient reviews undertaken. 16.1% of interventions were related to safety. Potential drug cost savings were estimated at £812,441 over 5 years, of which £431, 493 (53%) was attributed to deprescribing	Medication reviews undertaken by primary care pharmacists in care homes generate a wide range of interventions, commonly involving deprescribing. The service contributes to the continuous optimisation of prescribing and monitoring of medicines and offers potential drug cost savings.	Strengths: Collection of data from 'real world' implementation of intervention over 5 years Limitations: No control group, cost saving estimates not based on full economic evaluation
Baqir 2017[20]	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Care homes in two CCG areas in North East England	Medicines optimisation by a pharmacist acting independently or jointly with a GP. Shared decision making with the patient or their advocate	Of the 422 patients reviewed, 298 (70.6%) had at least one medicine deprescribed with 704 medicines (19.5%) being stopped. There was no statistically significant difference between pharmacist only and pharmacist plus GP in terms of deprescribing. Assuming that each medicine stopped would have been taken for another	Medicines optimisation reviews can lead to a reduction in polypharmacy for care home residents through a deprescribing process. Patients' medicine regimens were simplified and optimised while making financial savings for the NHS	Strengths: Compares two approaches to delivering medication review Limitations: Short-term uncontrolled study; intervention quality/fidelity not measured

				year, annualised cost savings were estimated at £65,471		
Birt 2021[21]	Mixed methods process evaluation of cluster RCT Intervention arm comprised 25 triads: Care homes (staff and up to 24 residents), GP and pharmacist Independent Prescriber (PIP); 22 PIPs contributed data	Care homes in England, Scotland and Northern Ireland	Integration of PIPs into care homes to assume central responsibility for medicines management	All stakeholders reported some benefits from PIPs having responsibility for medicine management and identified no safety concerns. PIPs reported an increase in their knowledge and identified the value of having time to engage with care home staff and residents during reviews. PIPs recorded 566 clinical interventions, many involving deprescribing; 93.8% of changes were sustained at 6 months. For 284 (50.2%) residents a medicine was stopped, and for a quarter of residents, changes involved a medicine linked to increased falls risk. Qualitative data indicated participants noted increased medication safety and improved resident quality of life. Contextual barriers to implementation were apparent in the few triads where PIP was not known to the GP and care home before the trial. In three triads, PIPs did not deliver the intervention.	The intervention was generally implemented as intended, and well-received by most stakeholders. Whilst there was widespread deprescribing, Contextual factors effected PIP engagement. Implementation was most effective when communication pathways between PIP and GP had been previously established.	Strengths: Involved three UK nations with differing healthcare systems; used study records to supplement qualitative data Limitations: Interview participants may not be representative; limited access to care home residents

Howard 2014[11]	Process evaluation of data from cluster RCT 36 intervention and 36 control practices; 1946 patients identified as at risk in intervention practices	General practice surgeries in an 80 km radius around Manchester and Nottingham	Pharmacist-led IT enabled intervention (PINCER). Patients potentially at risk from hazardous medicines management were identified using Quest Browser software to search GP electronic records. Intervention practices were assigned a pharmacist who educated practice staff about medication management and recommended improvements to practice. Pharmacists also reviewed	Pharmacists judged 72% (95% CI 70, 74; 1463/2026) of cases of hazardous medicines management to be clinically relevant. Pharmacists recommended 2105 interventions in 74% (95% CI 73, 76; 1516/2038) of cases and 1685 actions were taken in 61% (95% CI 59, 63; 1246/2038) of cases; 66% (95% CI 64, 68; 1383/2105) of interventions recommended by pharmacists were completed and 5% were accepted by GPs but not completed at the end of the pharmacists' placement; the remaining recommendations were rejected or considered not relevant by GPs.	Recommendations from the pharmacists were broadly acceptable to GPs and led to ameliorative action in the majority of cases. It seems likely that the approach used by the PINCER pharmacists could be employed by other practice pharmacists following appropriate training.	Strengths: Uses data from a large cluster RCT Limitations: Pharmacists did not record detailed reasons for their judgements and these were not peer reviewed

			cases of potentially hazardous medication and recommended interventions to GPs			
Jeffries 2017[13]	Qualitative realist evaluation Interviews: 3 GPs, 2 CCG pharmacists; Focus groups: 2 GPs, 4 community pharmacists, 4 patients, 4 practice managers	CCG in the South of England	Electronic Medicines Optimisation System (EMOS). The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of adverse drug events (ADEs)	Effective use of the EMOS depended upon engagement with the system, the flow of information between different health professionals centrally placed at the CCG and those locally placed at individual general practices, and upon adaptation of work practices to facilitate the use of the system. The use of the system was undermined by perceptions of ownership, lack of access, lack of knowledge and awareness, and time pressures.	The use of an electronic medicines optimisation system may improve medication safety in primary care settings by identifying those patients at risk of an ADE. To fully realise the potential benefits there needs to be better utilisation across primary care and with a wider range of stakeholders. Engaging with all potential stakeholders and users prior to implementation might allay perceptions that the system is owned centrally and increase knowledge of the potential benefits.	Strengths: Realist methodology enabled detailed examination of how the EMOS was used and its potential effects Limitations: Study involved only one CCG so may not be representative
Jeffries 2018[12]	Qualitative process evaluation 28 staff members from 23 general practices (9	43 general practices in Salford, Greater Manchester	Electronic audit and feedback surveillance dashboard to identify patients potentially at	Engagement with the dashboard involved a process of 'sense-making' by pharmacists. The intervention helped to build respect, improve trust and develop relationships between pharmacists and GPs. Collaboration and	Medicine optimisation in primary care may be enhanced by the implementation of a pharmacist-led electronic audit and feedback system. This intervention established a rapid learning health system that enabled data from electronic	Strengths: Use of Normalization Process Theory as a framework to understand implementation

	GPs, 12 pharmacists, 7 other GP staff)		risk of hazardous prescribing or monitoring of medicines	communication between pharmacists and clinicians was primarily initiated by pharmacists and was important for establishing the intervention.	health records to be used to make changes in practice to improve patient care.	Limitations: Evaluation team also developed the intervention; number of follow-up interviews was limited
Lane 2020[22]	Qualitative focus groups and interviews 85 (72 in focus groups and 13 in semi-structured interviews)	Care homes (4 sites in England (2), Scotland and Northern Ireland)	Integration of PIPs into care homes to take responsibility for medicines management	A PIP service was seen as offering benefits for residents, care homes and doctors but stakeholders raised challenges including agreement on areas where PIPs might prescribe, contextual barriers in chronic disease management, PIPs' knowledge of older people's medicine, and implementation barriers in integrated team-working and ensuring role clarity. Introducing a PIP was welcomed in principle but conditional on: a clearly defined PIP role communicated to stakeholders; collaboration between doctors, PIPs and care-home staff; and dialogue about developing the service with residents and relatives.	The overarching theme from this research was that everyone must "understand each other's systems". In particular, PIPs need to understand care homes' systems in advance of implementing a new service	Strengths: Purposively selected sample; use of TDF as a framework to analyse data Limitations: Data relate to proposed service model in advance of implementation
Madden 2022[14]	Qualitative interview study	General practice in England	Structured medication review (SMR) for people at risk of harm or	SMR implementation was largely delegated to individual pharmacists. Established pharmacists appeared more ready for implementation than	Early implementation of SMRs did not match the intention of providing patients with a holistic review and shared decision-making. The author identified	Strengths: based on detailed, in-depth interviews

	10 newly appointed pharmacists working in primary care networks (PCNs) in Northern England; 10 established pharmacists working in GP practices in other PCNs		medication-related problems	newly appointed staff. New pharmacists were learning about working in primary care settings and tended to follow procedures with which they were already familiar, particularly when they lacked patient-facing expertise. Implementation was affected by ongoing backlogs and workforce issues in general practices	an important opportunity cost of SMR implementation without prior adequate skills development, testing, and refining	Limitations: Authors note interviews need to be complemented by data on actual practice and longer term follow-up
Peek 2020[15]	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	General practice in England	Pharmacist-led Safety Medication dASHboard (SMASH). SMASH involved (1) training of clinical pharmacists to deliver the intervention; (2) a web-based dashboard providing actionable, patient-level feedback; and	The study used an interrupted time series analysis of rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring, comparing observed rates post-intervention to extrapolations from a 24-month pre-intervention trend. At baseline, 95% of practices had rates of potentially hazardous prescribing (composite of 10 indicators) between 0.88% and 6.19%. The prevalence of potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p <$ 0.001) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p <$	The SMASH intervention was associated with reduced rates of potentially hazardous prescribing and inadequate blood-test monitoring in general practices. This reduction was sustained over 52 months for prescribing but not for monitoring of medication. There was a marked reduction in the variation in rates of hazardous prescribing between practices.	Strengths: Authors noted pragmatic design, evaluation of clinically relevant outcomes and large number of practices taking part Limitations: Not a randomised study so possibility of unrecognised confounding cannot be excluded

			(3) pharmacists reviewing individual at-risk patients, and initiating remedial actions or advising GPs on doing so.	0.001) at 12 months after introduction of SMASH. The rate of inadequate blood-test monitoring (composite of 2 indicators) reduced by 22.0% (95% CI 0.2% to 50.7%, *p* = 0.046) at 24 weeks; the change at 12 months (23.5%) was no longer significant (95% CI −4.5% to 61.6%, *p* = 0.127). After 12 months, 95% of practices had rates of potentially hazardous prescribing between 0.74% and 3.02%.		
Rodgers 2022[16]	Multiple interrupted time series 393 general practices covering approximately 3 million patients	General practice in the East Midlands region of England	Pharmacist-led IT intervention to reduce hazardous prescribing (PINCER)	Successive groups of general practices received the PINCER intervention between September 2015 and April 2017. Eleven prescribing safety indicators were used to identify potentially hazardous prescribing and data were collected over a maximum of 16 quarterly time periods. PINCER was implemented in 370 (94.1%) of 393 general practices; data were successfully extracted from 343 (92.7%) of these practices. For the primary composite outcome, the PINCER intervention was associated with a decrease in the rate of hazardous prescribing of	The PINCER intervention, when rolled out at scale in routine clinical practice, was associated with a reduction in hazardous prescribing by 9.7% and 15% at 6 and 12 months post-intervention. The greatest reductions in hazardous prescribing were for indicators associated with risk of GI bleeding. These findings support the wider national rollout of PINCER in England.	Strengths: Suggests intervention was implemented successfully in routine practice and was associated with significant reductions in hazardous prescribing Limitations: The authors adjusted for calendar time and practice, but since this was an observational study, the findings may

				16.7% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6 months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention. The unadjusted rate of hazardous prescribing reduced from 26.4% to 20.1% at 6 months and 19.1% at 12 months. The greatest reduction was for hazardous prescribing indicators related to GI bleeding		have been influenced by unknown confounding factors or behavioural changes unrelated to the PINCER intervention. Data were also not collected for all practices at 6 and 12 months post-intervention
Syafhan 2021[17]	Individual RCT 356 patients at risk of medication-related problems (MRPs) from 8 GP practices	General practice in England (6 practices) and Northern Ireland (2)	Medicines optimisation with shared decision-making and agreed treatment goals. Intervention repeated at 2 and 4 months, building on progress towards agreed goals	Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p < 0.001$) in patients who received the full intervention schedule. Medication Appropriateness Index (MAI) scores were reduced (medications more appropriate) for the intervention group, but not for control group patients. Using the intention-to-treat (ITT) approach, the number of telephone consultations in intervention group patients was reduced and different from the control group. No significant differences between groups were found in unplanned hospital admissions, length of	The pharmacist service reduced MRPs, inappropriateness of medications and telephone consultations in general practice in a cost-effective manner	Strengths: Pragmatic randomised design Limitations: Sample smaller than planned; high loss to follow-up; MRP analysis only covered patients who attended 3 appointments

				hospital stay, number of A&E attendances or outpatient visits. The mean overall healthcare cost per intervention patient fell from £1041.7 ± 1446.7 to £859.1 ± 1235.2 (p = 0.032). Cost utility analysis showed an incremental cost per patient of − £229.0 (95% CI − 594.6, 128.2) and a mean QALY gained of 0.024 (95% CI − 0.021 to 0.065),. indicative of a health status gain at a reduced cost (2016/2017).		
Thayer 2021[23]	Service evaluation 160 care home residents with intellectual disabilities (ID)	Care homes for people with ID in the Wirral	Pharmacist review of residents' medicines and lifestyle risk factors between November 2019 and May 2020.	The 160 residents were prescribed 1207 medicines, 74% were prescribed ≥5 medicines and 507 interventions/recommendations were made, averaging 3.3 per resident. The highest proportion (30.4%) were lifestyle risk related, while changing and stopping medicines accounted for 17.9% and 12.8%, respectively. Of the recommendations discussed with GPs/psychiatrists, 86% were accepted.	There was considerable polypharmacy among the residents and a high level of pharmacists' interventions/recommendations about medicines and lifestyle risk, most of which were accepted by GPs/psychiatrists. Wider adoption of collaborative pharmacist review models could have benefits for residential populations with ID and potentially reduce pressure on other health services.	Strengths: Drew on skills of pharmacists from different sectors to address wide range of care needs; recommendations addressed national priorities Limitations: Study limited to one CCG area; limited access to patient records; observational study with no control/comparator arm

Twigg 2015[24]	Service evaluation 620 patients (aged over 65 years and prescribed ≥ 4 medications)	Community pharmacies in England	Four or More Medicines (FOMM) support service. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the patient's medication using STOPP/START criteria. Data were analysed	Of 620 patients recruited, 441 (71.1%) completed the 6-month study period. Pharmacists made 142 recommendations to prescribers in 110 patients, largely centred on potentially inappropriate prescribing of NSAIDs, PPIs or duplication of therapy. At follow-up, there was a significant decrease in the total number of falls experienced and a significant increase in medicine adherence and quality of life. Cost per quality-adjusted life year estimates ranged from£11 885 to £32 466 depending on the assumptions made.	By focussing on patients over the age of 65 years with four or more medicines, community pharmacists can improve medicine adherence and patient quality of life.	Strengths: Large sample of patients and providers; use of validated outcome measures Limitations: No control/comparator group; authors note some patients were probably reviewed independently by their GP during the study period; relatively high attrition rate

			for the first 6 months of participation in the service.			

Appendix Table 2: TIDieR Lite for UK pharmacist studies

Intervention name and study ID(s)	By whom	What	Where	Intensity	How often
CHIPPS Alharthi 2023[18]; Birt 2021[21]; Lane 2020 [22]; Bond 2020[25]; Holland 2023[29]	Trained pharmacist independent prescribers (PIPs). The training programme comprised 2 days of face-to-face instruction, time in practice to develop relationships with the GP and care home staff, and to address any self-assessed competency gaps supported by a mentor, and a formal final sign-off by a GP independent of the research	PIP, in collaboration with the care home resident's GP, assumes responsibility for managing the medicines of the resident, including: • Reviewing resident's medication and developing and implementing a pharmaceutical care plan • Assuming prescribing responsibilities • Supporting systematic ordering, prescribing and administration processes with each care home, GP practice and supplying	Participating care homes	PIPs committed a minimum of 16 hours/month to deliver the service. Each PIP provided care to approximately 20 residents	PIPs visited care homes weekly over 6 months

		pharmacy where needed • Providing training in care home and GP practice • Communicating with GP practice, care home, supplying community pharmacy and study team			
Care home medication reviews Alves 2019[19]	Primary care pharmacists and GPs in Somerset CCG area and CCG staff	Medicines optimisation visits to care homes. Primary care pharmacists visited homes on behalf of GP practices; GPs could participate in visits or hold discussions with pharmacists prior to the visit; screening of safety interventions was done by CCG pharmacist leads	Care homes with and without nursing in Somerset	The time and level of support allocated for the service was agreed with the respective CCG Locality Pharmacist Manager and influenced by a number of factors such as engagement from GP practices; primary care pharmacists' availability; skills and confidence; number of care home patients registered with each GP practice; and geographic area covered by the prescribing support pharmacists	The aim of the programme was to offer at least one visit to as many care homes as possible (appears to be one visit per year but not explicitly stated)
Shine Medication Optimisation Project Baqir 2017[20]	Pharmacists together with care home nurses and other members of the multi-disciplinary team (MDT), including GPs and mental health professionals as needed. Two different models: pharmacists made prescribing decisions (as part of	A notes based, pharmacist-led review of medicines, where the Northumbria 3Q approach was applied to each medicine, that is, was there an indication, was the indication appropriate and was it safe?. Additionally, medicines missing that could be beneficial (eg, START medicines) were identified. This	Care homes in North East England	Intensity of intervention not reported. Prescribing decisions could be made by pharmacists alone or in conjunction with GPs	Once, as a funded quality improvement (QI) project

	shared decision-making) independently or in conjunction with GPs	was followed by a MDT meeting where the information from the pharmacist-led review was discussed and an action plan was formulated. Whenever possible, the final decisions were made with patients and their families. After the review, the project database was updated to show medicines taken before review, medicines stopped, started or changed and any other interventions made.			
PINCER Howard 2014[11]; Rodgers 2022[16]	Pharmacists specifically trained to deliver the intervention; GPs, other practice staff and pharmacy technicians involved in implementation	Computer systems of general practices are searched to identify patients at risk of potentially hazardous prescribing using a set of prescribing safety indicators. Pharmacists then provide an educational outreach intervention where they meet with GPs and other practice staff to: • Discuss the search results and highlight the importance of the hazardous prescribing identified using brief educational materials. These feedback	General practices	When PINCER was rolled out in the East Midlands, time spent by pharmacists delivering the intervention varied by CCG depending on the resourcing level of the local Medicines Optimisation Team	Data collected quarterly up to 12 months after starting the intervention[16]

		sessions were to be held straight after running the searches and then at regular intervals. • Agree on an action plan, retained within the practice, for reviewing patients identified as high risk and improving prescribing and medication monitoring systems using root cause analysis Pharmacists (sometimes supported by pharmacy technicians) then work with, and support, general practice staff to implement the agreed action plan, sometimes making the necessary changes themselves			
Eclipse Live (electronic medicines optimisation system (EMOS))	Developed by a private company (Eclipse Solutions) and made available to stakeholders (including doctors, pharmacists, practice managers and	Web-based user interface which securely extracts patient data from general practice patient records. Accessed separately from the GPs' clinical systems, it allows different stakeholders access to real time anonymized	General practices covered by the participating CCG	Not reported (qualitative study)	Not reported (qualitative study)

Jeffries 2017[13]	patients) by a CCG in the South of England	patient data including medical histories of diagnoses, prescribed medications and test results. The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of ADEs, or not appropriately monitored. Patients can access the system through a "Patient Passport"			
Safety Medication dASHboard (SMASH) Jeffries 2018[12]; Peek 2020[15]; Jeffries 2020[26]	Clinical pharmacists working in general practices and other general practice staff	Pharmacists were trained to deliver the intervention and apply root cause analysis techniques to identify, explore, resolve, and prevent medication errors in partnership with general practice staff. Pharmacists and practice staff were given access to a web-based, interactive dashboard that provided feedback on 12 indicators of potentially hazardous prescribing. The dashboard also provided practice-level summary data as well as educational material.	General practices covered by the participating CCG	Practices interacted with the dashboard a median of 12.0 (interquartile range, 5.0–15.2) times per month during the first quarter of use. Over time, dashboard use transitioned towards regular but less frequent (median of 5.5 [3.5–7.9] times per month) checks to identify and resolve new cases. The frequency of dashboard use was higher in practices with a larger number of at-risk patients.	Dashboard was updated daily. Frequency of use varied by practice and over time (see previous column)
Structured Medication Review (SMR)	Clinical pharmacists within general practice primary care networks (PCNs)	Invited, personalised, holistic review of all medicines and their benefits to health for people at risk of harm or medicine-related problems	General practices	Reviews are recommended to be scheduled for at least 30 minutes to allow time for shared decision-making	Once

Madden 2022[14]; Stewart 2021[27]					
Medicines optimisation intervention Syafhan 2021[17]	GP practice-based pharmacists operating as part of the wider primary care team	Each pharmacist received 2 days of intensive specialist training on medicines optimisation (including training on motivational interviewing). The intervention included: review of patient records prior to meeting; medication history; individual medicines optimisation plan that could include recommending/making changes to medication regimens (in collaboration with GPs), personalised education and counselling on medication management, the correct use of medication administration devices and lifestyle factors; and an agreed list of treatment goals. Pharmacists could also refer patients to another health professional within the practice. Having completed the intervention, the pharmacist	Eight general practices in four regions of the UK	Initial meeting with further appointments available at 2 and 4 months building on patient progress towards agreed goals	Once per patient (up to three appointments)

		produced a short report for the patient's GP outlining actions taken and any further recommendations requiring GP input			
Collaborative pharmacist review Thayer 2021[23]	Community and specialist mental health pharmacists	Medicine review using a structured framework based on recommendations of the 2018 Learning Disability Mortality Review (LeDeR) report. Pharmacists visited care homes to conduct the reviews using individual residents' care home records. The specialist mental health pharmacist also had access to the care record held by the Specialist Mental Health Trust, if the resident was under the Trust's care, and remote access to the local data sharing platform. Assessments included medicines adherence and burden (particularly the anticholinergic burden), respiratory care, vaccination status, constipation risk, sepsis prevention, dysphagia risk and lifestyle risk issues, especially smoking. Finally, pharmacists were asked to detail actions taken/advice provided, any	Care homes for people with intellectual disabilities	507 interventions/recommendations for 160 residents reviewed (3.3 per resident)	Once

		recommendations made and make referrals, as necessary. Following the review, GP surgeries and psychiatrists were contacted by the pharmacists to arrange a review of their recommendations. As the pharmacists were not prescribers, decisions on accepting recommendations were made by the resident's GP/psychiatrist (after reviewing the resident's full clinical record) in consultation with the pharmacists			
Four or More Medicines (FOMM) support service Twigg 2015[24]	Community pharmacists and pharmacy team members	Pharmacists were trained via distance learning and face to face, which included how to use the various different tools and assessments. Training was then cascaded to other pharmacy members. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the	Participating community pharmacies	Pharmacist time estimated at 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review	After the first consultation, patients met with the pharmacist on a regular basis depending on when they collected their repeat medication or they felt a need.

		patient's medication using STOPP/START criteria.			

Full paper excludes with reasons for exclusion

Excluded on country

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SEARCH STRATEGIES in full (for Appendix / supplementary material)

Ovid MEDLINE(R) ALL <1946 to February 06, 2023>

1 Inappropriate Prescribing/ 4485

2 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 8188

3 (overprescri* or over-prescri*).mp. 1975

4 Polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 12777

5 1 or 2 or 3 or 4 21236

6 exp Primary Health Care/ or (primary health care or primary healthcare or primary care).mp. 289526

7 general practice/ or family practice/ 78114

8 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 751694

9 6 or 7 or 8 997387

10 (deprescri* or de-prescri*).mp. 2577

11 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 16563

12 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 3182

13 10 or 11 or 12 21842

14 5 and 9 and 13 540

15 *Medication Errors/ and 9 and 13 232

16 5 and 9 and pc.fs. 835

17 14 or 15 or 16 1416

18 limit 17 to yr="2013 -Current" 1152

19 remove duplicates from 18 1145

Embase <1974 to 2023 Week 05>

1 Potentially inappropriate medication/ 2458

2 unnecessary prescribing/ [+NT] 51

3 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 11262

4 (overprescri* or over-prescri*).mp. 3064

5 Polypharmacy/ or inappropriate polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 26382

6 1 or 2 or 3 or 4 or 5 39236

7 exp Primary Health Care/ or primary medical care/ or (primary health care or primary healthcare or primary care).mp. 281889

8 general practice/ or family practice/ 83634

9 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 766031

10 7 or 8 or 9 974647

11 (deprescri* or de-prescri*).mp. 3587

12 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 28235

13 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 6755

14 11 or 12 or 13 37710

15 6 and 10 and 14 813

16 6 and 10 and pc.fs. 308

17 15 or 16 1089

18 limit 17 to yr="2013 -Current" 903

19 remove duplicates from 18 886

APA PsycInfo <1806 to January Week 5 2023>

1 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 788

2 (overprescri* or over-prescri*).mp. 329

3 (polypharmacy or poly-pharmacy).mp. 3128

4 1 or 2 or 3 4078

5 (primary health care or primary healthcare or primary care).mp. 44486

6 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 34287

7 5 or 6 71196

8 (deprescri* or de-prescri*).mp. 336

9 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 3969

10 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 242

11 8 or 9 or 10 4505

12 4 and 7 and 11 44

#	Query	Limiters/Expanders	Last Run Via	Results
		Limiters - Published Date: 20130101-20231231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	
S16	S6 AND S10 AND S14			307
S15	S6 AND S10 AND S14			327
S14	S11 OR S12 OR S13			13,914
S13	(intervention* or initiative* or campaign*) n3 pharmacist*			1,981
S12	"structured medication review" or "medication reconciliation" or "medicine* optimi#ation" or "shared decision making" or "personalised care" or "personalized care"			10,941
S11	deprescri* or de-prescri*			1,345
S10	S7 OR S8 OR S9			336,381
S9	("primary care" or "primary health care" or "primary healthcare" or "primary medical care") OR (GP or "general			333,015

	practi*" or "family practi*" or "family physician*" or "community pharmac*" or dental or dentist* or optometrist* or optician*)	
S8	(MH "Family Practice")	26,910
S7	(MH "Primary Health Care") OR (MH "Physicians, Family")	90,488
S6	S1 OR S2 OR S3 OR S4 OR S5	12,727
S5	polypharmacy or poly-pharmacy	7,664
S4	(MH "Polypharmacy (Saba CCC)") OR (MH "Polypharmacy+")	5,635
S3	overprescri* or "over prescri*"	1,026
S2	(hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) n3 prescri*	4,996
S1	(MH "Inappropriate Prescribing")	3,448

Search Name: THE COCHRANE LIBRARY

Date Run: 08/02/2023 13:50:34

Comment:

ID	Search	Hits
#1	MeSH descriptor: [Inappropriate Prescribing] explode all trees	234
#2	MeSH descriptor: [Polypharmacy] explode all trees	312
#3	((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or "non essential" or inessential) near/3 prescri*):ti,ab,kw	771
#4	(overprescri* or "over-prescri*"):ti,ab,kw	161
#5	(polypharmacy or poly-pharmacy):ti,ab,kw	1288
#6	#1 or #2 or #3 or #4 or #5	2045
#7	MeSH descriptor: [Primary Health Care] explode all trees	9989
#8	MeSH descriptor: [General Practice] explode all trees	2877
#9	MeSH descriptor: [Family Practice] explode all trees	2242
#10	("primary health care" or "primary healthcare" or "primary care"):ti,ab,kw	24053
#11	(GP or "general practi*" or "family practice" or "family physician*" or "community pharmac*" or dental or dentist* or optometr* or optician*):ti,ab,kw	44879
#12	#7 or #8 or #9 or #10 or #11	70362
#13	MeSH descriptor: [Deprescriptions] explode all trees	68
#14	(deprescri* or de-prescri*):ti,ab,kw	364
#15	("structured medication review" or "medication reconciliation" or "medicine* optimi*" or "shared decision making" or "personalised care" or "personalized care"):ti,ab,kw	2425
#16	((intervention* or initiative* or campaign*) near/3 (pharmacist* or pharmacy)):ti,ab,kw	1559
#17	#13 or #14 or #15 or #16	4166
#18	#6 and #12 and #17	130

(3 reviews, 127 trials)

MMAT quality assessment results

Reference	Screening questions	Type of study	MMAT questions and answers
Alharthi 2023[18]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (identifying perceived barriers and facilitators)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Can't tell (secondary analysis of existing data)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Alves 2019[19]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Can't tell (partial data presented)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (fidelity not monitored)*
Baqir 2017[20]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*

Birt 2021[21]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Mixed methods	**5.1. Is there an adequate rationale for using a mixed methods design to address the research question?** *Yes (qualitative and quantitative data relevant to process evaluation)* **5.2. Are the different components of the study effectively integrated to answer the research question**? *Yes (integrated in results and discussion)* **5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?** *Yes (see discussion)* **5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?** *Yes (page 11 column 2)* **5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?** *Yes*
Howard 2014[11]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative descriptive	**4.1. Is the sampling strategy relevant to address the research question?** *Yes* **4.2. Is the sample representative of the target population?** *Yes (all interventions recorded)* **4.3. Are the measurements appropriate?** *Yes* **4.4. Is the risk of nonresponse bias low?** *Yes (data from intervention arm only)* **4.5. Is the statistical analysis appropriate to answer the research question?** *Yes*
Jeffries 2017[13]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews and focus groups)* **1.3. Are the findings adequately derived from the data?** *Yes (context-mechanism-outcome groups identified)* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of realist analysis)*
Jeffries 2018[12]	**S1. Are there clear research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)*

	S2. Do the collected data allow to address the research questions? *Yes*		**1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Normalisation Process Theory)*
Lane 2020[22]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (gather opinions about proposed service)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (focus groups and interviews with different staff groups at different sites)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Madden 2022[14]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (pharmacists' experience of SMR implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews with newly employed and established pharmacists)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by thematic analysis)*
Peek 2020[15]	**S1. Are there clear research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)*

	S2. Do the collected data allow to address the research questions? *Yes*		**3.3. Are there complete outcome data?** *Yes* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Rodgers 2022[16]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)* **3.3. Are there complete outcome data?** *No (6- and 12-month data not collected from all practices)* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Syafhan 2021[17]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative randomised controlled trial	**2.1. Is randomisation appropriately performed?** *Can't tell (method of randomisation not reported)* **2.2. Are the groups comparable at baseline?** *Yes* **2.3. Are there complete outcome data?** *No (30% lost to follow-up or withdrew)* **2.4. Are outcome assessors blinded to the intervention provided?** *Can't tell (outcome data from GP electronic records)* **2.5 Did the participants adhere to the assigned intervention?** *No (30% lost to follow-up or withdrew)*
Thayer 2021[23]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents with intellectual disabilities)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (details recorded for each review and associated outcomes)* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)*

			3.5. During the study period, is the intervention administered (or exposure occurred) as intended? *Yes (one-off review mainly based on records)*
Twigg 2015[24]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Can't tell (no indication of attempts to recruit a representative sample)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (data is recorded for intervention components and associated outcomes)* **3.3. Are there complete outcome data?** *Can't tell (limited response for resource use outcomes)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (approx. 30% withdrawal rate)*

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction (pp4-5)
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Methods (p6)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods (p6)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods (p7)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary file
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p7)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods (pp7-8)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods (pp7-8)
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods (pp7-8)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p8)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	See methods (p8)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	See methods (p8)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A (summary tables only)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods (p8)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Results (p8)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P10 and Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary table
Study characteristics	17	Cite each included study and present its characteristics.	Tables 1-4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary table
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1-4 where available and appropriate
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results (p22)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results (p22)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion (especially p27)
	23b	Discuss any limitations of the evidence included in the review.	Discussion (especially p26)
	23c	Discuss any limitations of the review processes used.	Discussion (pp27-28)
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion (pp28-29)
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Title page

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Title page
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P9
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data sharing statement (p30)

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

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Pharmacist-led primary care interventions to promote medicines optimisation and reduce overprescribing: a systematic review of UK studies and initiatives

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Pharmacist-led primary care interventions to promote medicines optimisation and reduce overprescribing: a systematic review of UK studies and initiatives

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Abstract

Objectives: To systematically review and synthesise evidence on the effectiveness and implementation barriers/facilitators of pharmacist-led interventions to promote medicines optimisation and reduce overprescribing in UK primary care.

Design: Systematic review

Setting: UK primary care

Methods: We searched MEDLINE, Embase, CINAHL PsycINFO and The Cochrane Library for UK-based studies published between January 2013 and February 2023. Targeted searches for grey literature were conducted in May 2023. Quantitative and qualitative studies (including conference abstracts and grey literature) that addressed a relevant intervention and reported a primary outcome related to changes in prescribing were eligible for inclusion. Quality of included studies was assessed using the Multiple Methods Appraisal Tool (MMAT). We performed a narrative synthesis, grouping studies by publication status, setting and type of data reported (effectiveness or implementation).

Results: We included 14 peer reviewed journal articles and 11 conference abstracts, together with four case study reports. The journal articles reported 10 different interventions, five delivered in general practice, four in care homes and one in community pharmacy. The quality of evidence was higher in general practice than in care home settings. It was consistently reported that the intervention improved outcomes related to prescribing, although the limited number of studies and wide range of outcomes reported made it difficult to estimate the size of any effect.

Implementation was strongly influenced by relationships between pharmacists and other health and care professionals, especially GPs. Implementation in care homes appeared to be more complex than in general practice because of differences in systems and 'culture' between health and social care.

Conclusions: Pharmacist-led interventions have been reported to reduce overprescribing in primary care settings in the UK but a shortage of high-quality evidence means that more rigorous studies using high-quality designs are needed. More research is also needed in community pharmacy settings; to assess intervention effects on patient outcomes other than prescribing; and to investigate how reducing overprescribing can impact on health inequalities.

Registration: PROSPERO [CRD42023396366].

Strengths and limitations of this study

- We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness.

- Many of the studies lacked a control group and the research took place in a highly complex and evolving system, meaning that results could have been influenced by confounding factors such as other interventions in the health and social care system.
- Some review processes were performed by a single reviewer and meta-analysis was not feasible.

Introduction

This evidence review was performed to support implementation of the National Overprescribing Review for England (NOR; see below)) by examining research on pharmacist-led overprescribing interventions in UK primary care settings. Pharmacists are trained to provide advice and support to patients and other health professionals, pharmacist independent prescribers (PIPs) have existed since 2006 and patients are increasingly asked to consider the community pharmacy as a first source of support for minor health conditions. Alongside community pharmacies, many general practices have pharmacists as members of the practice team. Pharmacists, working with GPs and other healthcare professionals, are thus well placed to support interventions directed towards medicines optimisation and the reduction of overprescribing. Such interventions include carrying out structured medication reviews directly with patients and carers and/or reviewing data from patient records. The aims and objectives of the review are outlined below, following a brief clarification of terminology.

Overprescribing has been defined as 'the use of a medicine where there is a better non-medicine alternative, or the use is inappropriate for that patients' circumstances and wishes'[1]. Overprescribing is often related to the concept of problematic polypharmacy, where harmful effects result from the prescription of multiple medications. However, there is no agreed definition of polypharmacy and patients with complex health conditions may require multiple medications.

Medicines optimisation is an umbrella term for interventions designed to ensure that medicines are used safely and effectively, producing the best possible outcomes for patients. In this context, deprescribing refers to the process of stopping medications that are no longer appropriate to a patient's needs. Deprescribing is a response to overprescribing and problematic polypharmacy and involves collaboration between health professionals and patients and/or carers to ensure shared decision-making. Shared decision-making with patients and/or carers is fundamental to successful medicines optimisation[2] but the need for time and resources to ensure that this takes place can create barriers to service delivery. Another related term, medicines reconciliation, is a more technical process to ensure consistency between prescription records and the medications the patient is actually receiving and taking. The terminology around overprescribing and other forms of medicines misuse was recently reviewed by Singier et al[3]. Medication review involves examining a patient's prescriptions as a whole and is separate from measures to reduce inappropriate prescribing of specific medications or types of medication such as antibiotics or proton pump inhibitors.

Overprescribing can cause direct harm to patients in a variety of ways. It has been estimated that about 6.5% of hospital admissions are caused by harmful effects of medication, rising to 20% for people aged over 65[1]. In addition to physiological harms, long-term use of some medications can lead to dependency and problems when attempting to withdraw the medication.

Issues relating to prescribed medication can arise from a whole range of causes, including patients requiring treatment for multiple conditions, lack of co-ordination between different health professionals or organisations and failures of communication between health professionals and patients (for example failing to gather information because of time constraints on appointments). Availability of new medications and increasing numbers of people living with long-term conditions such as arthritis and diabetes have resulted in patients being prescribed more medications and continuing to take them for long periods of time, often for life. The average number of prescription

items per head of population doubled between 1996 and 2016, and over 75% of prescriptions are repeat prescriptions[1].

Pharmacists are thus well placed to support processes of medicines optimisation, which involve them working closely with medical professionals (particularly GPs), commissioners of health care and patients. The report of the National Overprescribing Review for England, published in 2021, provides numerous examples and case studies[1].

The National Overprescribing Review (NOR) for England was set up in 2018 to evaluate the extent of overprescribing in the NHS and recommend measures to reduce it, particularly in primary care. A review of existing research (overview of systematic reviews) was commissioned to support the national review[4]. The NOR identified a need for a more consistent and effective approach to medication review, which requires both the identification of effective interventions and an understanding of the factors that need to be addressed in terms of organisational and cultural barriers to implementation. The national review's recommendations included changes to systems (patient records, transfers of care and clinical guidance) and culture (reduced dependence on medication and support for shared decision-making), as well as the appointment of a National Clinical Director for Prescribing[1].

This evidence review was commissioned to support implementation of the NOR recommendations by examining research on pharmacist-led overprescribing interventions in UK primary care settings. We aimed to assess the effects of relevant interventions on outcomes related to prescribing, identify key characteristics of the interventions and examine barriers and facilitators to implementation in routine practice. A further aim was to assess the quality of the evidence base and identify priorities for further research. In addition to this UK-focused paper, outputs from the project include a broader scoping review of reviews of interventions for overprescribing in primary care (Preston et al. in preparation) and an evidence-based analysis of factors for service commissioners and providers to consider in developing and delivering services to reduce overprescribing and optimise medication use.

Methods

Review aims and objectives

We aimed to perform a systematic review of published literature and published or informally published evaluations reporting UK-based, pharmacist-led interventions for overprescribing, including the following components:

i. A review and synthesis of outcomes of effective interventions

ii. A review of the characteristics of effective interventions using the TIDieR framework

iii. Evaluation of the UK evidence base in terms of quality and risk of bias

iv. Identification of case study examples of effectively implemented interventions in the UK

Inclusion and exclusion criteria

Inclusion criteria for the review were as follows

- Population/setting: UK primary care
- Intervention: Pharmacist-led interventions aimed at review and optimisation of prescribed medications
- Comparator: Not required
- Outcomes: Studies had to report a primary outcome related to changes in prescribing. Secondary outcomes were other patient and health service outcomes, including but not limited to changes to type of medicines prescribed, quality of life, hospital admissions and deaths.
- Study design: Quantitative and qualitative studies were eligible for inclusion, with no exclusions based on study design or quality. Reports of local initiatives published as grey literature reports or conference abstracts were included to give a fuller picture of activity across the NHS.
- Other: Studies published in English between January 2013 and February 2023

We excluded interventions aimed at reducing overprescribing of specific medications or types of medication, e.g. antibiotics or proton pump inhibitors. Studies of children and young people were also excluded.

Search methods

A common literature search was performed for this review and the associated scoping review of reviews (Preston et al. in preparation). Searches were conducted by an information specialist (MC) in order to identify published and unpublished evidence on primary care interventions to reduce overprescribing.

Phase 1: peer reviewed literature

A first phase of database searches was run in February 2023 to retrieve relevant peer-reviewed literature. Searches were designed around the following concepts:

PROBLEM	INTERVENTION	SETTING
Overprescribing; Inappropriate prescribing; polypharmacy	Deprescribing; Structured medication review; medication reconciliation; medicines optimisation; shared decision making; personalised care	Primary Care (including international terms for primary care where relevant)

While we are aware of the Morel filter (2022) for identifying studies of deprescribing[5], our focus was specifically on a primary care setting. Search strategies are provided in supplementary file 1.

Searches covered the databases MEDLINE, Embase, CINAHL, PsycINFO and The Cochrane Library and were limited to studies published since 2013 and in OECD countries with healthcare systems similar to the UK.

Phase 2: grey literature

A further phase of targeted searches was conducted in May 2023 to identify unpublished or "grey" literature. This involved searching for the case studies identified by the National Overprescribing Review (to identify any which had produced a report or evaluation), and then searching the Overton.io platform for pharmacist-led deprescribing/overprescribing and medicines optimisation.

Searches were complemented by input from stakeholders (internal and external topic advisers) to minimise the risk of missing any other relevant evidence.

Study selection

Records retrieved by the literature search were stored in a shared EndNote library and de-duplicated. Screening for inclusion at the title level was performed by single reviewers after piloting of a test set. Reviewers could refer records to another team member in the event of uncertainty and a 20% sample of records was screened by a second reviewer to validate title level inclusion decisions.

Screening for inclusion at the abstract and full text level was performed by pairs of reviewers acting independently. Disagreements were resolved by discussion among the reviewers involved (AC, DC and LP). A good level of agreement was achieved, values of kappa between pairs of reviewers ranging from 0.67 to 0.96. Reasons for exclusion at the full text stage were recorded.

Data extraction

Data extraction tables and summary tables were developed in Microsoft Word. Extraction was performed by a single reviewer, with a 10% sample being checked for consistency and accuracy. In addition to standard data extraction fields (study design/sample size, setting, intervention, key findings and strengths/limitations) , we used the TIDieR Lite framework to collect information on the features of interventions reported as 'successful' to determine whether service commissioners and providers should consider specific factors when commissioning/delivering services. TIDieR Lite is a simplified version of the TIDieR (Template for Intervention Description and Replication) checklist [6].

Quality assessment

Methodological quality of peer reviewed journal articles was assessed using the Mixed Methods Appraisal Tool (MMAT) version 2018[7]. The tool includes screening questions and methodological quality questions for different study designs (qualitative, randomised trials, non-randomised quantitative studies, descriptive studies and mixed methods). Quality assessment results were combined with identified strengths and limitations (including those reported by study authors) to characterise the contribution of individual studies and groups of studies to the overall evidence base.

Data synthesis

We performed a narrative synthesis of the included studies using text and tables to describe study and intervention characteristics in line with methodological and reporting guidelines[8, 9]. We initially grouped studies by publication status, considering peer-reviewed journal articles (regardless of study design and quality) separately from conference abstracts and case studies. Within these three categories, we grouped studies by setting (general practice, care homes or community settings). We also distinguished between studies reporting effectiveness of interventions and those reporting implementation of interventions (e.g. qualitative studies and process evaluations). In view of study heterogeneity and reporting limitations, effectively implemented interventions were defined as those where the study authors' conclusions indicated that the service was regarded as a success and was planned to continue or be expanded.

Studies reported a wide variety of outcomes using diverse effect measures. For this reason we did not attempt to calculate a standardised metric to compare effect sizes across outcomes. The synthesis used a 'vote-counting' method (number and proportion of studies reporting positive, negative or neutral outcomes), prioritising prescribing-related outcomes over patient and other outcomes. Reported effect measures and associated 95% CIs were recorded in the text and tables. Tables of study characteristics and findings were presented alphabetically by author for consistency. While reporting results from all study designs we prioritised stronger study designs (experimental and quasi-experimental) over those of uncontrolled observational studies. In terms of exploring heterogeneity, the structure of the synthesis allowed consideration of potential modifiers including study design, study quality and setting. Intervention components and aspects of implementation were examined using modifications of existing frameworks, the component analysis was pre-specified in the review protocol.

We did not use the GRADE approach to assess certainty of evidence because of its emphasis on randomised trials and downgrading of other study designs. Instead we distinguished between controlled and uncontrolled studies, identified areas of consistency and inconsistency and highlighted areas of particularly limited evidence (e.g. settings or outcomes represented by single studies). A similar approach has been used by team members in previous reviews[10].

Public involvement

The review was supported by a public panel who provided feedback on public perceptions that informed the review and are reflected in the Discussion.

Variations from protocol

We used Tidier Lite instead of the full TIDieR framework. This was because the full framework is designed to allow the replication of interventions and therefore goes beyond the degree of detail required for evidence synthesis.

Results

Results of literature search

The PRISMA flow diagram (Figure 1) summarises the study selection process. After screening 1774 records at the title and abstract stage and 215 full-text articles, we included 14 published articles, 11 conference abstracts and four case study reports. The majority of exclusions were of studies conducted outside the UK, with a smaller number excluded because the intervention was not pharmacist–led or the article did not report empirical data. Characteristics of the included studies are reported in the following sections.

Please insert Figure 1: PRISMA flow diagram near here

Research studies

Study characteristics

Study characteristics are summarised in Table 1, with full data extraction tables in supplementary file 2 . The 14 publications reported on ten interventions, of which five were delivered in general practice (seven publications[11-17]), three in care homes for older people (five publications[18-22]), one in care homes for people with intellectual disabilities (ID) [23] and one in community pharmacies[24].

All the interventions involved medication review in some form. Distinctive features of interventions included use of IT to identify patients for review[11-13, 15, 16]; a key role for pharmacist independent prescribers in medication management in care homes[21, 22]; and employment of pharmacists by groups of general practices (primary care networks, PCNs) to provide a holistic patient-centred service specified by NHS England[14]. Intervention characteristics are considered in more detail below.

Study designs used included one individual RCT[17] and two cluster RCTs (CHIPPS[18, 21] and PINCER[11]), although the primary publications of the latter two trials fell outside the time period covered by this review. Two studies used an interrupted time series (ITS) design[15, 16] and five used qualitative approaches[12-14, 18, 22]. One study was a mixed methods process evaluation[21]. The remaining studies were described as service evaluations or quality improvement reports with an uncontrolled before vs. after design [19, 20, 23, 24].

Included studies reported a wide range of outcomes (Table 1). For further analysis, see below under ‘effects of interventions’ and ‘Implementation/system issues, respectively. None of the studies reported details of participants other than age and sex, making it difficult to assess equity, diversity and inclusion across the evidence base.

Table 1: Summary of research study characteristics

Reference	Population	Intervention	Study design	Outcome measures
Quantitative controlled studies				
Howard 2014[11]	Pharmacists delivering intervention	IT-enabled pharmacist-led review to reduce medication errors	Cluster RCT (PINCER trial)	Time taken to complete reviews; recommended interventions and whether these were implemented
Peek 2020[15]	General practice patients with one or more risk factors for hazardous prescribing or inadequate blood test monitoring	Pharmacist-led Safety Medication dASHboard (SMASH) intervention	Interrupted time series analysis	Rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring
Rodgers 2022[16]	General practices in the East Midlands	Pharmacist-led IT intervention (PINCER)	Multiple interrupted time series	Incidence of potentially hazardous prescribing
Syafhan 2021[17]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness plus clinical outcomes and costs
Quantitative uncontrolled studies				
Alves 2019[19]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (5 year uncontrolled study)	Interventions by pharmacist (including deprescribing and changes to prescriptions)
Baqir 2017[20]	Care home residents	Medication review by pharmacist with or without GP	Retrospective analysis of data from QI programme	Number and type of medications stopped
Thayer 2021[23]	Care home residents with intellectual disabilities	Collaborative service initiative involving community pharmacists and a specialist mental health pharmacist providing review of medicines and lifestyle risk factors	Service evaluation	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists

Twigg 2015[24]	Patients over 65 prescribed four or more medications	Community pharmacist consultation including medication review using STOPP/START rules	Service evaluation	Number of recommendations; falls, medication adherence, quality of life and costs at 6 months
Qualitative/mixed methods				
Alharthi 2023[18]	Care home residents	Deprescribing by pharmacist independent prescriber	Qualitative interviews with participants in a cluster RCT (CHIPPS study)	Barriers and facilitators to deprescribing
Birt 2021;[21]	Care home residents	Pharmacist independent prescribers responsible for medicines management (CHIPPS)	Mixed methods process evaluation	PR activities, perceived benefits and barriers to implementation
Jeffries 2018[12]	Pharmacists delivering intervention, GPs and CCG staff	Pharmacist-led intervention involving the use of an electronic audit and feedback surveillance dashboard to identify patients potentially at risk of hazardous prescribing or monitoring of medicines in general practice	Qualitative interviews	Themes related to implementation of the intervention and role of practice pharmacists and others
Jeffries 2017[13]	Stakeholders in general practice and CCG	Electronic medicines optimisation system	Qualitative realist evaluation	Suggestions to support implementation of the system
Lane 2020[22]	Doctors, pharmacists, care-home managers and staff, residents and relatives	Pharmacist independent prescriber service	Qualitative focus groups and interviews	Perceived benefits of the service and barriers and facilitators to implementation
Madden 2022[14]	Pharmacists working in general practice within PCNs	Structured medication review (SMR) service within Primary Care Networks	Qualitative interview study	Themes related to early implementation of SMR service

Table 2: Summary of studies reporting effects of interventions

Reference	Intervention	Setting	Study design and sample size	Outcome measure and effect size
Alves 2019[19]	Medication review	Care homes	Service evaluation 10,405 patient reviews over 5 years	Interventions by pharmacis
Baqir 2017[20]	Medication review	Care homes	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Number and type of medicines stopped 19.5% reduction in number of medicines being prescribed relative to baseline
Peek 2020[15]	Safety medication dashboard	General practice	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	Potentially hazardous prescribing (composite of 10 indicators) Potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p < 0.001$) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p < 0.001$) at 12 months
Rodgers 2022[16]	Pharmacist-led IT-assisted intervention (PINCER)	General practice	Multiple interrupted time series 393 general practices covering approximately 3 million patients	Indicators of potentially hazardous prescribing The PINCER intervention was associated with a decrease in the rate of hazardous prescribing of 16.1% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6 months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention
Syafhan 2021[17]	Pharmacist-led medicines optimisation	General practice	Individual RCT 356 patients at risk of medication-related	Medication-related problems (MRP); Medicines Appropriateness Index (MAI) Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p < 0.00$ in patients who received the full

			problems (MRPs) from 8 GP practices	intervention schedule. MAI scores were reduced (medications more appropriate) for the intervention group, but not for control group.
Thayer 2021[23]	Review of medicines and lifestyle risk factors	Care homes for adults with intellectual disabilities (ID)	Service evaluation 160 care home residents with ID	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists
Twigg 2015[24]	Community pharmacist consultation including medication review	Community pharmacies	Service evaluation 620 patients (aged over 65 years and prescribed ≥ 4 medications	Number of recommendations, falls, medication adherence, quality of life and costs at 6 months

Intervention characteristics

Table 2 in supplementary file 2 summarises characteristics of the included interventions using the TIDieR Lite checklist. The table includes limited data extracted from studies cited by included studies but not themselves included in the review [25-27].

The pharmacists involved in delivering the interventions were variously described as pharmacist independent prescribers[21]; trained pharmacists and pharmacy technicians[11, 16]; primary care pharmacists[19]; clinical pharmacists working in general practice[13-15]; GP practice-based pharmacists working as part of a wider primary care team[17]; community and specialist mental health pharmacists[23]; and community pharmacists and pharmacy team members[24]. One study simply referred to 'pharmacists'[13].

Four interventions were explicitly stated to require training of pharmacists to deliver them[11, 17, 21, 24]; the extent of training was described for three of these[17, 21, 24]. Training pharmacists to deliver the PINCER intervention was described in a separate paper[11]. Interventions were delivered with other primary care team members depending on the setting of the study and in some cases with staff employed by clinical commissioning groups (CCGs). In particular, only the CHIPPS study involved pharmacists with the power to prescribe medication independently; in other studies recommendations were passed to the patient's GP or another medically qualified professional for implementation. Shared decision-making with patients and/or families was specifically reported for three interventions[14, 17, 20].

Reporting of interventions varied between studies. Most studies reported the process of medication review including patient selection for review and the review itself in more detail than resulting follow-up actions. Two qualitative studies reported limited details of the review process[12, 14], although a service specification was available for the NHS England structured medication review (SMR) investigated by Madden et al.[14]. For studies where the intervention was primarily directed at improving medication review processes using general practice data[11-13], it was unclear whether there was a standard process to discuss findings with the patient and make changes to their prescriptions. All studies reporting on effectiveness of medication reviews stated that the person undertaking the review had access to relevant patient records[15-17, 19, 20, 23, 24].

Intensity of interventions was also variably reported. In the CHIPPS study, PIPs committed a minimum of 16 hours/month to deliver care to approximately 20 care home residents[25]. Madden et al. reported that SMR appointments were recommended to allow at least 30 minutes for review and shared decision-making[14]. The medicines optimisation intervention evaluated by Syafhan et al. involved up to three meetings between patient and pharmacist[17], while the FOMM study in community pharmacies estimated times of 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review[24]. Other studies reported that time and level of support allocated to interventions varied between and within CCG areas depending on local resources and priorities[16, 19]. Another measure of intervention intensity was the number of recommended actions, averaging 3.3/resident in care home residents with intellectual disabilities[23].

Most included studies reported on a single round of medication reviews with variable periods of follow-up. As noted above, some interventions required multiple interactions between pharmacists and patients.

Effects of interventions

Seven studies reported on effects of pharmacist-led interventions in some form (Table 2): three in general practice[15-17], three in care homes[19, 20, 23] (including one in a care home for people with ID[23]) and one in community pharmacies[24].

The strongest evidence for the effectiveness of interventionscame from the studies in general practice. The interrupted time series (ITS) studies of Peek et al.[15] and Rodgers et al.[16], which used indicators of inappropriate prescribing to identify patients for intervention, reported significant decreases in inappropriate prescribing at 6 and 12 months after intervention (Table 2). Estimated reductions were larger in Peek et al. (27.9% and 40.7%) compared with Rodgers et al. (16.7% and 15.3%)[15, 16]. The 95% confidence intervals of the two studies at 12 months did not overlap, suggesting some uncertainty about the magnitude of the effect. The randomised trial by Syafhan et al.[17] preferentially recruited patients based on prescription of six or more medications and a history of recent unplanned hospital admission. The intervention was associated with a reduction in medication-related problems in those who completed the full programme (up to three appointments) and an improvement in MAI scores.

Of the three studies set in care homes, only Baqir et al. reported a direct effect on prescribing associated with medication review, a 19.5% reduction in number of prescribed medicines[20]. Alves et al.[28] reported on pharmacist interventions and potential financial savings over 5 years. In the one year reported in detail, 24.5% of interventions involved deprescribing. Potential drug cost savings were estimated at £812,441 annually, of which £431, 493 (55%) was attributed to deprescribing. The study of Thayer et al.[23] differed from the others in involving care home residents with intellectual disabilities. There was a high level of polypharmacy at baseline and pharmacists made an average of 3.3 interventions/recommendations per resident, of which 12.8% involved deprescribing. A large majority of pharmacist recommendations were accepted by GPs/psychiatrists caring for the residents.

The one study in a community pharmacy setting recruited patients aged 65 or older who were prescribed four or more medications[24]. Of 620 patients recruited, 441 (71.1%) completed the 6-month study. Pharmacists made 142 recommendations related to 110 patients, largely dealing with potentially inappropriate prescribing of NSAIDs and PPIs or duplication of therapy. The study also reported a significant decrease in falls and improvements in medication adherence and quality of life at follow-up.

The review included two publications from the CHIPPS Care Homes Independent Pharmacist Prescriber Study) trial[18, 21] but the paper reporting effectiveness and safety results from this cluster RCT[29] was published too late for formal consideration for inclusion in our review. The primary outcome was rate of falls, with Drug Burden Index (DBI) being one of the secondary outcomes. Fall rate at 6 months did not differ significantly between intervention and control groups

but DBI was lower in the intervention group (mean 0.66 vs. 0.73; adjusted rate ratio 0.83, 95% CI 0.74 to 0.92).

Implementation/system issues

Seven studies provided quantitative and/or qualitative evidence on factors affecting implementation of pharmacist-led interventions, of which four were performed in general practice[11-14] and three in care homes[18, 21, 22].

The general practice studies focused on different parts of the implementation pathway. Two dealt with implementation of IT systems to support detection of potentially hazardous prescribing[12, 13]; one was a process evaluation of the PINCER trial[11]; and one focused on implementation of structured medication reviews as recommended by NHS England in routine practice[14]. The studies of IT-supported interventions were broadly positive about the potential for implementation and sustainability, but the study of NHS England's SMR programme concluded that its early implementation failed to deliver the planned holistic and patient-centred approach.

Other evidence

Conference abstracts

We included 11 conference abstracts (Table 4), of which two were earlier reports of studies subsequently published as full papers[28, 30]. All of the included abstracts focused on intervention effects on prescribing and related outcomes.

Five abstracts reported research in general practice, of which three involved patients with polypharmacy identified from the overall practice population[31-33]. As a group, these three abstracts provided weak evidence of associations between pharmacist-led medication reviews and changes in medication and cost savings together with high levels of patient satisfaction (Table 3),

Two abstracts reported on selected general practice populations. The only comparative study in this group reported that patients living with frailty who were reviewed by a pharmacist as part of a multi-disciplinary team review had a reduction in total medications compared with a control cohort[34]. When patients recently discharged from hospital were reviewed by a pharmacist working in their general practice, 16 out of 35 had changes made to their medication, with 74% of changes involving deprescribing[35].

Turning to studies performed in care homes, two abstracts by Doherty et al. (2020)[36, 37] evaluated an intervention entitled Medicines Optimisation in Older People (MOOP) which involved case management by pharmacists. The authors reported that inappropriate prescribing (based on the MAI) was highly prevalent at baseline *84%) but declined significantly following the intervention. Swift et al. reported that a team comprising pharmacists and pharmacy technicians who both performed medication reviews and supported care home staff significantly reduced inappropriate polypharmacy (measured by prescribing quality indicators) between 2024 and 2017[38]. For care home residents receiving palliative care, structured medication reviews involving shared decision-

making were associated with high rates of changes to medication (1787 suggested changes from 574 reviews, 76% of which were implemented) and associated cost savings[39].

Grey literature case studies

We included reports of four case studies reporting on local initiatives in three areas of England (see Table 4).Details of all case studies may be found in Annex C of the National Overprescribing Review report[1]. Case studies were submitted by NHS organisations (mainly CCGs) and included varying amounts of data on intervention characteristics, support for implementation and outcome measures. Three interventions were delivered in general practice and one in care homes. The initiative developed by Swale CCG was distinctive in using pharmacy technicians to review less complex cases, although the initiative was targeted at patients considered high-risk for ADRs. Although not classified as research, such case studies can provide useful data on implementation of interventions and outcomes achieved in routine practice

Table 3: Summary of studies published as conference abstracts

Reference	Population	Intervention	Study design	Outcome measures and key findings
Alves 2016[28]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (retrospective analysis and interviews)	Interventions by pharmacist; barriers and facilitators A total of 2916 interventions were made in 1047 patients, of which deprescribing represented 22%
Bryant 2019[31]	Primary care patients taking ten or more medications	Polypharmacy clinics in GP surgeries	Service evaluation (retrospective data analysis)	Reductions in prescribing; cost savings; hospital admissions avoided April 2017 to March 2018, 370 patients reviewed and £50,766.63 saved. Figures for April to December 2018 were 209 and £1[illegible]2, respectively
Chauhan 2022[35]	Patients recently discharged from hospital	Post-discharge medication review by clinical pharmacist linked to GP practice	Formative service evaluation (uncontrolled)	Medication changes following review 16/35 patients had medications changed; 74% (25/34) of changes were medications stopped
Din 2020[32]	Patients referred by GPs	Polypharmacy review clinics led by pharmacist independent prescriber with shared decision-making	Service evaluation (uncontrolled)	Changes to medication, feedback from patients and MDT Pharmacist medication reviews were effective, with positive feedback received from patients and members of the MDT. Deprescribing and inhaler counselling were the most common interventions.
Din 2022[34]	Primary care patients living with frailty	Frailty review involving pharmacist as part of MDT	Comparative cohort	Changes in medication (including cholinergic burden), practice contacts and falls Intervention group had a reduction in total number of medications when compared with non-intervention cohort. Anti-cholinergic burden scores were reduced by a mean of 26%

Doherty 2020a[36], 2020b[37]	Care home residents	Medicines Optimisation in Older People (MOOP) involving case management by pharmacists	Uncontrolled before/after	Inappropriate prescribing; unplanned hospital admissions; GP visits; clinical interventions Inappropriate prescribing was highly prevalent at baseline (84.1%) but improved significantly from baseline (M = 14.87, SD = 13.11) to post-intervention (M = 0.70, SD = 2.04, Z = 25.97, p<.001).
Donyai 2017[33]	Patients aged at least 75 years and prescribed 15 or more medication	Pharmacist-led polypharmacy review clinic in primary care	Survey	Patient satisfaction and related outcomes Of the 166 patients who returned a satisfaction questionnaire (40% response rate), 83% found the service helpful, 13% did not, 2% did not know and 2% did not respond
Kolovetsios 2018[39]	Care home residents needing palliative care	Structured medication reviews carried out in agreement with patient, nurse, family/carer and GP	Service evaluation	Changes to medication, estimated cost savings From January 2017 to January 2018, 574 medication reviews took place resulting in 1787 suggested medication changes. Approximately 76% of these changes were agreed and actioned by patients' GPs, with estimated savings of £169,986.96.
Swift 2018[38]	Care home residents	Care home team (pharmacists and pharmacy technicians) delivering medication reviews and supporting care home staff	Service evaluation	Prescribing quality indicators (including reduced inappropriate polypharmacy); CQC ratings Medication reviews were completed for 749 care home residents between August 2014 and March 2017. Of the recommendations made to prescribers, 85% were accepted and resulted in a reduction in inappropriate polypharmacy
Syafhan 2019[30]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness A total of 356 adult patients (175 control and 181 intervention) were recruited. Among 108 intervention patients who had three pharmacist face-to- face contacts, 346 MRPs were identified at baseline and 83 MRPs at 6 months. Median values were 3 MRPs at baseline and 1 at 6 months (p<0.001).

Table 4: Summary of selected grey literature case studies

Setting	Name of initiative	Key findings	Comments
Brighton and Hove CCG	An evaluation of a clinical pharmacist medication review service in primary care	A total of 1,300 patients were referred into the service and reviewed between April 2017 and March 2018; 9% of patients were deprescribed high-risk medicines	The target patient cohort of frail or older persons prescribed polypharmacy was identified from searches within GP clinical systems and through referrals from clinical practitioners, voluntary and social care services
Swale CCG	Medicines Optimisation Review Programme	In 2018/19, pharmacists and pharmacy technicians reviewed 5281 patients and made 3859 interventions, 37% for adverse drug reactions (ADRs). Estimated in-year cost savings were £239,546	Targeted 'high-risk' patients Key feature is use of technicians for less complex cases
NE Hampshire and Farnham CCG	Care homes pharmacist	Pharmacist accompanying GPs visiting care homes carried out over 250 medication reviews and 800 interventions. Average number of medicines per resident fell from 9.4 to 7.6	Limited data reported
NE Hampshire and Farnham CCG	Polypharmacy prescribing comparators	Tool developed by Wessex AHSN was used to identify patients at risk of harm, resulting in significant reductions in percentage of patients aged over 75 prescribed 15 or more medications and percentage with an anticholinergic burden score of 6 or more	Limited data reported

Study quality

Quality assessment results using the MMAT are presented in supplementary file 3. The results should be read in conjunction with the study strengths and limitations (see Table 1 in supplementary file 1).

Five different checklists within the MMAT were used to assess the 14 studies. The sample included one RCT[17]; six studies were classified as quantitative non-randomised[15, 16, 19, 20, 23, 24]; one as quantitative descriptive[11]; one as mixed methods[21]; and five as qualitative[12-14, 18, 22]. All studies passed the screening questions (are there clear research questions? and do the collected data allow to address the research questions?)

The RCT by Syafhan et al. was described as a pragmatic trial and was at relatively high risk of bias for this type of design. The trial did not achieve the planned number of participants and there was a high rate of attrition (about 30%), meaning that many participants did not receive the full intervention or provide outcome data. The trial also suffered from unclear reporting: method of randomisation and whether outcome assessors were blinded was not reported, making it difficult to assess overall risk of bias.

The quantitative non-randomised studies comprised four observational studies at high risk of bias because of the absence of a control group[19, 20, 23, 24] and two large ITS studies[15, 16]. The MMAT tool identified some limitations of these studies, including some risk of confounding and incomplete outcome data in one study[16]. However, these were large studies conducted in routine practice and providing evidence of a statistically significant effect at 12 months post-intervention. The process evaluations of the CHIPPS[21] and PINCER[11] studies both scored highly on the MMAT assessment.

The qualitative studies were generally of good quality, with sufficient data presented in support of conclusions and appropriate use of frameworks and thematic analysis to organise presentation of the findings. The study by Alharthi et al.[18] was a secondary analysis of data collected for another purpose, making it unclear whether qualitative data collection methods were adequate.

Using the system applied by the authors in previous studies of complex health service interventions[10], the overall strength of evidence was classified as borderline 'stronger' (generally consistent findings in multiple studies with a comparator group) for general practice, 'weaker' (generally consistent findings in one study with a comparator group design and several non-comparator studies or multiple non-comparator studies) for care homes and 'very limited' (single study) for community pharmacies.

Effectively implemented interventions

Three research studies met the criteria for 'effectively implemented' interventions: the closely related PINCER[16] and SMASH[15] interventions in general practice and the Somerset model of medication review in care homes[19]. Further examples of effectively implemented medication review in care homes were identified among the included conference abstracts[36-39]. Case studies from Brighton and Hove and Swale CCGs appeared to report effectively implemented interventions

targeted at high-risk patients in general practice (Table 5). An evaluation of the early implementation of SMRs in primary care networks indicated that the service as provided did not match the vision of a patient-centred holistic review with an emphasis on shared decision-making[14].

.Discussion

Summary of findings

In spite of its broad inclusion criteria, this review identified a relatively small number of studies of pharmacist-led interventions in UK primary care (14 peer reviewed journal articles, 11 conference abstracts and four case studies). Overall, the bulk of evidence came from the care home sector but most of the better quality evidence was derived from studies conducted in general practice. The majority (8/14) of peer reviewed papers were published in 2020 or later, suggesting that this is a developing area of research and practice in the context of encouraging patients to consult pharmacists initially for minor conditions and to increase pharmacists' prescribing rights. It was encouraging that we identified a number of effectively implemented interventions and initiatives in both care homes and general practice.

Outcomes of effective interventions

This systematic review suggests that pharmacist-led interventions may reduce overprescribing in primary care settings in the UK, although more controlled studies are needed. The evidence is strongest for interventions implemented in general practice, where we identified a small randomised trial[17] as well as two large quasi-experimental studies (interrupted time series)[15, 16] and various uncontrolled studies and service evaluations. Evidence from care home settings was of lower quality with the exception of the CHIPPS study involving pharmacist independent prescribers working in care homes[21]. We located only one uncontrolled study based in UK community pharmacies[24].

Although the direction of reported effects was clear, the limited number of controlled studies combined with the wide range of outcomes reported makes it difficult to estimate the size of any effect. For example, the two ITS studies using similar interventions reported markedly different reductions in measures of inappropriate prescribing at 6 and 12 months after implementation of the intervention[15, 16]. Uncertainty about effect sizes is increased because many of the studies lacked a control group and the results could have been influenced by other interventions in the health and social care system, for example the Enhanced Health in Care Homes programme implemented in England. While our review focused primarily on outcomes related to prescribing, data on cost savings were also widely reported but the evidence was generally of low quality. We also found limited evidence of a link between reductions in measures of overprescribing and clinical outcomes, mainly because of lack of reporting. The CHIPPS study found no significant difference in its primary outcome of fall rate, although there was a reduction in Drug Burden Index (a secondary outcome) in the intervention group at 6 months[29].

Characteristics of effective interventions

The TIDieR Lite checklist provided a suitable structure for describing intervention characteristics for evidence synthesis purposes and this discussion follows its structure. Lack of reporting (especially of

intervention intensity/frequency) was a limiting factor, as was reporting of varying intervention information across multiple publications.

Medication reviews were undertaken by pharmacists acting independently or in conjunction with GPs or care home staff. In a study in care homes for people with intellectual disabilities, psychiatrists were also involved in review where appropriate[23]. Pharmacy technicians were also involved in the PINCER study and could potentially have a greater role in relatively straightforward medication reviews[11, 16]. The included studies reported a variety of models of employment of pharmacists, including direct employment by GP practices, CCG Medicines Optimisation Teams, PIPs and community pharmacists. PCNs support employment of pharmacists by general practices and are the route chosen by NHS England to implement its model of SMR.

A major difference between settings is the need to identify patients requiring medication review in general practice, whereas most care home residents take multiple medications and could be considered candidates for review as part of their routine health care. A key element of the PINCER[11, 16] and SMASH[15] interventions is the use of information technology to search electronic patient records efficiently across large numbers of general practices. Effective interventions were also characterised by attention to training and tools to support and sustain change in practice, e.g. an 'audit and feedback' dashboard[15].

Training of pharmacists and other staff to deliver interventions was reported to varying degrees, reflecting in part the publication channel of the research. For example, in the CHIPPS study PIPS had comprised 2 days of face-to-face instruction plus time in practice to develop relationships with the GP and care home staff.[21] Specification and provision of appropriate training will be important for future development of pharmacist-led interventions, as also highlighted by the evaluation of NHS England's SMR programme[14].

Intervention intensity is another important factor in developing and delivering interventions. For the CHIPPS study, participating PIPs committed a minimum of 16 hours/month to the service. [21] In general practice settings, NHS England recommended allowing 30 minutes for an SMR to give time for shared decision-making; this was interpreted to include time for preparation and writing-up[14]. This level of time requirement was also reported in the one study from a community setting, which estimated pharmacist time at 25 minutes for an initial consultation[24].

In terms of intensity more generally, resourcing of interventions was reported to vary between commissioning groups (CCGs) depending on staff availability and other priorities[11, 16, 19]. General practices varied in their use of a medication safety dashboard[26]. Frequency of intervention was rarely reported, reflecting the short time frame of most included studies but it seems possible that there could be an ongoing need for review as patients get older and/or their health state changes.

Quality and risk of bias

The MMAT provided a good alternative to the use of multiple tools to assess risk of bias across diverse study designs. The only randomised trial assessed was designed as a pragmatic trial[17] and the assessment confirmed a relatively high risk of bias. Publications from the CHIPPS study were included but the trial *per se* was not assessed for risk of bias because of the publication date of the main study report. Similarly, the PINCER intervention was supported by a randomised trial published in 2012, before the cut-off date for our review [40]). Well-conducted studies included in the review included large ITS studies[15, 16], process evaluations[11, 12, 21] and qualitative studies[13, 14].

Service evaluations and other lower quality evidence tended to support higher quality studies by highlighting implementation and results achieved in routine practice, although a causal relationship between intervention and outcome remains uncertain in studies without a parallel control group.

Implementation barriers and facilitators

Implementation of pharmacist-led interventions was strongly influenced by factors affecting relationships between pharmacists and other health and care professionals, especially GPs. Given that most pharmacists are not prescribers, their recommendations around (de)prescribing need to be seen as 'legitimate' by GPs who are generally responsible for acting on the recommendations. This is facilitated by continuity at the system level, including existing links between pharmacists and GPs[21] and good access to data[12]. Jeffries et al. reported that pharmacists took the lead in developing relationships with GPs, enabling a 'learning health system'[12]. The benefits of continuity at the system level could help to explain why early implementation of the SMR programme through the relatively new medium of PCNs was reported to be less successful than initially hoped[14].

Implementation in care homes may be more complex than in general practice because of differences in systems and 'culture' between health and social care[22]. Patients and their families may be supportive of medication review or oppose it based on real or perceived benefits of medication[18].

The main message regarding implementation of pharmacist-led interventions across all settings is the need for involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers[22].

Identification of effectively implemented interventions/initiatives:

Our simple criteria for 'effectively implemented' interventions/initiatives identified a number of examples published as research papers, conference abstracts or case studies (see 'Effectively implemented interventions' above). Despite limitations as research, some of the abstracts and case studies provided valuable information about how commissioners and providers had supported interventions and their commitment to continue the programme[36-39]. In other studies, despite promising results, it was unclear whether the intervention would be implemented more widely[17].

Relationship to previous research

To our knowledge, this is the first systematic review of pharmacist-led interventions and initiatives specifically in UK settings. A scoping review of reviews by the same authors (Preston et al., in preparation) included 20 systematic reviews published between 2014 and 2023. The most recent review covered pharmacist integration into general practice to optimise prescribing and outcomes for patients with polypharmacy[41]. The review included 23 studies, of which just three were from the UK. The conclusion that pharmacist integration probably reduced PIP and number of medicines (moderate certainty evidence) was in line with the findings of the present review. A 2016 systematic review by Riordan et al. focused on pharmacist-led interventions to optimise prescribing in older community-dwelling adults in primary care[42]. The authors concluded that pharmacist-led interventions may improve appropriateness of prescribing but the quality of evidence was low. The

review included randomised and quasi-randomised studies published before December 2015, giving it limited overlap with our review.

Strengths and limitations

The UK focus is both a strength and limitation of this review. We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness. The dual focus reflects the fact that pharmacist-led medicines optimisation and deprescribing in primary care is both an area of active research and of implementation within the health care system. Nevertheless, some of the evidence is not of high quality and we have tried to be appropriately cautious in our conclusions and identified implications.

Our broad review questions and UK focus resulted in a heterogeneous group of included studies. Meta-analysis was not possible so we performed a narrative synthesis in line with appropriate guidelines[8, 9]. The review was undertaken by a small but experienced team with expertise in systematic review methods and prescribing.

Implications for service delivery

Several studies indicate that barriers to successful service delivery often arise from 'system' issues and differences in 'culture'[14, 22]. Commissioners and providers engaged in developing new pharmacist-led services should ensure equitable access to data and information to avoid perceptions of 'ownership' by certain groups at the expense of others[13]. In care homes, where medication review is an important component of health care for residents[19], implementation requires health and social care professionals to work together and 'understand each other's systems'[22]. The holistic patient-centred SMR envisaged by NHS England may require culture change/training to foster an emphasis on direct patient contact and shared decision-making. Removal of financial incentives for PCNs to carry out SMRs as reported recently (https://pharmaceutical-journal.com/article/news/nhs-england-removes-financial-incentives-for-structured-medication-reviews-in-2023-2024) may complicate delivery, although the service remains a contractual requirement.

Services have been delivered successfully through CCGs Medicines Optimisation Teams with suitable training[11, 16]. The review also found evidence that services provided by PIPs appear to be a valid alternative to approaches requiring action by GPs or other medical professionals[21].

Implications for research

A major priority for research is to further evaluate the effectiveness of medication review in community pharmacy settings and how pharmacies might be best supported to deliver the service. A related need is for research to better understand public perceptions of community pharmacies as a

setting for medication review and their pros and cons compared with alternative settings such as GP surgeries. Research is needed to support the development of the PIP role and how PIPs might best be used in combination with GPs and other professionals to support optimal prescribing across the health and care system.

Shared decision-making is key to the success of pharmacist-led interventions. Research is needed to better understand patient and family attitudes to shared decision-making in the context of deprescribing and the barriers and facilitators operating in different settings and with different professionals.

The present review focused on outcomes related to prescribing and a review of effects on patient and health system outcomes would be a logical follow-up. Finally, further research is needed to understand the effects of implementing pharmacist-led medication review in general practice on health inequalities and how to reduce unwarranted variations in service delivery between different practices or regions.

Conclusions

The evidence base for pharmacist-led interventions varies widely in terms of quality but studies have consistently reported improvements relative to a comparator group or baseline. The diversity of interventions and outcomes reported makes it difficult to generalise about effect sizes but given the reported extent of the problem, even small relative reductions could be beneficial for patients and the health and care system.

The existing evidence base requires cautious interpretation because of a shortage of controlled studies and this is particularly the case for studies in community pharmacy settings. Further rigorous evaluation of interventions, particularly those delivered in community pharmacies, is required. Although not a focus of this review, there appears to be a shortage of high-quality economic evidence to guide decision-making by service commissioners and providers.

The problems encountered in the early implementation of NHS England's SMR programme[14] suggest a need for further research on the implementation of pharmacist-led interventions. Implementation of this type of interventions requires the involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers.

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Conflict of interest

The authors have no conflicts of interest to declare.

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Contribution of authors

Duncan Chambers contributed to all review processes and wrote the first draft of the paper. Louise Preston managed the review team, and contributed to all review processes and to writing the paper. Mark Clowes developed search strategies, performed literature searches and contributed to writing the paper. Anna Cantrell contributed to all review processes and to writing the paper. Elizabeth Goyder provided topic expertise and contributed to writing the paper. All authors have approved the version to be submitted.

Data sharing

Any additional data not included in this report and its appendices are available on request. All queries should be submitted to the corresponding author.

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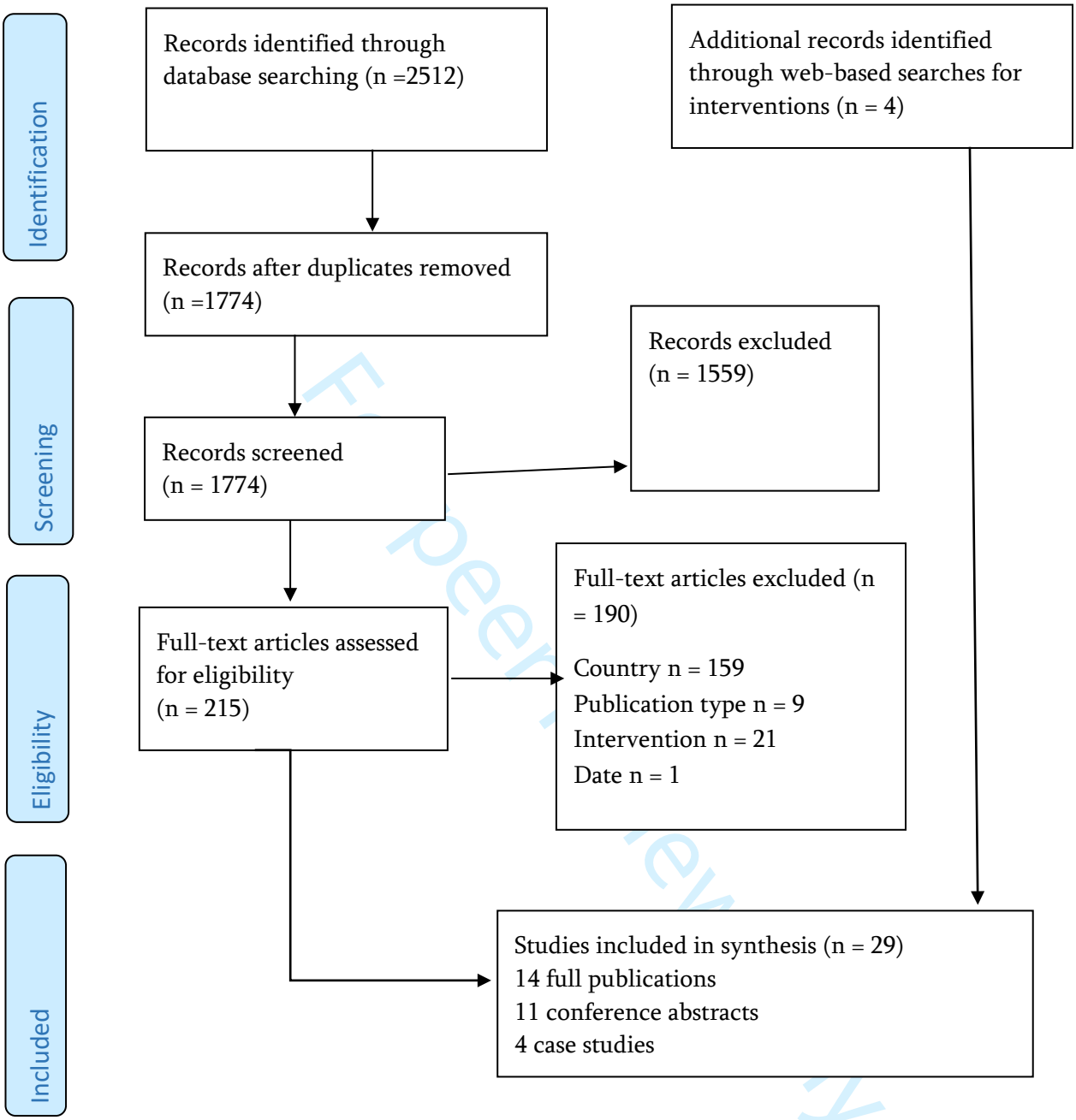

SEARCH STRATEGIES in full (for Appendix / supplementary material)

Ovid MEDLINE(R) ALL <1946 to February 06, 2023>

1 Inappropriate Prescribing/ 4485

2 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 8188

3 (overprescri* or over-prescri*).mp. 1975

4 Polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 12777

5 1 or 2 or 3 or 4 21236

6 exp Primary Health Care/ or (primary health care or primary healthcare or primary care).mp. 289526

7 general practice/ or family practice/ 78114

8 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 751694

9 6 or 7 or 8 997387

10 (deprescri* or de-prescri*).mp. 2577

11 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 16563

12 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 3182

13 10 or 11 or 12 21842

14 5 and 9 and 13 540

15 *Medication Errors/ and 9 and 13 232

16 5 and 9 and pc.fs. 835

17 14 or 15 or 16 1416

18 limit 17 to yr="2013 -Current" 1152

19 remove duplicates from 18 1145

Embase <1974 to 2023 Week 05>

1 Potentially inappropriate medication/ 2458

2 unnecessary prescribing/ [+NT] 51

3 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 11262

4 (overprescri* or over-prescri*).mp. 3064

5 Polypharmacy/ or inappropriate polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 26382

6 1 or 2 or 3 or 4 or 5 39236

7 exp Primary Health Care/ or primary medical care/ or (primary health care or primary healthcare or primary care).mp. 281889

8 general practice/ or family practice/ 83634

9 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 766031

10 7 or 8 or 9 974647

11 (deprescri* or de-prescri*).mp. 3587

12 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 28235

13 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 6755

14 11 or 12 or 13 37710

15 6 and 10 and 14 813

16 6 and 10 and pc.fs. 308

17 15 or 16 1089

18 limit 17 to yr="2013 -Current" 903

19 remove duplicates from 18 886

APA PsycInfo <1806 to January Week 5 2023>

1 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 788

2 (overprescri* or over-prescri*).mp. 329

3 (polypharmacy or poly-pharmacy).mp. 3128

4 1 or 2 or 3 4078

5 (primary health care or primary healthcare or primary care).mp. 44486

6 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 34287

7 5 or 6 71196

8 (deprescri* or de-prescri*).mp. 336

9 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 3969

10 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 242

11 8 or 9 or 10 4505

12 4 and 7 and 11 44

MY

EBSCOhost

#	Query	Limiters/Expanders	Last Run Via	Results
		Limiters - Published Date: 20130101-20231231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	
S16	S6 AND S10 AND S14			307
S15	S6 AND S10 AND S14			327
S14	S11 OR S12 OR S13			13,914
S13	(intervention* or initiative* or campaign*) n3 pharmacist*			1,981
S12	"structured medication review" or "medication reconciliation" or "medicine* optimi#ation" or "shared decision making" or "personalised care" or "personalized care"			10,941
S11	deprescri* or de-prescri*			1,345
S10	S7 OR S8 OR S9			336,381
S9	("primary care" or "primary health care" or "primary healthcare" or "primary medical care") OR (GP or "general practi*" or "family practi*" or "family physician*" or "community pharmac*" or dental or dentist* or optometrist* or optician*)			333,015
S8	(MH "Family Practice")			26,910
S7	(MH "Primary Health Care") OR (MH "Physicians, Family")			90,488
S6	S1 OR S2 OR S3 OR S4 OR S5			12,727

S5	polypharmacy or poly-pharmacy	7,664
S4	(MH "Polypharmacy (Saba CCC)") OR (MH "Polypharmacy+")	5,635
S3	overprescri* or "over prescri*"	1,026
S2	(hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) n3 prescri*	4,996
S1	(MH "Inappropriate Prescribing")	3,448

Search Name: THE COCHRANE LIBRARY

Date Run: 08/02/2023 13:50:34

Comment:

ID	Search	Hits
#1	MeSH descriptor: [Inappropriate Prescribing] explode all trees	234
#2	MeSH descriptor: [Polypharmacy] explode all trees	312
#3	((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or "non essential" or inessential) near/3 prescri*):ti,ab,kw	771
#4	(overprescri* or "over-prescri*"):ti,ab,kw	161
#5	(polypharmacy or poly-pharmacy):ti,ab,kw	1288
#6	#1 or #2 or #3 or #4 or #5	2045
#7	MeSH descriptor: [Primary Health Care] explode all trees	9989
#8	MeSH descriptor: [General Practice] explode all trees	2877
#9	MeSH descriptor: [Family Practice] explode all trees	2242
#10	("primary health care" or "primary healthcare" or "primary care"):ti,ab,kw	24053
#11	(GP or "general practi*" or "family practice" or "family physician*" or "community pharmac*" or dental or dentist* or optometr* or optician*):ti,ab,kw	44879
#12	#7 or #8 or #9 or #10 or #11	70362
#13	MeSH descriptor: [Deprescriptions] explode all trees	68
#14	(deprescri* or de-prescri*):ti,ab,kw	364
#15	("structured medication review" or "medication reconciliation" or "medicine* optimi*" or "shared decision making" or "personalised care" or "personalized care"):ti,ab,kw	2425
#16	((intervention* or initiative* or campaign*) near/3 (pharmacist* or pharmacy)):ti,ab,kw	1559
#17	#13 or #14 or #15 or #16	4166
#18	#6 and #12 and #17	130

(3 reviews, 127 trials)

Data extraction tables

Table 1: Study characteristics of included research studies (full data extraction table)

Study ID	Study design/sample size	Setting	Intervention	Key findings	Authors' conclusions	Study strengths/limitations
Alharthi 2023[18]	Secondary analysis of qualitative interview data 11 pharmacist independent prescribers (PIPs) who participated in a cluster randomised trial	Care homes in England and Scotland	Integration of PIPs into care homes to improve medication management	Factors that acted as both enablers and barriers were PIP relationship with General Practitioner (GP), care home staff and residents/families, awareness of the PIP role and family trust in PIPs' deprescribing activities *(social influences)*; PIPs' independent prescribing confidence, previous experience and ability dealing with residents' medications *(beliefs about capabilities)*; understanding of PIP role and PIP confidence in their role as an independent prescriber *(social/professional role and identity)*; access to residents' records, deprescribing decision support, regular follow-up from care home staff, resident difficulties with medications,	PiPs' involvement in care homes is influenced by numerous barriers and enablers that can be addressed to improve intervention effectiveness	Strengths: Diverse PIP contexts and perspectives on deprescribing; theory-informed analysis using Theoretical Domains Framework to identify barriers and enablers Limitations: Only PIP perspective considered; analysis used data from interviews focused on the whole intervention process rather than exclusively on deprescribing

				teamwork, and time restraints *(environmental context and resources)*. Belief that the negatives of deprescribing outweigh benefits regarding certain medications *(beliefs about consequences) acted as a barrier.*		
Alves 2019[19]	Service evaluation 10,405 patient reviews over 5 years	Care homes in Somerset	Medication review by primary care pharmacists linked to GP practices	Pharmacists made 23,955 interventions (mean 2.3 per patient) from the 10,405 patient reviews undertaken. 16.1% of interventions were related to safety. Potential drug cost savings were estimated at £812,441 over 5 years, of which £431, 493 (53%) was attributed to deprescribing	Medication reviews undertaken by primary care pharmacists in care homes generate a wide range of interventions, commonly involving deprescribing. The service contributes to the continuous optimisation of prescribing and monitoring of medicines and offers potential drug cost savings.	Strengths: Collection of data from 'real world' implementation of intervention over 5 years Limitations: No control group, cost saving estimates not based on full economic evaluation
Baqir 2017[20]	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Care homes in two CCG areas in North East England	Medicines optimisation by a pharmacist acting independently or jointly with a GP. Shared decision making with the patient or their advocate	Of the 422 patients reviewed, 298 (70.6%) had at least one medicine deprescribed with 704 medicines (19.5%) being stopped. There was no statistically significant difference between pharmacist only and pharmacist plus GP in terms of deprescribing. Assuming that each medicine stopped would have been taken for another year, annualised cost savings were estimated at £65,471	Medicines optimisation reviews can lead to a reduction in polypharmacy for care home residents through a deprescribing process. Patients' medicine regimens were simplified and optimised while making financial savings for the NHS	Strengths: Compares two approaches to delivering medication review Limitations: Short-term uncontrolled study; intervention quality/fidelity not measured

Birt 2021[21]	Mixed methods process evaluation of cluster RCT Intervention arm comprised 25 triads: Care homes (staff and up to 24 residents), GP and pharmacist Independent Prescriber (PIP); 22 PIPs contributed data	Care homes in England, Scotland and Northern Ireland	Integration of PIPs into care homes to assume central responsibility for medicines management	All stakeholders reported some benefits from PIPs having responsibility for medicine management and identified no safety concerns. PIPs reported an increase in their knowledge and identified the value of having time to engage with care home staff and residents during reviews. PIPs recorded 566 clinical interventions, many involving deprescribing; 93.8% of changes were sustained at 6 months. For 284 (50.2%) residents a medicine was stopped, and for a quarter of residents, changes involved a medicine linked to increased falls risk. Qualitative data indicated participants noted increased medication safety and improved resident quality of life. Contextual barriers to implementation were apparent in the few triads where PIP was not known to the GP and care home before the trial. In three triads, PIPs did not deliver the intervention.	The intervention was generally implemented as intended, and well-received by most stakeholders. Whilst there was widespread deprescribing, contextual factors effected PIP engagement. Implementation was most effective when communication pathways between PIP and GP had been previously established.	Strengths: Involved three UK nations with differing healthcare systems; used study records to supplement qualitative data Limitations: Interview participants may not be representative; limited access to care home residents
Howard 2014[11]	Process evaluation of data from cluster RCT	General practice surgeries in an 80 km	Pharmacist-led IT enabled intervention (PINCER).	Pharmacists judged 72% (95% CI 70, 74; 1463/2026) of cases of hazardous medicines management to be clinically	Recommendations from the pharmacists were broadly	Strengths: Uses data from a large cluster RCT

	36 intervention and 36 control practices; 1946 patients identified as at risk in intervention practices	radius around Manchester and Nottingham	Patients potentially at risk from hazardous medicines management were identified using Quest Browser software to search GP electronic records. Intervention practices were assigned a pharmacist who educated practice staff about medication management and recommended improvements to practice. Pharmacists also reviewed cases of potentially hazardous medication	relevant. Pharmacists recommended 2105 interventions in 74% (95% CI 73, 76; 1516/2038) of cases and 1685 actions were taken in 61% (95% CI 59, 63; 1246/2038) of cases; 66% (95% CI 64, 68; 1383/2105) of interventions recommended by pharmacists were completed and 5% were accepted by GPs but not completed at the end of the pharmacists' placement; the remaining recommendations were rejected or considered not relevant by GPs.	acceptable to GPs and led to ameliorative action in the majority of cases. It seems likely that the approach used by the PINCER pharmacists could be employed by other practice pharmacists following appropriate training.	Limitations: Pharmacists did not record detailed reasons for their judgements and these were not peer reviewed

			and recommended interventions to GPs			
Jeffries 2017[13]	Qualitative realist evaluation Interviews: 3 GPs, 2 CCG pharmacists; Focus groups: 2 GPs, 4 community pharmacists, 4 patients, 4 practice managers	CCG in the South of England	Electronic Medicines Optimisation System (EMOS). The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of adverse drug events (ADEs)	Effective use of the EMOS depended upon engagement with the system, the flow of information between different health professionals centrally placed at the CCG and those locally placed at individual general practices, and upon adaptation of work practices to facilitate the use of the system. The use of the system was undermined by perceptions of ownership, lack of access, lack of knowledge and awareness, and time pressures.	The use of an electronic medicines optimisation system may improve medication safety in primary care settings by identifying those patients at risk of an ADE. To fully realise the potential benefit, there needs to be better utilisation across primary care and with a wider range of stakeholders. Engaging with all potential stakeholders and users prior to implementation might allay perceptions that the system is owned centrally and increase knowledge of the potential benefits.	Strengths: Realist methodology enabled detailed examination of how the EMOS was used and its potential effects Limitations: Study involved only one CCG so may not be representative
Jeffries 2018[12]	Qualitative process evaluation 28 staff members from 23 general practices (9 GPs, 12 pharmacists, 7 other GP staff)	43 general practices in Salford, Greater Manchester	Electronic audit and feedback surveillance dashboard to identify patients potentially at risk of hazardous prescribing or	Engagement with the dashboard involved a process of 'sense-making' by pharmacists. The intervention helped to build respect, improve trust and develop relationships between pharmacists and GPs. Collaboration and communication between pharmacists and clinicians was primarily initiated by	Medicine optimisation in primary care may be enhanced by the implementation of a pharmacist-led electronic audit and feedback system. This intervention established a rapid learning health system that enabled data from electronic health records to be used to make changes in practice to improve patient care.	Strengths: Use of Normalization Process Theory as a framework to understand implementation Limitations: Evaluation team also developed the intervention; number of follow-up

			monitoring of medicines	pharmacists and was important for establishing the intervention.		interviews was limited
Lane 2020[22]	Qualitative focus groups and interviews 85 (72 in focus groups and 13 in semi-structured interviews)	Care homes (4 sites in England (2), Scotland and Northern Ireland)	Integration of PIPs into care homes to take responsibility for medicines management	A PIP service was seen as offering benefits for residents, care homes and doctors but stakeholders raised challenges including agreement on areas where PIPs might prescribe, contextual barriers in chronic disease management, PIPs' knowledge of older people's medicine, and implementation barriers in integrated team-working and ensuring role clarity. Introducing a PIP was welcomed in principle but conditional on: a clearly defined PIP role communicated to stakeholders; collaboration between doctors, PIPs and care-home staff; and dialogue about developing the service with residents and relatives.	The overarching theme from this research was that everyone must "understand each other's systems". In particular, PIPs need to understand care homes' systems in advance of implementing a new service	Strengths: Purposively selected sample; use of TDF as a framework to analyse data Limitations: Data relate to proposed service model in advance of implementation
Madden 2022[14]	Qualitative interview study 10 newly appointed pharmacists working in primary care	General practice in England	Structured medication review (SMR) for people at risk of harm or medication-related problems	SMR implementation was largely delegated to individual pharmacists. Established pharmacists appeared more ready for implementation than newly appointed staff. New pharmacists were learning about working in primary care settings and tended to follow procedures	Early implementation of SMRs did not match the intention of providing patients with a holistic review and shared decision-making. The authors identified an important opportunity cost of SMR implementation without prior adequate skills	Strengths: based on detailed, in-depth interviews Limitations: Authors note interviews need to be complemented by data on actual

	networks (PCNs) in Northern England; 10 established pharmacists working in GP practices in other PCNs			with which they were already familiar, particularly when they lacked patient-facing expertise. Implementation was affected by ongoing backlogs and workforce issues in general practices	development, testing, and refining	practice and longer term follow-up
Peek 2020[15]	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	General practice in England	Pharmacist-led Safety Medication dASHboard (SMASH). SMASH involved (1) training of clinical pharmacists to deliver the intervention; (2) a web-based dashboard providing actionable, patient-level feedback; and (3) pharmacists reviewing individual at-risk patients,	The study used an interrupted time series analysis of rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring, comparing observed rates post-intervention to extrapolations from a 24-month pre-intervention trend. At baseline, 95% of practices had rates of potentially hazardous prescribing (composite of 10 indicators) between 0.88% and 6.19%. The prevalence of potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p < 0.001$) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p < 0.001$) at 12 months after introduction of SMASH. The rate of inadequate blood-test monitoring (composite of 2 indicators) reduced by 22.0%	The SMASH intervention was associated with reduced rates of potentially hazardous prescribing and inadequate blood-test monitoring in general practices. This reduction was sustained over 12 months for prescribing but not for monitoring of medication. There was a marked reduction in the variation in rates of hazardous prescribing between practices.	Strengths: Authors noted pragmatic design, evaluation of clinically relevant outcomes and large number of practices taking part Limitations: Not a randomised study so possibility of unrecognised confounding cannot be excluded

			and initiating remedial actions or advising GPs on doing so.	(95% CI 0.2% to 50.7%, *p* = 0.046) at 24 weeks; the change at 12 months (23.5%) was no longer significant (95% CI −4.5% to 61.6%, *p* = 0.127). After 12 months, 95% of practices had rates of potentially hazardous prescribing between 0.74% and 3.02%.		
Rodgers 2022[16]	Multiple interrupted time series 393 general practices covering approximately 3 million patients	General practice in the East Midlands region of England	Pharmacist-led IT intervention to reduce hazardous prescribing (PINCER)	Successive groups of general practices received the PINCER intervention between September 2015 and April 2017. Eleven prescribing safety indicators were used to identify potentially hazardous prescribing and data were collected over a maximum of 16 quarterly time periods. PINCER was implemented in 370 (94.1%) of 393 general practices; data were successfully extracted from 343 (92.7%) of these practices. For the primary composite outcome, the PINCER intervention was associated with a decrease in the rate of hazardous prescribing of 16.7% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6	The PINCER intervention, when rolled out at scale in routine clinical practice, was associated with a reduction in hazardous prescribing by 17% and 15% at 6 and 12 months post-intervention. The greatest reductions in hazardous prescribing were for indicators associated with risk of GI bleeding. These findings support the wider national rollout of PINCER in England.	Strengths: Suggests intervention was implemented successfully in routine practice and was associated with significant reductions in hazardous prescribing Limitations: The authors adjusted for calendar time and practice, but since this was an observational study, the findings may have been influenced by unknown confounding factors or behavioural changes unrelated to

				months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention. The unadjusted rate of hazardous prescribing reduced from 26.4% to 20.1% at 6 months and 19.1% at 12 months. The greatest reduction was for hazardous prescribing indicators related to GI bleeding		the PINCER intervention. Data were also not collected for all practices at 6 and 12 months post-intervention
Syafhan 2021[17]	Individual RCT 356 patients at risk of medication-related problems (MRPs) from 8 GP practices	General practice in England (6 practices) and Northern Ireland (2)	Medicines optimisation with shared decision-making and agreed treatment goals. Intervention repeated at 2 and 4 months, building on progress towards agreed goals	Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p <$ 0.001) in patients who received the full intervention schedule. Medication Appropriateness Index (MAI) scores were reduced (medications more appropriate) for the intervention group, but not for control group patients. Using the intention-to-treat (ITT) approach, the number of telephone consultations in intervention group patients was reduced and different from the control group. No significant differences between groups were found in unplanned hospital admissions, length of hospital stay, number of A&E attendances or outpatient visits. The mean overall healthcare	The pharmacist intervention reduced MRPs, inappropriateness of medications and telephone consultations in general practice in a cost-effective manner	Strengths: Pragmatic randomised design Limitations: Sample smaller than planned; high loss to follow-up; MRP analysis only covered patients who attended 3 appointments

				cost per intervention patient fell from £1041.7 ± 1446.7 to £859.1 ± 1235.2 (p = 0.032). Cost utility analysis showed an incremental cost per patient of − £229.0 (95% CI − 594.6, 128.2) and a mean QALY gained of 0.024 (95% CI − 0.021 to 0.065),. indicative of a health status gain at a reduced cost (2016/2017).		
Thayer 2021[23]	Service evaluation 160 care home residents with intellectual disabilities (ID)	Care homes for people with ID in the Wirral	Pharmacist review of residents' medicines and lifestyle risk factors between November 2019 and May 2020.	The 160 residents were prescribed 1207 medicines, 74% were prescribed ⩾5 medicines and 507 interventions/recommendations were made, averaging 3.3 per resident. The highest proportion (30.4%) were lifestyle risk related, while changing and stopping medicines accounted for 17.9% and 12.8%, respectively. Of the recommendations discussed with GPs/psychiatrists, 86% were accepted.	There was considerable polypharmacy among the residents and a high level of pharmacists' interventions/recommendations about medicines and lifestyle risk, most of which were accepted by GPs/psychiatrists. Wider adoption of collaborative pharmacist review models could have benefits for residential populations with ID and potentially reduce pressure on other health services.	Strengths: Drew on skills of pharmacists from different sectors to address wide range of care needs; recommendations addressed national priorities Limitations: Study limited to one CCG area; limited access to patient records; observational study with no control/comparator arm
Twigg 2015[24]	Service evaluation	Community pharmacies in England	Four or More Medicines (FOMM) support	Of 620 patients recruited, 441 (71.1%) completed the 6-month study period. Pharmacists made 142	By focussing on patients over the age of 65 years with four or more medicines, community pharmacists can improve	Strengths: Large sample of patients and providers; use of

	620 patients (aged over 65 years and prescribed ≥ 4 medications)		service. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the patient's medication using STOPP/START criteria. Data were analysed for the first 6 months of participation in the service.	recommendations to prescribers in 110 patients, largely centred on potentially inappropriate prescribing of NSAIDs, PPIs or duplication of therapy. At follow-up, there was a significant decrease in the total number of falls experienced and a significant increase in medicine adherence and quality of life. Cost per quality-adjusted life year estimates ranged from£11 885 to £32 466 depending on the assumptions made.	medicine adherence and patient quality of life.	validated outcome measures Limitations: No control/comparator group; authors note some patients were probably reviewed independently by their GP during the study period; relatively high attrition rate

Appendix Table 2: TIDieR Lite for UK pharmacist studies

Intervention name and study ID(s)	By whom	What	Where	Intensity	How often
CHIPPS Alharthi 2023[18]; Birt 2021[21]; Lane 2020 [22]; Bond 2020[25]; Holland 2023[29]	Trained pharmacist independent prescribers (PIPs). The training programme comprised 2 days of face-to-face instruction, time in practice to develop relationships with the GP and care home staff, and to address any self-assessed competency gaps supported by a mentor, and a formal final sign-off by a GP independent of the research	PIP, in collaboration with the care home resident's GP, assumes responsibility for managing the medicines of the resident, including: • Reviewing resident's medication and developing and implementing a pharmaceutical care plan • Assuming prescribing responsibilities • Supporting systematic ordering, prescribing and administration processes with each care home, GP practice and supplying pharmacy where needed • Providing training in care home and GP practice • Communicating with GP practice, care home,	Participating care homes	PIPs committed a minimum of 16 hours/month to deliver the service. Each PIP provided care to approximately 20 residents	PIPs visited care homes weekly over 6 months

		supplying community pharmacy and study team			
Care home medication reviews Alves 2019[19]	Primary care pharmacists and GPs in Somerset CCG area and CCG staff	Medicines optimisation visits to care homes. Primary care pharmacists visited homes on behalf of GP practices; GPs could participate in visits or hold discussions with pharmacists prior to the visit; screening of safety interventions was done by CCG pharmacist leads	Care homes with and without nursing in Somerset	The time and level of support allocated for the service was agreed with the respective CCG Local Pharmacist Manager and influenced by a number of factors such as engagement from GP practices; primary care pharmacists' availability; skills and confidence; number of care home patients registered with each GP practice; and geographic area covered by the prescribing support pharmacists	The aim of the programme was to offer at least one visit to as many care homes as possible (appears to be one visit per year but not explicitly stated)
Shine Medication Optimisation Project Baqir 2017[20]	Pharmacists together with care home nurses and other members of the multi-disciplinary team (MDT), including GPs and mental health professionals as needed. Two different models: pharmacists made prescribing decisions (as part of shared decision-making) independently or in conjunction with GPs	A notes based, pharmacist-led review of medicines, where the Northumbria 3Q approach was applied to each medicine, that is, was there an indication, was the indication appropriate and was it safe?. Additionally, medicines missing that could be beneficial (eg, START medicines) were identified. This was followed by a MDT meeting where the information from the pharmacist-led review was discussed and an action plan was formulated. Whenever possible, the final decisions were made with patients and their families. After the review,	Care homes in North East England	Intensity of intervention not reported. Prescribing decisions could be made by pharmacists alone or in conjunction with GPs	Once, as a funded quality improvement (QI) project

		the project database was updated to show medicines taken before review, medicines stopped, started or changed and any other interventions made.			
PINCER Howard 2014[11]; Rodgers 2022[16]	Pharmacists specifically trained to deliver the intervention; GPs, other practice staff and pharmacy technicians involved in implementation	Computer systems of general practices are searched to identify patients at risk of potentially hazardous prescribing using a set of prescribing safety indicators. Pharmacists then provide an educational outreach intervention where they meet with GPs and other practice staff to: • Discuss the search results and highlight the importance of the hazardous prescribing identified using brief educational materials. These feedback sessions were to be held straight after running the searches and then at regular intervals. • Agree on an action plan, retained within the practice, for	General practices	When PINCER was rolled out in the East Midlands, time spent by pharmacists delivering the intervention varied by CCG depending on the resourcing level of the local Medicines Optimisation Team	Data collected quarterly up to 12 months after starting the intervention[16]

		reviewing patients identified as high risk and improving prescribing and medication monitoring systems using root cause analysis Pharmacists (sometimes supported by pharmacy technicians) then work with, and support, general practice staff to implement the agreed action plan, sometimes making the necessary changes themselves			
Eclipse Live (electronic medicines optimisation system (EMOS)) Jeffries 2017[13]	Developed by a private company (Eclipse Solutions) and made available to stakeholders (including doctors, pharmacists, practice managers and patients) by a CCG in the South of England	Web-based user interface which securely extracts patient data from general practice patient records. Accessed separately from the GPs' clinical systems, it allows different stakeholders access to real time anonymized patient data including medical histories of diagnoses, prescribed medications and test results. The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of ADEs, or not appropriately monitored.	General practices covered by the participating CCG	Not reported (qualitative study)	Not reported (qualitative study)

		Patients can access the system through a "Patient Passport"			
Safety Medication dASHboard (SMASH) Jeffries 2018[12]; Peek 2020[15]; Jeffries 2020[26]	Clinical pharmacists working in general practices and other general practice staff	Pharmacists were trained to deliver the intervention and apply root cause analysis techniques to identify, explore, resolve, and prevent medication errors in partnership with general practice staff. Pharmacists and practice staff were given access to a web-based, interactive dashboard that provided feedback on 12 indicators of potentially hazardous prescribing. The dashboard also provided practice-level summary data as well as educational material.	General practices covered by the participating CCG	Practices interacted with the dashboard a median of 12.0 (interquartile range, 5.0–15.2) times per month during the first quarter of use. Over time, dashboard use transitioned towards regular but less frequent (median of 5.5 [3.5–8.5] times per month) checks to identify and resolve new cases. The frequency of dashboard use was higher in practices with a larger number of at-risk patients.	Dashboard was updated daily. Frequency of use varied by practice and over time (see previous column)
Structured Medication Review (SMR) Madden 2022[14]; Stewart 2021[27]	Clinical pharmacists within general practice primary care networks (PCNs)	Invited, personalised, holistic review of all medicines and their benefits to health for people at risk of harm or medicine-related problems	General practices	Reviews are recommended to be scheduled for at least 30 minutes to allow time for shared decision-making	Once
Medicines optimisation intervention	GP practice-based pharmacists operating as part of the wider primary care team	Each pharmacist received 2 days of intensive specialist training	Eight general practices in four regions of the UK	Initial meeting with further appointments available at 2 and 4 months building on patient progress towards agreed goals	Once per patient (up to three appointments)

Syafhan 2021[17]		on medicines optimisation (including training on motivational interviewing). The intervention included: review of patient records prior to meeting; medication history; individual medicines optimisation plan that could include recommending/making changes to medication regimens (in collaboration with GPs), personalised education and counselling on medication management, the correct use of medication administration devices and lifestyle factors; and an agreed list of treatment goals. Pharmacists could also refer patients to another health professional within the practice. Having completed the intervention, the pharmacist produced a short report for the patient's GP outlining actions taken and any further recommendations requiring GP input			

Collaborative pharmacist review Thayer 2021[23]	Community and specialist mental health pharmacists	Medicine review using a structured framework based on recommendations of the 2018 Learning Disability Mortality Review (LeDeR) report. Pharmacists visited care homes to conduct the reviews using individual residents' care home records. The specialist mental health pharmacist also had access to the care record held by the Specialist Mental Health Trust, if the resident was under the Trust's care, and remote access to the local data sharing platform. Assessments included medicines adherence and burden (particularly the anticholinergic burden), respiratory care, vaccination status, constipation risk, sepsis prevention, dysphagia risk and lifestyle risk issues, especially smoking. Finally, pharmacists were asked to detail actions taken/advice provided, any recommendations made and make referrals, as necessary. Following the review, GP surgeries and psychiatrists were contacted by the pharmacists to arrange a review of their	Care homes for people with intellectual disabilities	507 interventions/recommendations for 160 residents reviewed (3.3 per resident)	Once

		recommendations. As the pharmacists were not prescribers, decisions on accepting recommendations were made by the resident's GP/psychiatrist (after reviewing the resident's full clinical record) in consultation with the pharmacists			
Four or More Medicines (FOMM) support service Twigg 2015[24]	Community pharmacists and pharmacy team members	Pharmacists were trained via distance learning and face to face, which included how to use the various different tools and assessments. Training was then cascaded to other pharmacy members. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the patient's medication using STOPP/START criteria.	Participating community pharmacies	Pharmacist time estimated at 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review	After the first consultation, patients met with the pharmacist on a regular basis depending on when they collected their repeat medication or they felt a need.

MMAT quality assessment results

Reference	Screening questions	Type of study	MMAT questions and answers
Alharthi 2023[18]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (identifying perceived barriers and facilitators)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Can't tell (secondary analysis of existing data)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Alves 2019[19]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Can't tell (partial data presented)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (fidelity not monitored)*
Baqir 2017[20]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*

Birt 2021[21]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Mixed methods	**5.1. Is there an adequate rationale for using a mixed methods design to address the research question?** *Yes (qualitative and quantitative data relevant to process evaluation)* **5.2. Are the different components of the study effectively integrated to answer the research question**? *Yes (integrated in results and discussion)* **5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?** *Yes (see discussion)* **5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?** *Yes (page 11 column 2)* **5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?** *Yes*
Howard 2014[11]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative descriptive	**4.1. Is the sampling strategy relevant to address the research question?** *Yes* **4.2. Is the sample representative of the target population?** *Yes (all interventions recorded)* **4.3. Are the measurements appropriate?** *Yes* **4.4. Is the risk of nonresponse bias low?** *Yes (data from intervention arm only)* **4.5. Is the statistical analysis appropriate to answer the research question?** *Yes*
Jeffries 2017[13]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews and focus groups)* **1.3. Are the findings adequately derived from the data?** *Yes (context-mechanism-outcome groups identified)* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of realist analysis)*
Jeffries 2018[12]	**S1. Are there clear research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)*

	S2. Do the collected data allow to address the research questions? *Yes*		**1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Normalisation Process Theory)*
Lane 2020[22]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (gather opinions about proposed service)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (focus groups and interviews with different staff groups at different sites)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Madden 2022[14]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (pharmacists' experience of SMR implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews with newly employed and established pharmacists)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by thematic analysis)*
Peek 2020[15]	**S1. Are there clear research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)*

	S2. Do the collected data allow to address the research questions? *Yes*		**3.3. Are there complete outcome data?** *Yes* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Rodgers 2022[16]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)* **3.3. Are there complete outcome data?** *No (6- and 12-month data not collected from all practices)* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Syafhan 2021[17]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative randomised controlled trial	**2.1. Is randomisation appropriately performed?** *Can't tell (method of randomisation not reported)* **2.2. Are the groups comparable at baseline?** *Yes* **2.3. Are there complete outcome data?** *No (30% lost to follow-up or withdrew)* **2.4. Are outcome assessors blinded to the intervention provided?** *Can't tell (outcome data from GP electronic records)* **2.5 Did the participants adhere to the assigned intervention?** *No (30% lost to follow-up or withdrew)*
Thayer 2021[23]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents with intellectual disabilities)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (details recorded for each review and associated outcomes)* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)*

			3.5. During the study period, is the intervention administered (or exposure occurred) as intended? *Yes (one-off review mainly based on records)*
Twigg 2015[24]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Can't tell (no indication of attempts to recruit a representative sample)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (data is recorded for intervention components and associated outcomes)* **3.3. Are there complete outcome data?** *Can't tell (limited response for resource use outcomes)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (approx. 30% withdrawal rate)*

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction (pp4-5)
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Methods (p6)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods (p6)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods (p7)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary file
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p7)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods (pp7-8)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods (pp7-8)
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods (pp7-8)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p8)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	See methods (p8)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	See methods (p8)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A (summary tables only)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods (p8)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Results (p8)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P10 and Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary table
Study characteristics	17	Cite each included study and present its characteristics.	Tables 1-4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary table
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1-4 where available and appropriate
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results (p22)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results (p22)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion (especially p27)
	23b	Discuss any limitations of the evidence included in the review.	Discussion (especially p26)
	23c	Discuss any limitations of the review processes used.	Discussion (pp27-28)
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion (pp28-29)
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Title page

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Title page
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P9
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data sharing statement (p30)

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

BMJ Open

Pharmacist-led primary care interventions to promote medicines optimisation and reduce overprescribing: a systematic review of UK studies and initiatives

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Secondary Subject Heading:	Pharmacology and therapeutics
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Pharmacist-led primary care interventions to promote medicines optimisation and reduce overprescribing: a systematic review of UK studies and initiatives

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Abstract

Objectives: To systematically review and synthesise evidence on the effectiveness and implementation barriers/facilitators of pharmacist-led interventions to promote medicines optimisation and reduce overprescribing in UK primary care.

Design: Systematic review

Setting: UK primary care

Methods: We searched MEDLINE, Embase, CINAHL PsycINFO and The Cochrane Library for UK-based studies published between January 2013 and February 2023. Targeted searches for grey literature were conducted in May 2023. Quantitative and qualitative studies (including conference abstracts and grey literature) that addressed a relevant intervention and reported a primary outcome related to changes in prescribing were eligible for inclusion. Quality of included studies was assessed using the Multiple Methods Appraisal Tool (MMAT). We performed a narrative synthesis, grouping studies by publication status, setting and type of data reported (effectiveness or implementation).

Results: We included 14 peer reviewed journal articles and 11 conference abstracts, together with four case study reports. The journal articles reported 10 different interventions, five delivered in general practice, four in care homes and one in community pharmacy. The quality of evidence was higher in general practice than in care home settings. It was consistently reported that the intervention improved outcomes related to prescribing, although the limited number of studies and wide range of outcomes reported made it difficult to estimate the size of any effect.

Implementation was strongly influenced by relationships between pharmacists and other health and care professionals, especially GPs. Implementation in care homes appeared to be more complex than in general practice because of differences in systems and 'culture' between health and social care.

Conclusions: Pharmacist-led interventions have been reported to reduce overprescribing in primary care settings in the UK but a shortage of high-quality evidence means that more rigorous studies using high-quality designs are needed. More research is also needed in community pharmacy settings; to assess intervention effects on patient outcomes other than prescribing; and to investigate how reducing overprescribing can impact on health inequalities.

Registration: PROSPERO [CRD42023396366].

Strengths and limitations of this study

- We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness.

- Many of the studies lacked a control group and the research took place in a highly complex and evolving system, meaning that results could have been influenced by confounding factors such as other interventions in the health and social care system.
- Some review processes were performed by a single reviewer and meta-analysis was not feasible.

Introduction

This evidence review was performed to support implementation of the National Overprescribing Review for England (NOR; see below)) by examining research on pharmacist-led overprescribing interventions in UK primary care settings. Pharmacists are trained to provide advice and support to patients and other health professionals, pharmacist independent prescribers (PIPs) have existed since 2006 and patients are increasingly asked to consider the community pharmacy as a first source of support for minor health conditions. Alongside community pharmacies, many general practices have pharmacists as members of the practice team. Pharmacists, working with GPs and other healthcare professionals, are thus well placed to support interventions directed towards medicines optimisation and the reduction of overprescribing. Such interventions include carrying out structured medication reviews directly with patients and carers and/or reviewing data from patient records. The aims and objectives of the review are outlined below, following a brief clarification of terminology.

Overprescribing has been defined as 'the use of a medicine where there is a better non-medicine alternative, or the use is inappropriate for that patients' circumstances and wishes'[1]. Overprescribing is often related to the concept of problematic polypharmacy, where harmful effects result from the prescription of multiple medications. However, there is no agreed definition of polypharmacy and patients with complex health conditions may require multiple medications.

Medicines optimisation is an umbrella term for interventions designed to ensure that medicines are used safely and effectively, producing the best possible outcomes for patients. In this context, deprescribing refers to the process of stopping medications that are no longer appropriate to a patient's needs. Deprescribing is a response to overprescribing and problematic polypharmacy and involves collaboration between health professionals and patients and/or carers to ensure shared decision-making. Shared decision-making with patients and/or carers is fundamental to successful medicines optimisation[2] but the need for time and resources to ensure that this takes place can create barriers to service delivery. Another related term, medicines reconciliation, is a more technical process to ensure consistency between prescription records and the medications the patient is actually receiving and taking. The terminology around overprescribing and other forms of medicines misuse was recently reviewed by Singier et al[3]. Medication review involves examining a patient's prescriptions as a whole and is separate from measures to reduce inappropriate prescribing of specific medications or types of medication such as antibiotics or proton pump inhibitors.

Overprescribing can cause direct harm to patients in a variety of ways. It has been estimated that about 6.5% of hospital admissions are caused by harmful effects of medication, rising to 20% for people aged over 65[1]. In addition to physiological harms, long-term use of some medications can lead to dependency and problems when attempting to withdraw the medication.

Issues relating to prescribed medication can arise from a whole range of causes, including patients requiring treatment for multiple conditions, lack of co-ordination between different health professionals or organisations and failures of communication between health professionals and patients (for example failing to gather information because of time constraints on appointments). Availability of new medications and increasing numbers of people living with long-term conditions such as arthritis and diabetes have resulted in patients being prescribed more medications and continuing to take them for long periods of time, often for life. The average number of prescription

items per head of population doubled between 1996 and 2016, and over 75% of prescriptions are repeat prescriptions[1].

Pharmacists are thus well placed to support processes of medicines optimisation, which involve them working closely with medical professionals (particularly GPs), commissioners of health care and patients. The report of the National Overprescribing Review for England, published in 2021, provides numerous examples and case studies[1].

The National Overprescribing Review (NOR) for England was set up in 2018 to evaluate the extent of overprescribing in the NHS and recommend measures to reduce it, particularly in primary care. A review of existing research (overview of systematic reviews) was commissioned to support the national review[4]. The NOR identified a need for a more consistent and effective approach to medication review, which requires both the identification of effective interventions and an understanding of the factors that need to be addressed in terms of organisational and cultural barriers to implementation. The national review's recommendations included changes to systems (patient records, transfers of care and clinical guidance) and culture (reduced dependence on medication and support for shared decision-making), as well as the appointment of a National Clinical Director for Prescribing[1].

This evidence review was commissioned to support implementation of the NOR recommendations by examining research on pharmacist-led overprescribing interventions in UK primary care settings. Our focus on pharmacist-led interventions complements recent research on deprescribing in the UK context. The TAILOR evidence synthesis sought to identify how best to support deprescribing in older people living with multimorbidity and polypharmacy. The authors concluded that effective deprescribing requires 'attention to providing an enabling infrastructure, access to data, tailored explanations and trust'[5]. More recently, Radcliffe et al. conducted a realist review and synthesis examining multidisciplinary medication review and deprescribing interventions for older people in primary care[6]. This study identified a number of key mechanisms that could contribute to the design of effective interventions, including integration of pharmacists into the multidisciplinary team delivering the intervention. Pharmacist-led interventions could fall within the scope of both of these studies, but characterisation of the evidence base is required to support the application of insights derived from these more general, theory-based reviews.

We aimed to assess the effects of relevant interventions on outcomes related to prescribing, identify key characteristics of the interventions and examine barriers and facilitators to implementation in routine practice. A further aim was to assess the quality of the evidence base and identify priorities for further research.

Methods

Review aims and objectives

We aimed to perform a systematic review of published literature and published or informally published evaluations reporting UK-based, pharmacist-led interventions for overprescribing, including the following components:

i. A review and synthesis of outcomes of effective interventions

ii. A review of the characteristics of effective interventions using the TIDieR framework

iii. Evaluation of the UK evidence base in terms of quality and risk of bias

iv. Identification of case study examples of effectively implemented interventions in the UK

Inclusion and exclusion criteria

Inclusion criteria for the review were as follows

- Population/setting: UK primary care
- Intervention: Pharmacist-led interventions aimed at review and optimisation of prescribed medications
- Comparator: Not required
- Outcomes: Studies had to report a primary outcome related to changes in prescribing. Secondary outcomes were other patient and health service outcomes, including but not limited to changes to type of medicines prescribed, quality of life, hospital admissions and deaths.
- Study design: Quantitative and qualitative studies were eligible for inclusion, with no exclusions based on study design or quality. Reports of local initiatives published as grey literature reports or conference abstracts were included to give a fuller picture of activity across the NHS.
- Other: Studies published in English between January 2013 and February 2023

We excluded interventions aimed at reducing overprescribing of specific medications or types of medication, e.g. antibiotics or proton pump inhibitors. Studies of children and young people were also excluded.

Search methods

The literature search harnessed economies of scale by identifying primary studies for inclusion in this review and reviews for inclusion in a scoping review for internal use to inform the wider project. Searches were conducted by an information specialist (MC) in order to identify published and unpublished evidence on primary care interventions to reduce overprescribing.

Phase 1: peer reviewed literature

A first phase of database searches was run in February 2023 to retrieve relevant peer-reviewed literature. Searches were designed around the following concepts:

PROBLEM	INTERVENTION	SETTING
Overprescribing; Inappropriate prescribing; polypharmacy	Deprescribing; Structured medication review; medication reconciliation; medicines optimisation; shared decision making; personalised care	Primary Care (including international terms for primary care where relevant)

While we are aware of the Morel filter (2022) for identifying studies of deprescribing[7], our focus was specifically on a primary care setting. Search strategies are provided in supplementary file 1.

Searches covered the databases MEDLINE, Embase, CINAHL, PsycINFO and The Cochrane Library and were limited to studies published since 2013 and in OECD countries with healthcare systems similar to the UK.

Phase 2: grey literature

A further phase of targeted searches was conducted in May 2023 to identify unpublished or "grey" literature. This involved searching for the case studies identified by the National Overprescribing Review (to identify any which had produced a report or evaluation), and then searching the Overton.io platform for pharmacist-led deprescribing/overprescribing and medicines optimisation.

Searches were complemented by input from stakeholders (internal and external topic advisers) to minimise the risk of missing any other relevant evidence.

Study selection

Records retrieved by the literature search were stored in a shared EndNote library and de-duplicated. Screening for inclusion at the title level was performed by single reviewers after piloting of a test set. Reviewers could refer records to another team member in the event of uncertainty and a 20% sample of records was screened by a second reviewer to validate title level inclusion decisions.

Screening for inclusion at the abstract and full text level was performed by pairs of reviewers acting independently. Disagreements were resolved by discussion among the reviewers involved (AC, DC and LP). A good level of agreement was achieved, values of kappa between pairs of reviewers ranging from 0.67 to 0.96. Reasons for exclusion at the full text stage were recorded.

Data extraction

Data extraction tables and summary tables were developed in Microsoft Word. Extraction was performed by a single reviewer, with a 10% sample being checked for consistency and accuracy. In addition to standard data extraction fields (study design/sample size, setting, intervention, key findings and strengths/limitations) , we used the TIDieR Lite framework to collect information on the features of interventions reported as 'successful' to determine whether service commissioners and providers should consider specific factors when commissioning/delivering services. TIDieR Lite is a simplified version of the TIDieR (Template for Intervention Description and Replication) checklist [8].

Quality assessment

Methodological quality of peer reviewed journal articles was assessed using the Mixed Methods Appraisal Tool (MMAT) version 2018[9]. The tool includes screening questions and methodological quality questions for different study designs (qualitative, randomised trials, non-randomised quantitative studies, descriptive studies and mixed methods). Quality assessment results were combined with identified strengths and limitations (including those reported by study authors) to characterise the contribution of individual studies and groups of studies to the overall evidence base.

Data synthesis

We performed a narrative synthesis of the included studies using text and tables to describe study and intervention characteristics in line with methodological and reporting guidelines[10, 11]. We initially grouped studies by publication status, considering peer-reviewed journal articles (regardless of study design and quality) separately from conference abstracts and case studies. Within these three categories, we grouped studies by setting (general practice, care homes or community settings). We also distinguished between studies reporting effectiveness of interventions and those reporting implementation of interventions (e.g. qualitative studies and process evaluations). In view of study heterogeneity and reporting limitations, effectively implemented interventions were defined as those where the study authors' conclusions indicated that the service was regarded as a success and was planned to continue or be expanded.

Studies reported a wide variety of outcomes using diverse effect measures. For this reason we did not attempt to calculate a standardised metric to compare effect sizes across outcomes. The synthesis used a 'vote-counting' method (number and proportion of studies reporting positive, negative or neutral outcomes), prioritising prescribing-related outcomes over patient and other outcomes. Reported effect measures and associated 95% CIs were recorded in the text and tables. Tables of study characteristics and findings were presented alphabetically by author for consistency. While reporting results from all study designs we prioritised stronger study designs (experimental and quasi-experimental) over those of uncontrolled observational studies. In terms of exploring heterogeneity, the structure of the synthesis allowed consideration of potential modifiers including study design, study quality and setting. Intervention components and aspects of implementation were examined using modifications of existing frameworks, the component analysis was pre-specified in the review protocol.

We did not use the GRADE approach to assess certainty of evidence because of its emphasis on randomised trials and downgrading of other study designs. Instead we distinguished between controlled and uncontrolled studies, identified areas of consistency and inconsistency and highlighted areas of particularly limited evidence (e.g. settings or outcomes represented by single studies). A similar approach has been used by team members in previous reviews[12].

Public involvement

The review was supported by a public panel who provided feedback on public perceptions that informed the review and are reflected in the Discussion.

Variations from protocol

We used Tidier Lite instead of the full TIDieR framework. This was because the full framework is designed to allow the replication of interventions and therefore goes beyond the degree of detail required for evidence synthesis. The scoping review of reviews referred to in the protocol was not completed (see @Search methods' above).

Results

Results of literature search

The PRISMA flow diagram (Figure 1) summarises the study selection process. After screening 1774 records at the title and abstract stage and 215 full-text articles, we included 14 published articles, 11 conference abstracts and four case study reports. The majority of exclusions were of studies conducted outside the UK, with a smaller number excluded because the intervention was not pharmacist–led or the article did not report empirical data. Characteristics of the included studies are reported in the following sections.

Please insert Figure 1: PRISMA flow diagram near here

Research studies

Study characteristics

Study characteristics are summarised in Table 1, with full data extraction tables in supplementary file 2 . The 14 publications reported on ten interventions, of which five were delivered in general practice (seven publications[13-19]), three in care homes for older people (five publications[20-24]), one in care homes for people with intellectual disabilities (ID) [25] and one in community pharmacies[26].

All the interventions involved medication review in some form. Distinctive features of interventions included use of IT to identify patients for review[13-15, 17, 18]; a key role for pharmacist independent prescribers in medication management in care homes[23, 24]; and employment of pharmacists by groups of general practices (primary care networks, PCNs) to provide a holistic patient-centred service specified by NHS England[16]. Intervention characteristics are considered in more detail below.

Study designs used included one individual RCT[19] and two cluster RCTs (CHIPPS[20, 23] and PINCER[13]), although the primary publications of the latter two trials fell outside the time period covered by this review. Two studies used an interrupted time series (ITS) design[17, 18] and five used qualitative approaches[14-16, 20, 24]. One study was a mixed methods process evaluation[23]. The remaining studies were described as service evaluations or quality improvement reports with an uncontrolled before vs. after design [21, 22, 25, 26].

Included studies reported a wide range of outcomes (Table 1). For further analysis, see below under ‘effects of interventions’ and ‘Implementation/system issues, respectively. None of the studies reported details of participants other than age and sex, making it difficult to assess equity, diversity and inclusion across the evidence base.

Table 1: Summary of research study characteristics

Reference	Population	Intervention	Study design	Outcome measures
Quantitative controlled studies				
Howard 2014[13]	Pharmacists delivering intervention	IT-enabled pharmacist-led review to reduce medication errors	Cluster RCT (PINCER trial)	Time taken to complete reviews; recommended interventions and whether these were implemented
Peek 2020[17]	General practice patients with one or more risk factors for hazardous prescribing or inadequate blood test monitoring	Pharmacist-led Safety Medication dASHboard (SMASH) intervention	Interrupted time series analysis	Rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring
Rodgers 2022[18]	General practices in the East Midlands	Pharmacist-led IT intervention (PINCER)	Multiple interrupted time series	Incidence of potentially hazardous prescribing
Syafhan 2021[19]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness plus clinical outcomes and costs
Quantitative uncontrolled studies				
Alves 2019[21]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (5 year uncontrolled study)	Interventions by pharmacist (including deprescribing and changes to prescriptions)
Baqir 2017[22]	Care home residents	Medication review by pharmacist with or without GP	Retrospective analysis of data from QI programme	Number and type of medications stopped
Thayer 2021[25]	Care home residents with intellectual disabilities	Collaborative service initiative involving community pharmacists and a specialist mental health pharmacist providing review of medicines and lifestyle risk factors	Service evaluation	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists

Twigg 2015[26]	Patients over 65 prescribed four or more medications	Community pharmacist consultation including medication review using STOPP/START rules	Service evaluation	Number of recommendations; falls, medication adherence, quality of life and costs at 6 months
Qualitative/mixed methods				
Alharthi 2023[20]	Care home residents	Deprescribing by pharmacist independent prescriber	Qualitative interviews with participants in a cluster RCT (CHIPPS study)	Barriers and facilitators to deprescribing
Birt 2021;[23]	Care home residents	Pharmacist independent prescribers responsible for medicines management (CHIPPS)	Mixed methods process evaluation	PR activities, perceived benefits and barriers to implementation
Jeffries 2018[14]	Pharmacists delivering intervention, GPs and CCG staff	Pharmacist-led intervention involving the use of an electronic audit and feedback surveillance dashboard to identify patients potentially at risk of hazardous prescribing or monitoring of medicines in general practice	Qualitative interviews	Themes related to implementation of the intervention and role of practice pharmacists and others
Jeffries 2017[15]	Stakeholders in general practice and CCG	Electronic medicines optimisation system	Qualitative realist evaluation	Suggestions to support implementation of the system
Lane 2020[24]	Doctors, pharmacists, care-home managers and staff, residents and relatives	Pharmacist independent prescriber service	Qualitative focus groups and interviews	Perceived benefits of the service and barriers and facilitators to implementation
Madden 2022[16]	Pharmacists working in general practice within PCNs	Structured medication review (SMR) service within Primary Care Networks	Qualitative interview study	Themes related to early implementation of SMR service

Table 2: Summary of studies reporting effects of interventions

Reference	Intervention	Setting	Study design and sample size	Outcome measure and effect size
Alves 2019[21]	Medication review	Care homes	Service evaluation 10,405 patient reviews over 5 years	Interventions by pharmacis
Baqir 2017[22]	Medication review	Care homes	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Number and type of medicines stopped 19.5% reduction in number of medicines being prescribed relative to baseline
Peek 2020[17]	Safety medication dashboard	General practice	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	Potentially hazardous prescribing (composite of 10 indicators) Potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p < 0.001$) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p < 0.001$) at 12 months
Rodgers 2022[18]	Pharmacist-led IT-assisted intervention (PINCER)	General practice	Multiple interrupted time series 393 general practices covering approximately 3 million patients	Indicators of potentially hazardous prescribing The PINCER intervention was associated with a decrease in the rate of hazardous prescribing of 16.1% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6 months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention
Syafhan 2021[19]	Pharmacist-led medicines optimisation	General practice	Individual RCT 356 patients at risk of medication-related	Medication-related problems (MRP); Medicines Appropriateness Index (MAI) Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p < 0.00$ in patients who received the full

			problems (MRPs) from 8 GP practices	intervention schedule. MAI scores were reduced (medications more appropriate) for the intervention group, but not for control group.
Thayer 2021[25]	Review of medicines and lifestyle risk factors	Care homes for adults with intellectual disabilities (ID)	Service evaluation 160 care home residents with ID	Pharmacist interventions/recommendations and acceptance by GPs and psychiatrists
Twigg 2015[26]	Community pharmacist consultation including medication review	Community pharmacies	Service evaluation 620 patients (aged over 65 years and prescribed ≥ 4 medications	Number of recommendations, falls, medication adherence, quality of life and costs at 6 months

Intervention characteristics

Table 2 in supplementary file 2 summarises characteristics of the included interventions using the TIDieR Lite checklist. The table includes limited data extracted from studies cited by included studies but not themselves included in the review [27-29].

The pharmacists involved in delivering the interventions were variously described as pharmacist independent prescribers[23]; trained pharmacists and pharmacy technicians[13, 18]; primary care pharmacists[21]; clinical pharmacists working in general practice[15-17]; GP practice-based pharmacists working as part of a wider primary care team[19]; community and specialist mental health pharmacists[25]; and community pharmacists and pharmacy team members[26]. One study simply referred to 'pharmacists'[15].

Four interventions were explicitly stated to require training of pharmacists to deliver them[13, 19, 23, 26]; the extent of training was described for three of these[19, 23, 26]. Training pharmacists to deliver the PINCER intervention was described in a separate paper[13]. Interventions were delivered with other primary care team members depending on the setting of the study and in some cases with staff employed by clinical commissioning groups (CCGs). In particular, only the CHIPPS study involved pharmacists with the power to prescribe medication independently; in other studies recommendations were passed to the patient's GP or another medically qualified professional for implementation. Shared decision-making with patients and/or families was specifically reported for three interventions[16, 19, 22].

Reporting of interventions varied between studies. Most studies reported the process of medication review including patient selection for review and the review itself in more detail than resulting follow-up actions. Two qualitative studies reported limited details of the review process[14, 16], although a service specification was available for the NHS England structured medication review (SMR) investigated by Madden et al.[16]. For studies where the intervention was primarily directed at improving medication review processes using general practice data[13-15], it was unclear whether there was a standard process to discuss findings with the patient and make changes to their prescriptions. All studies reporting on effectiveness of medication reviews stated that the person undertaking the review had access to relevant patient records[17-19, 21, 22, 25, 26].

Intensity of interventions was also variably reported. In the CHIPPS study, PIPs committed a minimum of 16 hours/month to deliver care to approximately 20 care home residents[27]. Madden et al. reported that SMR appointments were recommended to allow at least 30 minutes for review and shared decision-making[16]. The medicines optimisation intervention evaluated by Syafhan et al. involved up to three meetings between patient and pharmacist[19], while the FOMM study in community pharmacies estimated times of 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review[26]. Other studies reported that time and level of support allocated to interventions varied between and within CCG areas depending on local resources and priorities[18, 21]. Another measure of intervention intensity was the number of recommended actions, averaging 3.3/resident in care home residents with intellectual disabilities[25].

Most included studies reported on a single round of medication reviews with variable periods of follow-up. As noted above, some interventions required multiple interactions between pharmacists and patients.

Effects of interventions

Seven studies reported on effects of pharmacist-led interventions in some form (Table 2): three in general practice[17-19], three in care homes[21, 22, 25] (including one in a care home for people with ID[25]) and one in community pharmacies[26].

The strongest evidence for the effectiveness of interventionscame from the studies in general practice. The interrupted time series (ITS) studies of Peek et al.[17] and Rodgers et al.[18], which used indicators of inappropriate prescribing to identify patients for intervention, reported significant decreases in inappropriate prescribing at 6 and 12 months after intervention (Table 2). Estimated reductions were larger in Peek et al. (27.9% and 40.7%) compared with Rodgers et al. (16.7% and 15.3%)[17, 18]. The 95% confidence intervals of the two studies at 12 months did not overlap, suggesting some uncertainty about the magnitude of the effect. The randomised trial by Syafhan et al.[19] preferentially recruited patients based on prescription of six or more medications and a history of recent unplanned hospital admission. The intervention was associated with a reduction in medication-related problems in those who completed the full programme (up to three appointments) and an improvement in MAI scores.

Of the three studies set in care homes, only Baqir et al. reported a direct effect on prescribing associated with medication review, a 19.5% reduction in number of prescribed medicines[22]. Alves et al.[30] reported on pharmacist interventions and potential financial savings over 5 years. In the one year reported in detail, 24.5% of interventions involved deprescribing. Potential drug cost savings were estimated at £812,441 annually, of which £431, 493 (55%) was attributed to deprescribing. The study of Thayer et al.[25] differed from the others in involving care home residents with intellectual disabilities. There was a high level of polypharmacy at baseline and pharmacists made an average of 3.3 interventions/recommendations per resident, of which 12.8% involved deprescribing. A large majority of pharmacist recommendations were accepted by GPs/psychiatrists caring for the residents.

The one study in a community pharmacy setting recruited patients aged 65 or older who were prescribed four or more medications[26]. Of 620 patients recruited, 441 (71.1%) completed the 6-month study. Pharmacists made 142 recommendations related to 110 patients, largely dealing with potentially inappropriate prescribing of NSAIDs and PPIs or duplication of therapy. The study also reported a significant decrease in falls and improvements in medication adherence and quality of life at follow-up.

The review included two publications from the CHIPPS Care Homes Independent Pharmacist Prescriber Study) trial[20, 23] but the paper reporting effectiveness and safety results from this cluster RCT[31] was published too late for formal consideration for inclusion in our review. The primary outcome was rate of falls, with Drug Burden Index (DBI) being one of the secondary outcomes. Fall rate at 6 months did not differ significantly between intervention and control groups

but DBI was lower in the intervention group (mean 0.66 vs. 0.73; adjusted rate ratio 0.83, 95% CI 0.74 to 0.92).

Implementation/system issues

Seven studies provided quantitative and/or qualitative evidence on factors affecting implementation of pharmacist-led interventions, of which four were performed in general practice[13-16] and three in care homes[20, 23, 24].

The general practice studies focused on different parts of the implementation pathway. Two dealt with implementation of IT systems to support detection of potentially hazardous prescribing[14, 15]; one was a process evaluation of the PINCER trial[13]; and one focused on implementation of structured medication reviews as recommended by NHS England in routine practice[16]. The studies of IT-supported interventions were broadly positive about the potential for implementation and sustainability, but the study of NHS England's SMR programme concluded that its early implementation failed to deliver the planned holistic and patient-centred approach.

Other evidence

Conference abstracts

We included 11 conference abstracts (Table 4), of which two were earlier reports of studies subsequently published as full papers[30, 32]. All of the included abstracts focused on intervention effects on prescribing and related outcomes.

Five abstracts reported research in general practice, of which three involved patients with polypharmacy identified from the overall practice population[33-35]. As a group, these three abstracts provided weak evidence of associations between pharmacist-led medication reviews and changes in medication and cost savings together with high levels of patient satisfaction (Table 3),

Two abstracts reported on selected general practice populations. The only comparative study in this group reported that patients living with frailty who were reviewed by a pharmacist as part of a multi-disciplinary team review had a reduction in total medications compared with a control cohort[36]. When patients recently discharged from hospital were reviewed by a pharmacist working in their general practice, 16 out of 35 had changes made to their medication, with 74% of changes involving deprescribing[37].

Turning to studies performed in care homes, two abstracts by Doherty et al. (2020)[38, 39] evaluated an intervention entitled Medicines Optimisation in Older People (MOOP) which involved case management by pharmacists. The authors reported that inappropriate prescribing (based on the MAI) was highly prevalent at baseline *84%) but declined significantly following the intervention. Swift et al. reported that a team comprising pharmacists and pharmacy technicians who both performed medication reviews and supported care home staff significantly reduced inappropriate polypharmacy (measured by prescribing quality indicators) between 2024 and 2017[40]. For care home residents receiving palliative care, structured medication reviews involving shared decision-

making were associated with high rates of changes to medication (1787 suggested changes from 574 reviews, 76% of which were implemented) and associated cost savings[41].

Grey literature case studies

We included reports of four case studies reporting on local initiatives in three areas of England (see Table 4).Details of all case studies may be found in Annex C of the National Overprescribing Review report[1]. Case studies were submitted by NHS organisations (mainly CCGs) and included varying amounts of data on intervention characteristics, support for implementation and outcome measures. Three interventions were delivered in general practice and one in care homes. The initiative developed by Swale CCG was distinctive in using pharmacy technicians to review less complex cases, although the initiative was targeted at patients considered high-risk for ADRs. Although not classified as research, such case studies can provide useful data on implementation of interventions and outcomes achieved in routine practice

Table 3: Summary of studies published as conference abstracts

Reference	Population	Intervention	Study design	Outcome measures and key findings
Alves 2016[30]	Care home residents	Medication review by primary care pharmacists linked to GP practices	Service evaluation (retrospective analysis and interviews)	Interventions by pharmacist; barriers and facilitators A total of 2916 interventions were made in 1047 patients, of which deprescribing represented 22%
Bryant 2019[33]	Primary care patients taking ten or more medications	Polypharmacy clinics in GP surgeries	Service evaluation (retrospective data analysis)	Reductions in prescribing; cost savings; hospital admissions avoided April 2017 to March 2018, 370 patients reviewed and £50,766.63 saved. Figures for April to December 2018 were 209 and £1[illegible]2, respectively
Chauhan 2022[37]	Patients recently discharged from hospital	Post-discharge medication review by clinical pharmacist linked to GP practice	Formative service evaluation (uncontrolled)	Medication changes following review 16/35 patients had medications changed; 74% (25/34) of changes were medications stopped
Din 2020[34]	Patients referred by GPs	Polypharmacy review clinics led by pharmacist independent prescriber with shared decision-making	Service evaluation (uncontrolled)	Changes to medication, feedback from patients and MDT Pharmacist medication reviews were effective, with positive feedback received from patients and members of the MDT. Deprescribing and inhaler counselling were the most common interventions.
Din 2022[36]	Primary care patients living with frailty	Frailty review involving pharmacist as part of MDT	Comparative cohort	Changes in medication (including cholinergic burden), practice contacts and falls Intervention group had a reduction in total number of medications when compared with non-intervention cohort. Anti-cholinergic burden scores were reduced by a mean of 26%

Doherty 2020a[38], 2020b[39]	Care home residents	Medicines Optimisation in Older People (MOOP) involving case management by pharmacists	Uncontrolled before/after	Inappropriate prescribing; unplanned hospital admissions; GP visits; clinical interventions Inappropriate prescribing was highly prevalent at baseline (84.1%) but improved significantly from baseline (M = 14.87, SD = 13.11) to post-intervention (M = 0.70, SD = 2.04, Z = 25.97, p<.001).
Donyai 2017[35]	Patients aged at least 75 years and prescribed 15 or more medication	Pharmacist-led polypharmacy review clinic in primary care	Survey	Patient satisfaction and related outcomes Of the 166 patients who returned a satisfaction questionnaire (40% response rate), 83% found the service helpful, 13% did not, 2% did not know and 2% did not respond
Kolovetsios 2018[41]	Care home residents needing palliative care	Structured medication reviews carried out in agreement with patient, nurse, family/carer and GP	Service evaluation	Changes to medication, estimated cost savings From January 2017 to January 2018, 574 medication reviews took place resulting in 1787 suggested medication changes. Approximately 76% of these changes were agreed and actioned by patients' GPs, with estimated savings of £169,986.96.
Swift 2018[40]	Care home residents	Care home team (pharmacists and pharmacy technicians) delivering medication reviews and supporting care home staff	Service evaluation	Prescribing quality indicators (including reduced inappropriate polypharmacy); CQC ratings Medication reviews were completed for 749 care home residents between August 2014 and March 2017. Of the recommendations made to prescribers, 85% were accepted and resulted in a reduction in inappropriate polypharmacy
Syafhan 2019[32]	Patients in participating GP practices at risk of MRPs	Pharmacist-supplemented care focusing on medication optimisation	Individual RCT	Number of medication related problems (MRPs) and medication inappropriateness A total of 356 adult patients (175 control and 181 intervention) were recruited. Among 108 intervention patients who had three pharmacist face-to- face contacts, 346 MRPs were identified at baseline and 83 MRPs at 6 months. Median values were 3 MRPs at baseline and 1 at 6 months (p<0.001).

Table 4: Summary of selected grey literature case studies

Setting	Name of initiative	Key findings	Comments
Brighton and Hove CCG	An evaluation of a clinical pharmacist medication review service in primary care	A total of 1,300 patients were referred into the service and reviewed between April 2017 and March 2018; 9% of patients were deprescribed high-risk medicines	The target patient cohort of frail or older persons prescribed polypharmacy was identified from searches within GP clinical systems and through referrals from clinical practitioners, voluntary and social care services
Swale CCG	Medicines Optimisation Review Programme	In 2018/19, pharmacists and pharmacy technicians reviewed 5281 patients and made 3859 interventions, 37% for adverse drug reactions (ADRs). Estimated in-year cost savings were £239,546	Targeted 'high-risk' patients Key feature is use of technicians for less complex cases
NE Hampshire and Farnham CCG	Care homes pharmacist	Pharmacist accompanying GPs visiting care homes carried out over 250 medication reviews and 800 interventions. Average number of medicines per resident fell from 9.4 to 7.6	Limited data reported
NE Hampshire and Farnham CCG	Polypharmacy prescribing comparators	Tool developed by Wessex AHSN was used to identify patients at risk of harm, resulting in significant reductions in percentage of patients aged over 75 prescribed 15 or more medications and percentage with an anticholinergic burden score of 6 or more	Limited data reported

Study quality

Quality assessment results using the MMAT are presented in supplementary file 3. The results should be read in conjunction with the study strengths and limitations (see Table 1 in supplementary file 1).

Five different checklists within the MMAT were used to assess the 14 studies. The sample included one RCT[19]; six studies were classified as quantitative non-randomised[17, 18, 21, 22, 25, 26]; one as quantitative descriptive[13]; one as mixed methods[23]; and five as qualitative[14-16, 20, 24]. All studies passed the screening questions (are there clear research questions? and do the collected data allow to address the research questions?)

The RCT by Syafhan et al. was described as a pragmatic trial and was at relatively high risk of bias for this type of design. The trial did not achieve the planned number of participants and there was a high rate of attrition (about 30%), meaning that many participants did not receive the full intervention or provide outcome data. The trial also suffered from unclear reporting: method of randomisation and whether outcome assessors were blinded was not reported, making it difficult to assess overall risk of bias.

The quantitative non-randomised studies comprised four observational studies at high risk of bias because of the absence of a control group[21, 22, 25, 26] and two large ITS studies[17, 18]. The MMAT tool identified some limitations of these studies, including some risk of confounding and incomplete outcome data in one study[18]. However, these were large studies conducted in routine practice and providing evidence of a statistically significant effect at 12 months post-intervention. The process evaluations of the CHIPPS[23] and PINCER[13] studies both scored highly on the MMAT assessment.

The qualitative studies were generally of good quality, with sufficient data presented in support of conclusions and appropriate use of frameworks and thematic analysis to organise presentation of the findings. The study by Alharthi et al.[20] was a secondary analysis of data collected for another purpose, making it unclear whether qualitative data collection methods were adequate.

Using the system applied by the authors in previous studies of complex health service interventions[12], the overall strength of evidence was classified as borderline 'stronger' (generally consistent findings in multiple studies with a comparator group) for general practice, 'weaker' (generally consistent findings in one study with a comparator group design and several non-comparator studies or multiple non-comparator studies) for care homes and 'very limited' (single study) for community pharmacies.

Effectively implemented interventions

Three research studies met the criteria for 'effectively implemented' interventions: the closely related PINCER[18] and SMASH[17] interventions in general practice and the Somerset model of medication review in care homes[21]. Further examples of effectively implemented medication review in care homes were identified among the included conference abstracts[38-41]. Case studies from Brighton and Hove and Swale CCGs appeared to report effectively implemented interventions

targeted at high-risk patients in general practice (Table 4). An evaluation of the early implementation of SMRs in primary care networks indicated that the service as provided did not match the vision of a patient-centred holistic review with an emphasis on shared decision-making[16].

.Discussion

Summary of findings

In spite of its broad inclusion criteria, this review identified a relatively small number of studies of pharmacist-led interventions in UK primary care (14 peer reviewed journal articles, 11 conference abstracts and four case studies). Overall, the bulk of evidence came from the care home sector but most of the better quality evidence was derived from studies conducted in general practice. The majority (8/14) of peer reviewed papers were published in 2020 or later, suggesting that this is a developing area of research and practice in the context of encouraging patients to consult pharmacists initially for minor conditions and to increase pharmacists' prescribing rights. It was encouraging that we identified a number of effectively implemented interventions and initiatives in both care homes and general practice.

Outcomes of effective interventions

This systematic review suggests that pharmacist-led interventions may reduce overprescribing in primary care settings in the UK, although more controlled studies are needed. The evidence is strongest for interventions implemented in general practice, where we identified a small randomised trial[19] as well as two large quasi-experimental studies (interrupted time series)[17, 18] and various uncontrolled studies and service evaluations. Evidence from care home settings was of lower quality with the exception of the CHIPPS study involving pharmacist independent prescribers working in care homes[23]. We located only one uncontrolled study based in UK community pharmacies[26].

Although the direction of reported effects was clear, the limited number of controlled studies combined with the wide range of outcomes reported makes it difficult to estimate the size of any effect. For example, the two ITS studies using similar interventions reported markedly different reductions in measures of inappropriate prescribing at 6 and 12 months after implementation of the intervention[17, 18]. Uncertainty about effect sizes is increased because many of the studies lacked a control group and the results could have been influenced by other interventions in the health and social care system, for example the Enhanced Health in Care Homes programme implemented in England. While our review focused primarily on outcomes related to prescribing, data on cost savings were also widely reported but the evidence was generally of low quality. We also found limited evidence of a link between reductions in measures of overprescribing and clinical outcomes, mainly because of lack of reporting. The CHIPPS study found no significant difference in its primary outcome of fall rate, although there was a reduction in Drug Burden Index (a secondary outcome) in the intervention group at 6 months[31].

Characteristics of effective interventions

The TIDieR Lite checklist provided a suitable structure for describing intervention characteristics for evidence synthesis purposes and this discussion follows its structure. Lack of reporting (especially of

intervention intensity/frequency) was a limiting factor, as was reporting of varying intervention information across multiple publications.

Medication reviews were undertaken by pharmacists acting independently or in conjunction with GPs or care home staff. In a study in care homes for people with intellectual disabilities, psychiatrists were also involved in review where appropriate[25]. Pharmacy technicians were also involved in the PINCER study and could potentially have a greater role in relatively straightforward medication reviews[13, 18]. The included studies reported a variety of models of employment of pharmacists, including direct employment by GP practices, CCG Medicines Optimisation Teams, PIPs and community pharmacists. PCNs support employment of pharmacists by general practices and are the route chosen by NHS England to implement its model of SMR.

A major difference between settings is the need to identify patients requiring medication review in general practice, whereas most care home residents take multiple medications and could be considered candidates for review as part of their routine health care. A key element of the PINCER[13, 18] and SMASH[17] interventions is the use of information technology to search electronic patient records efficiently across large numbers of general practices. Effective interventions were also characterised by attention to training and tools to support and sustain change in practice, e.g. an 'audit and feedback' dashboard[17].

Training of pharmacists and other staff to deliver interventions was reported to varying degrees, reflecting in part the publication channel of the research. For example, in the CHIPPS study PIPS had comprised 2 days of face-to-face instruction plus time in practice to develop relationships with the GP and care home staff.[23] Specification and provision of appropriate training will be important for future development of pharmacist-led interventions, as also highlighted by the evaluation of NHS England's SMR programme[16].

Intervention intensity is another important factor in developing and delivering interventions. For the CHIPPS study, participating PIPs committed a minimum of 16 hours/month to the service. [23] In general practice settings, NHS England recommended allowing 30 minutes for an SMR to give time for shared decision-making; this was interpreted to include time for preparation and writing-up[16]. This level of time requirement was also reported in the one study from a community setting, which estimated pharmacist time at 25 minutes for an initial consultation[26].

In terms of intensity more generally, resourcing of interventions was reported to vary between commissioning groups (CCGs) depending on staff availability and other priorities[13, 18, 21]. General practices varied in their use of a medication safety dashboard[28]. Frequency of intervention was rarely reported, reflecting the short time frame of most included studies but it seems possible that there could be an ongoing need for review as patients get older and/or their health state changes.

Quality and risk of bias

The MMAT provided a good alternative to the use of multiple tools to assess risk of bias across diverse study designs. The only randomised trial assessed was designed as a pragmatic trial[19] and the assessment confirmed a relatively high risk of bias. Publications from the CHIPPS study were included but the trial *per se* was not assessed for risk of bias because of the publication date of the main study report. Similarly, the PINCER intervention was supported by a randomised trial published in 2012, before the cut-off date for our review [42]). Well-conducted studies included in the review included large ITS studies[17, 18], process evaluations[13, 14, 23] and qualitative studies[15, 16].

Service evaluations and other lower quality evidence tended to support higher quality studies by highlighting implementation and results achieved in routine practice, although a causal relationship between intervention and outcome remains uncertain in studies without a parallel control group.

Implementation barriers and facilitators

Implementation of pharmacist-led interventions was strongly influenced by factors affecting relationships between pharmacists and other health and care professionals, especially GPs. Given that most pharmacists are not prescribers, their recommendations around (de)prescribing need to be seen as 'legitimate' by GPs who are generally responsible for acting on the recommendations. This is facilitated by continuity at the system level, including existing links between pharmacists and GPs[23] and good access to data[14]. Jeffries et al. reported that pharmacists took the lead in developing relationships with GPs, enabling a 'learning health system'[14]. The benefits of continuity at the system level could help to explain why early implementation of the SMR programme through the relatively new medium of PCNs was reported to be less successful than initially hoped[16].

Implementation in care homes may be more complex than in general practice because of differences in systems and 'culture' between health and social care[24]. Patients and their families may be supportive of medication review or oppose it based on real or perceived benefits of medication[20].

The main message regarding implementation of pharmacist-led interventions across all settings is the need for involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers[24].

Identification of effectively implemented interventions/initiatives:

Our simple criteria for 'effectively implemented' interventions/initiatives identified a number of examples published as research papers, conference abstracts or case studies (see 'Effectively implemented interventions' above). Despite limitations as research, some of the abstracts and case studies provided valuable information about how commissioners and providers had supported interventions and their commitment to continue the programme[38-41]. In other studies, despite promising results, it was unclear whether the intervention would be implemented more widely[19].

Relationship to previous research

To our knowledge, this is the first systematic review of pharmacist-led interventions and initiatives specifically in UK settings. A scoping literature search identified 20 systematic reviews published between 2014 and 2023. The most recent review covered pharmacist integration into general practice to optimise prescribing and outcomes for patients with polypharmacy[43]. The review included 23 studies, of which just three were from the UK. The conclusion that pharmacist integration probably reduced PIP and number of medicines (moderate certainty evidence) was in line with the findings of the present review. A 2016 systematic review by Riordan et al. focused on pharmacist-led interventions to optimise prescribing in older community-dwelling adults in primary care[44]. The authors concluded that pharmacist-led interventions may improve appropriateness of

prescribing but the quality of evidence was low. The review included randomised and quasi-randomised studies published before December 2015, giving it limited overlap with our review.

Strengths and limitations

The UK focus is both a strength and limitation of this review. We included evidence often excluded from systematic reviews to get as full a picture as possible of how pharmacist-led interventions are implemented and sustained in practice as well as their characteristics and effectiveness. The dual focus reflects the fact that pharmacist-led medicines optimisation and deprescribing in primary care is both an area of active research and of implementation within the health care system. Nevertheless, some of the evidence is not of high quality and we have tried to be appropriately cautious in our conclusions and identified implications.

Our broad review questions and UK focus resulted in a heterogeneous group of included studies. Meta-analysis was not possible so we performed a narrative synthesis in line with appropriate guidelines[10, 11]. The review was undertaken by a small but experienced team with expertise in systematic review methods and prescribing.

Implications for service delivery

Several studies indicate that barriers to successful service delivery often arise from 'system' issues and differences in 'culture'[16, 24]. Commissioners and providers engaged in developing new pharmacist-led services should ensure equitable access to data and information to avoid perceptions of 'ownership' by certain groups at the expense of others[15]. In care homes, where medication review is an important component of health care for residents[21], implementation requires health and social care professionals to work together and 'understand each other's systems'[24]. The holistic patient-centred SMR envisaged by NHS England may require culture change/training to foster an emphasis on direct patient contact and shared decision-making. Removal of financial incentives for PCNs to carry out SMRs as reported recently (https://pharmaceutical-journal.com/article/news/nhs-england-removes-financial-incentives-for-structured-medication-reviews-in-2023-2024) may complicate delivery, although the service remains a contractual requirement.

Services have been delivered successfully through CCGs Medicines Optimisation Teams with suitable training[13, 18]. The review also found evidence that services provided by PIPs appear to be a valid alternative to approaches requiring action by GPs or other medical professionals[23].

Implications for research

A major priority for research is to further evaluate the effectiveness of medication review in community pharmacy settings and how pharmacies might be best supported to deliver the service. A related need is for research to better understand public perceptions of community pharmacies as a

setting for medication review and their pros and cons compared with alternative settings such as GP surgeries. Research is needed to support the development of the PIP role and how PIPs might best be used in combination with GPs and other professionals to support optimal prescribing across the health and care system.

Shared decision-making is key to the success of pharmacist-led interventions. Research is needed to better understand patient and family attitudes to shared decision-making in the context of deprescribing and the barriers and facilitators operating in different settings and with different professionals.

The present review focused on outcomes related to prescribing and a review of effects on patient and health system outcomes would be a logical follow-up. Finally, further research is needed to understand the effects of implementing pharmacist-led medication review in general practice on health inequalities and how to reduce unwarranted variations in service delivery between different practices or regions.

Conclusions

The evidence base for pharmacist-led interventions varies widely in terms of quality but studies have consistently reported improvements relative to a comparator group or baseline. The diversity of interventions and outcomes reported makes it difficult to generalise about effect sizes but given the reported extent of the problem, even small relative reductions could be beneficial for patients and the health and care system.

The existing evidence base requires cautious interpretation because of a shortage of controlled studies and this is particularly the case for studies in community pharmacy settings. Further rigorous evaluation of interventions, particularly those delivered in community pharmacies, is required. Although not a focus of this review, there appears to be a shortage of high-quality economic evidence to guide decision-making by service commissioners and providers.

The problems encountered in the early implementation of NHS England's SMR programme[16] suggest a need for further research on the implementation of pharmacist-led interventions. Implementation of this type of interventions requires the involvement of all relevant stakeholders, preferably before starting the process of implementation, to understand the context and anticipate possible barriers.

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Conflict of interest

The authors have no conflicts of interest to declare.

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Contribution of authors

Duncan Chambers (submitting author and guarantor) contributed to planning the study (writing the protocol), selected studies for inclusion, assessed study quality and wrote the first draft of the paper. Louise Preston managed the review team, contributed to planning the study (writing the protocol), selected studies for inclusion, assessed study quality and commented on drafts of the paper. Mark Clowes contributed to planning the study (writing the protocol), developed search strategies, performed literature searches and wrote up the searches and search results. Anna Cantrell selected studies for inclusion, assessed study quality and commented on drafts of the paper. Elizabeth Goyder contributed to planning the study (writing the protocol) and commented on drafts of the paper. Duncan Chambers, Louise Preston, Mark Clowes, Anna Cantrell and Elizabeth Goyder have approved the version to be submitted.

Data sharing

Any additional data not included in this report and its appendices are available on request. All queries should be submitted to the corresponding author.

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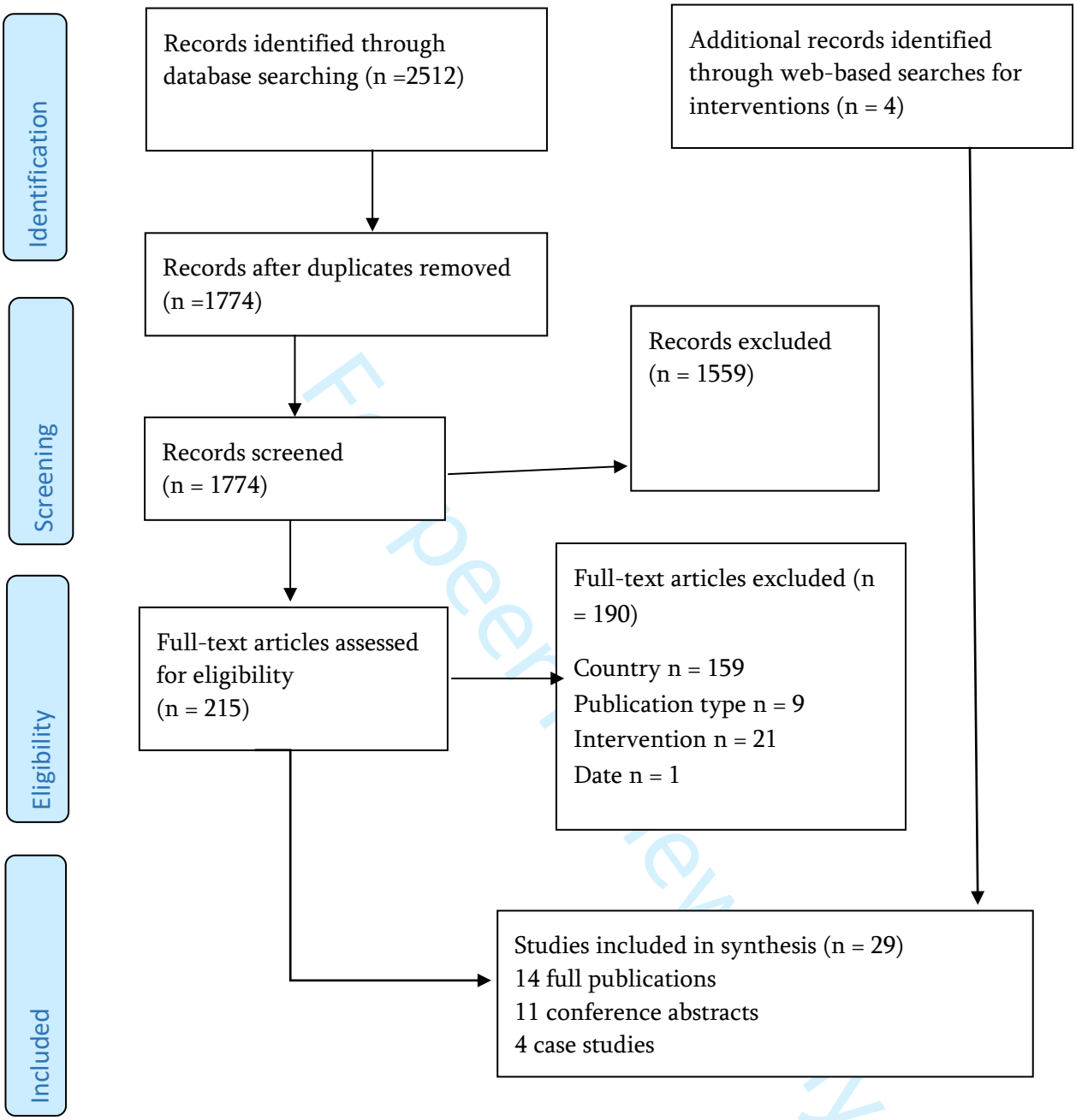

SEARCH STRATEGIES in full (for Appendix / supplementary material)

Ovid MEDLINE(R) ALL <1946 to February 06, 2023>

1 Inappropriate Prescribing/ 4485

2 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 8188

3 (overprescri* or over-prescri*).mp. 1975

4 Polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 12777

5 1 or 2 or 3 or 4 21236

6 exp Primary Health Care/ or (primary health care or primary healthcare or primary care).mp. 289526

7 general practice/ or family practice/ 78114

8 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 751694

9 6 or 7 or 8 997387

10 (deprescri* or de-prescri*).mp. 2577

11 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 16563

12 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 3182

13 10 or 11 or 12 21842

14 5 and 9 and 13 540

15 *Medication Errors/ and 9 and 13 232

16 5 and 9 and pc.fs. 835

17 14 or 15 or 16 1416

18 limit 17 to yr="2013 -Current" 1152

19 remove duplicates from 18 1145

Embase <1974 to 2023 Week 05>

1 Potentially inappropriate medication/ 2458

2 unnecessary prescribing/ [+NT] 51

3 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 11262

4 (overprescri* or over-prescri*).mp. 3064

5 Polypharmacy/ or inappropriate polypharmacy/ or (polypharmacy or poly-pharmacy).ti,ab. 26382

6 1 or 2 or 3 or 4 or 5 39236

7 exp Primary Health Care/ or primary medical care/ or (primary health care or primary healthcare or primary care).mp. 281889

8 general practice/ or family practice/ 83634

9 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 766031

10 7 or 8 or 9 974647

11 (deprescri* or de-prescri*).mp. 3587

12 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 28235

13 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 6755

14 11 or 12 or 13 37710

15 6 and 10 and 14 813

16 6 and 10 and pc.fs. 308

17 15 or 16 1089

18 limit 17 to yr="2013 -Current" 903

19 remove duplicates from 18 886

APA PsycInfo <1806 to January Week 5 2023>

1 ((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) adj3 prescri*).mp. 788

2 (overprescri* or over-prescri*).mp. 329

3 (polypharmacy or poly-pharmacy).mp. 3128

4 1 or 2 or 3 4078

5 (primary health care or primary healthcare or primary care).mp. 44486

6 (GP or general practi* or family practice or family physician* or community pharmac* or dental or dentist* or optometr* or optician*).mp. 34287

7 5 or 6 71196

8 (deprescri* or de-prescri*).mp. 336

9 (structured medication review or medication reconciliation or medicine* optimi#ation or shared decision making or personalised care).mp. 3969

10 ((intervention* or initiative* or campaign*) adj3 (pharmacist* or pharmacy technician*)).mp. 242

11 8 or 9 or 10 4505

12 4 and 7 and 11 44

#	Query	Limiters/Expanders	Last Run Via	Results
		Limiters - Published Date: 20130101-20231231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	
S16	S6 AND S10 AND S14			307
S15	S6 AND S10 AND S14			327
S14	S11 OR S12 OR S13			13,914
S13	(intervention* or initiative* or campaign*) n3 pharmacist*			1,981
S12	"structured medication review" or "medication reconciliation" or "medicine* optimi#ation" or "shared decision making" or "personalised care" or "personalized care"			10,941
S11	deprescri* or de-prescri*			1,345
S10	S7 OR S8 OR S9			336,381
S9	("primary care" or "primary health care" or "primary healthcare" or "primary medical care") OR (GP or "general practi*" or "family practi*" or "family physician*" or "community pharmac*" or dental or dentist* or optometrist* or optician*)			333,015
S8	(MH "Family Practice")			26,910
S7	(MH "Primary Health Care") OR (MH "Physicians, Family")			90,488
S6	S1 OR S2 OR S3 OR S4 OR S5			12,727

S5	polypharmacy or poly-pharmacy	7,664
S4	(MH "Polypharmacy (Saba CCC)") OR (MH "Polypharmacy+")	5,635
S3	overprescri* or "over prescri*"	1,026
S2	(hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or non-essential or inessential) n3 prescri*	4,996
S1	(MH "Inappropriate Prescribing")	3,448

Search Name: THE COCHRANE LIBRARY

Date Run: 08/02/2023 13:50:34

Comment:

ID	Search	Hits
#1	MeSH descriptor: [Inappropriate Prescribing] explode all trees	234
#2	MeSH descriptor: [Polypharmacy] explode all trees	312
#3	((hazardous* or excessive* or inappropriate* or unnecessar* or nonessential or "non essential" or inessential) near/3 prescri*):ti,ab,kw	771
#4	(overprescri* or "over-prescri*"):ti,ab,kw	161
#5	(polypharmacy or poly-pharmacy):ti,ab,kw	1288
#6	#1 or #2 or #3 or #4 or #5	2045
#7	MeSH descriptor: [Primary Health Care] explode all trees	9989
#8	MeSH descriptor: [General Practice] explode all trees	2877
#9	MeSH descriptor: [Family Practice] explode all trees	2242
#10	("primary health care" or "primary healthcare" or "primary care"):ti,ab,kw	24053
#11	(GP or "general practi*" or "family practice" or "family physician*" or "community pharmac*" or dental or dentist* or optometr* or optician*):ti,ab,kw	44879
#12	#7 or #8 or #9 or #10 or #11	70362
#13	MeSH descriptor: [Deprescriptions] explode all trees	68
#14	(deprescri* or de-prescri*):ti,ab,kw	364
#15	("structured medication review" or "medication reconciliation" or "medicine* optimi*" or "shared decision making" or "personalised care" or "personalized care"):ti,ab,kw	2425
#16	((intervention* or initiative* or campaign*) near/3 (pharmacist* or pharmacy)):ti,ab,kw	1559
#17	#13 or #14 or #15 or #16	4166
#18	#6 and #12 and #17	130

(3 reviews, 127 trials)

Data extraction tables

Table 1: Study characteristics of included research studies (full data extraction table)

Study ID	Study design/sample size	Setting	Intervention	Key findings	Authors' conclusions	Study strengths/limitations
Alharthi 2023[18]	Secondary analysis of qualitative interview data 11 pharmacist independent prescribers (PIPs) who participated in a cluster randomised trial	Care homes in England and Scotland	Integration of PIPs into care homes to improve medication management	Factors that acted as both enablers and barriers were PIP relationship with General Practitioner (GP), care home staff and residents/families, awareness of the PIP role and family trust in PIPs' deprescribing activities *(social influences)*; PIPs' independent prescribing confidence, previous experience and ability dealing with residents' medications *(beliefs about capabilities)*; understanding of PIP role and PIP confidence in their role as an independent prescriber *(social/professional role and identity)*; access to residents' records, deprescribing decision support, regular follow-up from care home staff, resident difficulties with medications,	PiPs' involvement in care homes is influenced by numerous barriers and enablers that can be addressed to improve intervention effectiveness	Strengths: Diverse PIP contexts and perspectives on deprescribing; theory-informed analysis using Theoretical Domains Framework to identify barriers and enablers Limitations: Only PIP perspective considered; analysis used data from interviews focused on the whole intervention process rather than exclusively on deprescribing

				teamwork, and time restraints *(environmental context and resources)*. Belief that the negatives of deprescribing outweigh benefits regarding certain medications *(beliefs about consequences) acted as a barrier.*		
Alves 2019[19]	Service evaluation 10,405 patient reviews over 5 years	Care homes in Somerset	Medication review by primary care pharmacists linked to GP practices	Pharmacists made 23,955 interventions (mean 2.3 per patient) from the 10,405 patient reviews undertaken. 16.1% of interventions were related to safety. Potential drug cost savings were estimated at £812,441 over 5 years, of which £431, 493 (53%) was attributed to deprescribing	Medication reviews undertaken by primary care pharmacists in care homes generate a wide range of interventions, commonly involving deprescribing. The service contributes to the continuous optimisation of prescribing and monitoring of medicines and offers potential drug cost savings.	Strengths: Collection of data from 'real world' implementation of intervention over 5 years Limitations: No control group, cost saving estimates not based on full economic evaluation
Baqir 2017[20]	Retrospective evaluation of quality improvement project 422 residents in 20 care homes	Care homes in two CCG areas in North East England	Medicines optimisation by a pharmacist acting independently or jointly with a GP. Shared decision making with the patient or their advocate	Of the 422 patients reviewed, 298 (70.6%) had at least one medicine deprescribed with 704 medicines (19.5%) being stopped. There was no statistically significant difference between pharmacist only and pharmacist plus GP in terms of deprescribing. Assuming that each medicine stopped would have been taken for another year, annualised cost savings were estimated at £65,471	Medicines optimisation reviews can lead to a reduction in polypharmacy for care home residents through a deprescribing process. Patients' medicine regimens were simplified and optimised while making financial savings for the NHS	Strengths: Compares two approaches to delivering medication review Limitations: Short-term uncontrolled study; intervention quality/fidelity not measured

Birt 2021[21]	Mixed methods process evaluation of cluster RCT Intervention arm comprised 25 triads: Care homes (staff and up to 24 residents), GP and pharmacist Independent Prescriber (PIP); 22 PIPs contributed data	Care homes in England, Scotland and Northern Ireland	Integration of PIPs into care homes to assume central responsibility for medicines management	All stakeholders reported some benefits from PIPs having responsibility for medicine management and identified no safety concerns. PIPs reported an increase in their knowledge and identified the value of having time to engage with care home staff and residents during reviews. PIPs recorded 566 clinical interventions, many involving deprescribing; 93.8% of changes were sustained at 6 months. For 284 (50.2%) residents a medicine was stopped, and for a quarter of residents, changes involved a medicine linked to increased falls risk. Qualitative data indicated participants noted increased medication safety and improved resident quality of life. Contextual barriers to implementation were apparent in the few triads where PIP was not known to the GP and care home before the trial. In three triads, PIPs did not deliver the intervention.	The intervention was generally implemented as intended, and well-received by most stakeholders. Whilst there was widespread deprescribing, contextual factors effected PIP engagement. Implementation was most effective when communication pathways between PIP and GP had been previously established.	Strengths: Involved three UK nations with differing healthcare systems; used study records to supplement qualitative data Limitations: Interview participants may not be representative; limited access to care home residents
Howard 2014[11]	Process evaluation of data from cluster RCT	General practice surgeries in an 80 km	Pharmacist-led IT enabled intervention (PINCER).	Pharmacists judged 72% (95% CI 70, 74; 1463/2026) of cases of hazardous medicines management to be clinically	Recommendations from the pharmacists were broadly	Strengths: Uses data from a large cluster RCT

	36 intervention and 36 control practices; 1946 patients identified as at risk in intervention practices	radius around Manchester and Nottingham	Patients potentially at risk from hazardous medicines management were identified using Quest Browser software to search GP electronic records. Intervention practices were assigned a pharmacist who educated practice staff about medication management and recommended improvements to practice. Pharmacists also reviewed cases of potentially hazardous medication	relevant. Pharmacists recommended 2105 interventions in 74% (95% CI 73, 76; 1516/2038) of cases and 1685 actions were taken in 61% (95% CI 59, 63; 1246/2038) of cases; 66% (95% CI 64, 68; 1383/2105) of interventions recommended by pharmacists were completed and 5% were accepted by GPs but not completed at the end of the pharmacists' placement; the remaining recommendations were rejected or considered not relevant by GPs.	acceptable to GPs and led to ameliorative action in the majority of cases. It seems likely that the approach used by the PINCER pharmacists could be employed by other practice pharmacists following appropriate training.	Limitations: Pharmacists did not record detailed reasons for their judgements and these were not peer reviewed

			and recommended interventions to GPs			
Jeffries 2017[13]	Qualitative realist evaluation Interviews: 3 GPs, 2 CCG pharmacists; Focus groups: 2 GPs, 4 community pharmacists, 4 patients, 4 practice managers	CCG in the South of England	Electronic Medicines Optimisation System (EMOS). The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of adverse drug events (ADEs)	Effective use of the EMOS depended upon engagement with the system, the flow of information between different health professionals centrally placed at the CCG and those locally placed at individual general practices, and upon adaptation of work practices to facilitate the use of the system. The use of the system was undermined by perceptions of ownership, lack of access, lack of knowledge and awareness, and time pressures.	The use of an electronic medicines optimisation system may improve medication safety in primary care settings by identifying those patients at risk of an ADE. To fully realise the potential benefit, there needs to be better utilisation across primary care and with a wide range of stakeholders. Engaging with all potential stakeholders and users prior to implementation might allay perceptions that the system is owned centrally and increase knowledge of the potential benefits.	Strengths: Realist methodology enabled detailed examination of how the EMOS was used and its potential effects Limitations: Study involved only one CCG so may not be representative
Jeffries 2018[12]	Qualitative process evaluation 28 staff members from 23 general practices (9 GPs, 12 pharmacists, 7 other GP staff)	43 general practices in Salford, Greater Manchester	Electronic audit and feedback surveillance dashboard to identify patients potentially at risk of hazardous prescribing or	Engagement with the dashboard involved a process of 'sense-making' by pharmacists. The intervention helped to build respect, improve trust and develop relationships between pharmacists and GPs. Collaboration and communication between pharmacists and clinicians was primarily initiated by	Medicine optimisation in primary care may be enhanced by the implementation of a pharmacist-led electronic audit and feedback system. This intervention established a rapid learning health system that enabled data from electronic health records to be used to make changes in practice to improve patient care.	Strengths: Use of Normalization Process Theory as a framework to understand implementation Limitations: Evaluation team also developed the intervention; number of follow-up

			monitoring of medicines	pharmacists and was important for establishing the intervention.		interviews was limited
Lane 2020[22]	Qualitative focus groups and interviews 85 (72 in focus groups and 13 in semi-structured interviews)	Care homes (4 sites in England (2), Scotland and Northern Ireland)	Integration of PIPs into care homes to take responsibility for medicines management	A PIP service was seen as offering benefits for residents, care homes and doctors but stakeholders raised challenges including agreement on areas where PIPs might prescribe, contextual barriers in chronic disease management, PIPs' knowledge of older people's medicine, and implementation barriers in integrated team-working and ensuring role clarity. Introducing a PIP was welcomed in principle but conditional on: a clearly defined PIP role communicated to stakeholders; collaboration between doctors, PIPs and care-home staff; and dialogue about developing the service with residents and relatives.	The overarching theme from this research was that everyone must "understand each other's systems". In particular, PIPs need to understand care homes' systems in advance of implementing a new service	Strengths: Purposively selected sample; use of TDF as a framework to analyse data Limitations: Data relate to proposed service model in advance of implementation
Madden 2022[14]	Qualitative interview study 10 newly appointed pharmacists working in primary care	General practice in England	Structured medication review (SMR) for people at risk of harm or medication-related problems	SMR implementation was largely delegated to individual pharmacists. Established pharmacists appeared more ready for implementation than newly appointed staff. New pharmacists were learning about working in primary care settings and tended to follow procedures	Early implementation of SMRs did not match the intention of providing patients with a holistic review and shared decision-making. The authors identified an important opportunity cost of SMR implementation without prior adequate skills	Strengths: based on detailed, in-depth interviews Limitations: Authors note interviews need to be complemented by data on actual

	networks (PCNs) in Northern England; 10 established pharmacists working in GP practices in other PCNs			with which they were already familiar, particularly when they lacked patient-facing expertise. Implementation was affected by ongoing backlogs and workforce issues in general practices	development, testing, and refining	practice and longer term follow-up
Peek 2020[15]	Interrupted time series 43 general practices covering 235,595 people in Salford, Greater Manchester	General practice in England	Pharmacist-led Safety Medication dASHboard (SMASH). SMASH involved (1) training of clinical pharmacists to deliver the intervention; (2) a web-based dashboard providing actionable, patient-level feedback; and (3) pharmacists reviewing individual at-risk patients,	The study used an interrupted time series analysis of rates (prevalence) of potentially hazardous prescribing and inadequate blood-test monitoring, comparing observed rates post-intervention to extrapolations from a 24-month pre-intervention trend. At baseline, 95% of practices had rates of potentially hazardous prescribing (composite of 10 indicators) between 0.88% and 6.19%. The prevalence of potentially hazardous prescribing reduced by 27.9% (95% CI 20.3% to 36.8%, $p < 0.001$) at 24 weeks and by 40.7% (95% CI 29.1% to 54.2%, $p < 0.001$) at 12 months after introduction of SMASH. The rate of inadequate blood-test monitoring (composite of 2 indicators) reduced by 22.0%	The SMASH intervention was associated with reduced rates of potentially hazardous prescribing and inadequate blood-test monitoring in general practices. This reduction was sustained over 12 months for prescribing but not for monitoring of medication. There was a marked reduction in the variation in rates of hazardous prescribing between practices.	Strengths: Authors noted pragmatic design, evaluation of clinically relevant outcomes and large number of practices taking part Limitations: Not a randomised study so possibility of unrecognised confounding cannot be excluded

			and initiating remedial actions or advising GPs on doing so.	(95% CI 0.2% to 50.7%, *p* = 0.046) at 24 weeks; the change at 12 months (23.5%) was no longer significant (95% CI −4.5% to 61.6%, *p* = 0.127). After 12 months, 95% of practices had rates of potentially hazardous prescribing between 0.74% and 3.02%.		
Rodgers 2022[16]	Multiple interrupted time series 393 general practices covering approximately 3 million patients	General practice in the East Midlands region of England	Pharmacist-led IT intervention to reduce hazardous prescribing (PINCER)	Successive groups of general practices received the PINCER intervention between September 2015 and April 2017. Eleven prescribing safety indicators were used to identify potentially hazardous prescribing and data were collected over a maximum of 16 quarterly time periods. PINCER was implemented in 370 (94.1%) of 393 general practices; data were successfully extracted from 343 (92.7%) of these practices. For the primary composite outcome, the PINCER intervention was associated with a decrease in the rate of hazardous prescribing of 16.7% (adjusted odds ratio (aOR) 0.83, 95% confidence interval (CI) 0.80 to 0.86) at 6	The PINCER intervention, when rolled out at scale in routine clinical practice, was associated with a reduction in hazardous prescribing by 17% and 15% at 6 and 12 months post-intervention. The greatest reductions in hazardous prescribing were for indicators associated with risk of GI bleeding. These findings support the wider national rollout of PINCER in England.	Strengths: Suggests intervention was implemented successfully in routine practice and was associated with significant reductions in hazardous prescribing Limitations: The authors adjusted for calendar time and practice, but since this was an observational study, the findings may have been influenced by unknown confounding factors or behavioural changes unrelated to

				months and 15.3% (aOR 0.85, 95% CI 0.80 to 0.90) at 12 months post-intervention. The unadjusted rate of hazardous prescribing reduced from 26.4% to 20.1% at 6 months and 19.1% at 12 months. The greatest reduction was for hazardous prescribing indicators related to GI bleeding		the PINCER intervention. Data were also not collected for all practices at 6 and 12 months post-intervention
Syafhan 2021[17]	Individual RCT 356 patients at risk of medication-related problems (MRPs) from 8 GP practices	General practice in England (6 practices) and Northern Ireland (2)	Medicines optimisation with shared decision-making and agreed treatment goals. Intervention repeated at 2 and 4 months, building on progress towards agreed goals	Median number of MRPs per intervention patient at 6 months was reduced from 3 to 0.5 ($p <$ 0.001) in patients who received the full intervention schedule. Medication Appropriateness Index (MAI) scores were reduced (medications more appropriate) for the intervention group, but not for control group patients. Using the intention-to-treat (ITT) approach, the number of telephone consultations in intervention group patients was reduced and different from the control group. No significant differences between groups were found in unplanned hospital admissions, length of hospital stay, number of A&E attendances or outpatient visits. The mean overall healthcare	The pharmacist intervention reduced MRPs, inappropriateness of medications and telephone consultations in general practice in a cost-effective manner	Strengths: Pragmatic randomised design Limitations: Sample smaller than planned; high loss to follow-up; MRP analysis only covered patients who attended 3 appointments

				cost per intervention patient fell from £1041.7 ± 1446.7 to £859.1 ± 1235.2 (p = 0.032). Cost utility analysis showed an incremental cost per patient of − £229.0 (95% CI − 594.6, 128.2) and a mean QALY gained of 0.024 (95% CI − 0.021 to 0.065),. indicative of a health status gain at a reduced cost (2016/2017).		
Thayer 2021[23]	Service evaluation 160 care home residents with intellectual disabilities (ID)	Care homes for people with ID in the Wirral	Pharmacist review of residents' medicines and lifestyle risk factors between November 2019 and May 2020.	The 160 residents were prescribed 1207 medicines, 74% were prescribed ⩾5 medicines and 507 interventions/recommendations were made, averaging 3.3 per resident. The highest proportion (30.4%) were lifestyle risk related, while changing and stopping medicines accounted for 17.9% and 12.8%, respectively. Of the recommendations discussed with GPs/psychiatrists, 86% were accepted.	There was considerable polypharmacy among the residents and a high level of pharmacists' interventions/recommendations about medicines and lifestyle risk, most of which were accepted by GPs/psychiatrists. Wider adoption of collaborative pharmacist review models could have benefits for residential populations with ID and potentially reduce pressure on other health services.	Strengths: Drew on skills of pharmacists from different sectors to address wide range of care needs; recommendations addressed national priorities Limitations: Study limited to one CCG area; limited access to patient records; observational study with no control/comparator arm
Twigg 2015[24]	Service evaluation	Community pharmacies in England	Four or More Medicines (FOMM) support	Of 620 patients recruited, 441 (71.1%) completed the 6-month study period. Pharmacists made 142	By focussing on patients over the age of 65 years with four or more medicines, community pharmacists can improve	Strengths: Large sample of patients and providers; use of

	620 patients (aged over 65 years and prescribed ≥ 4 medications)		service. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the patient's medication using STOPP/START criteria. Data were analysed for the first 6 months of participation in the service.	recommendations to prescribers in 110 patients, largely centred on potentially inappropriate prescribing of NSAIDs, PPIs or duplication of therapy. At follow-up, there was a significant decrease in the total number of falls experienced and a significant increase in medicine adherence and quality of life. Cost per quality-adjusted life year estimates ranged from£11 885 to £32 466 depending on the assumptions made.	medicine adherence and patient quality of life.	validated outcome measures Limitations: No control/comparator group; authors note some patients were probably reviewed independently by their GP during the study period; relatively high attrition rate

Appendix Table 2: TIDieR Lite for UK pharmacist studies

Intervention name and study ID(s)	By whom	What	Where	Intensity	How often
CHIPPS Alharthi 2023[18]; Birt 2021[21]; Lane 2020 [22]; Bond 2020[25]; Holland 2023[29]	Trained pharmacist independent prescribers (PIPs). The training programme comprised 2 days of face-to-face instruction, time in practice to develop relationships with the GP and care home staff, and to address any self-assessed competency gaps supported by a mentor, and a formal final sign-off by a GP independent of the research	PIP, in collaboration with the care home resident's GP, assumes responsibility for managing the medicines of the resident, including: • Reviewing resident's medication and developing and implementing a pharmaceutical care plan • Assuming prescribing responsibilities • Supporting systematic ordering, prescribing and administration processes with each care home, GP practice and supplying pharmacy where needed • Providing training in care home and GP practice • Communicating with GP practice, care home,	Participating care homes	PIPs committed a minimum of 16 hours/month to deliver the service. Each PIP provided care to approximately 20 residents	PIPs visited care homes weekly over 6 months

		supplying community pharmacy and study team			
Care home medication reviews Alves 2019[19]	Primary care pharmacists and GPs in Somerset CCG area and CCG staff	Medicines optimisation visits to care homes. Primary care pharmacists visited homes on behalf of GP practices; GPs could participate in visits or hold discussions with pharmacists prior to the visit; screening of safety interventions was done by CCG pharmacist leads	Care homes with and without nursing in Somerset	The time and level of support allocated for the service was agreed with the respective CCG Local Pharmacist Manager and influenced by a number of factors such as engagement from GP practices; primary care pharmacists' availability; skills and confidence; number of care home patients registered with each GP practice; and geographic area covered by the prescribing support pharmacists	The aim of the programme was to offer at least one visit to as many care homes as possible (appears to be one visit per year but not explicitly stated)
Shine Medication Optimisation Project Baqir 2017[20]	Pharmacists together with care home nurses and other members of the multi-disciplinary team (MDT), including GPs and mental health professionals as needed. Two different models: pharmacists made prescribing decisions (as part of shared decision-making) independently or in conjunction with GPs	A notes based, pharmacist-led review of medicines, where the Northumbria 3Q approach was applied to each medicine, that is, was there an indication, was the indication appropriate and was it safe?. Additionally, medicines missing that could be beneficial (eg, START medicines) were identified. This was followed by a MDT meeting where the information from the pharmacist-led review was discussed and an action plan was formulated. Whenever possible, the final decisions were made with patients and their families. After the review,	Care homes in North East England	Intensity of intervention not reported. Prescribing decisions could be made by pharmacists alone or in conjunction with GPs	Once, as a funded quality improvement (QI) project

		the project database was updated to show medicines taken before review, medicines stopped, started or changed and any other interventions made.			
PINCER Howard 2014[11]; Rodgers 2022[16]	Pharmacists specifically trained to deliver the intervention; GPs, other practice staff and pharmacy technicians involved in implementation	Computer systems of general practices are searched to identify patients at risk of potentially hazardous prescribing using a set of prescribing safety indicators. Pharmacists then provide an educational outreach intervention where they meet with GPs and other practice staff to: • Discuss the search results and highlight the importance of the hazardous prescribing identified using brief educational materials. These feedback sessions were to be held straight after running the searches and then at regular intervals. • Agree on an action plan, retained within the practice, for	General practices	When PINCER was rolled out in the East Midlands, time spent by pharmacists delivering the intervention varied by CCG depending on the resourcing level of the local Medicines Optimisation Team	Data collected quarterly up to 12 months after starting the intervention[16]

		reviewing patients identified as high risk and improving prescribing and medication monitoring systems using root cause analysis Pharmacists (sometimes supported by pharmacy technicians) then work with, and support, general practice staff to implement the agreed action plan, sometimes making the necessary changes themselves			
Eclipse Live (electronic medicines optimisation system (EMOS)) Jeffries 2017[13]	Developed by a private company (Eclipse Solutions) and made available to stakeholders (including doctors, pharmacists, practice managers and patients) by a CCG in the South of England	Web-based user interface which securely extracts patient data from general practice patient records. Accessed separately from the GPs' clinical systems, it allows different stakeholders access to real time anonymized patient data including medical histories of diagnoses, prescribed medications and test results. The EMOS is intended to facilitate clinical audits of prescribing activity to identify patients at risk of ADEs, or not appropriately monitored.	General practices covered by the participating CCG	Not reported (qualitative study)	Not reported (qualitative study)

		Patients can access the system through a "Patient Passport"			
Safety Medication dASHboard (SMASH) Jeffries 2018[12]; Peek 2020[15]; Jeffries 2020[26]	Clinical pharmacists working in general practices and other general practice staff	Pharmacists were trained to deliver the intervention and apply root cause analysis techniques to identify, explore, resolve, and prevent medication errors in partnership with general practice staff. Pharmacists and practice staff were given access to a web-based, interactive dashboard that provided feedback on 12 indicators of potentially hazardous prescribing. The dashboard also provided practice-level summary data as well as educational material.	General practices covered by the participating CCG	Practices interacted with the dashboard a median of 12.0 (interquartile range, 5.0–15.2) times per month during the first quarter of use. Over time, dashboard use transitioned towards regular but less frequent (median of 5.5 [3.5–8.5] times per month) checks to identify and resolve new cases. The frequency of dashboard use was higher in practices with a larger number of at-risk patients.	Dashboard was updated daily. Frequency of use varied by practice and over time (see previous column)
Structured Medication Review (SMR) Madden 2022[14]; Stewart 2021[27]	Clinical pharmacists within general practice primary care networks (PCNs)	Invited, personalised, holistic review of all medicines and their benefits to health for people at risk of harm or medicine-related problems	General practices	Reviews are recommended to be scheduled for at least 30 minutes to allow time for shared decision-making	Once
Medicines optimisation intervention	GP practice-based pharmacists operating as part of the wider primary care team	Each pharmacist received 2 days of intensive specialist training	Eight general practices in four regions of the UK	Initial meeting with further appointments available at 2 and 4 months building on patient progress towards agreed goals	Once per patient (up to three appointments)

Syafhan 2021[17]		on medicines optimisation (including training on motivational interviewing). The intervention included: review of patient records prior to meeting; medication history; individual medicines optimisation plan that could include recommending/making changes to medication regimens (in collaboration with GPs), personalised education and counselling on medication management, the correct use of medication administration devices and lifestyle factors; and an agreed list of treatment goals. Pharmacists could also refer patients to another health professional within the practice. Having completed the intervention, the pharmacist produced a short report for the patient's GP outlining actions taken and any further recommendations requiring GP input			

Collaborative pharmacist review Thayer 2021[23]	Community and specialist mental health pharmacists	Medicine review using a structured framework based on recommendations of the 2018 Learning Disability Mortality Review (LeDeR) report. Pharmacists visited care homes to conduct the reviews using individual residents' care home records. The specialist mental health pharmacist also had access to the care record held by the Specialist Mental Health Trust, if the resident was under the Trust's care, and remote access to the local data sharing platform. Assessments included medicines adherence and burden (particularly the anticholinergic burden), respiratory care, vaccination status, constipation risk, sepsis prevention, dysphagia risk and lifestyle risk issues, especially smoking. Finally, pharmacists were asked to detail actions taken/advice provided, any recommendations made and make referrals, as necessary. Following the review, GP surgeries and psychiatrists were contacted by the pharmacists to arrange a review of their	Care homes for people with intellectual disabilities	507 interventions/recommendations for 160 residents reviewed (3.3 per resident)	Once

		recommendations. As the pharmacists were not prescribers, decisions on accepting recommendations were made by the resident's GP/psychiatrist (after reviewing the resident's full clinical record) in consultation with the pharmacists			
Four or More Medicines (FOMM) support service Twigg 2015[24]	Community pharmacists and pharmacy team members	Pharmacists were trained via distance learning and face to face, which included how to use the various different tools and assessments. Training was then cascaded to other pharmacy members. Patients were invited to participate in the service by the community pharmacy team. The pharmacist held regular consultations with the patient and discussed risk of falls, pain management, adherence and general health. They also reviewed the patient's medication using STOPP/START criteria.	Participating community pharmacies	Pharmacist time estimated at 25 minutes for initial consultation, 10 minutes for monthly review and 11 minutes for quarterly review	After the first consultation, patients met with the pharmacist on a regular basis depending on when they collected their repeat medication or they felt a need.

MMAT quality assessment results

Reference	Screening questions	Type of study	MMAT questions and answers
Alharthi 2023[18]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (identifying perceived barriers and facilitators)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Can't tell (secondary analysis of existing data)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Alves 2019[19]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Can't tell (partial data presented)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (fidelity not monitored)*
Baqir 2017[20]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*

Birt 2021[21]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Mixed methods	**5.1. Is there an adequate rationale for using a mixed methods design to address the research question?** *Yes (qualitative and quantitative data relevant to process evaluation)* **5.2. Are the different components of the study effectively integrated to answer the research question**? *Yes (integrated in results and discussion)* **5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?** *Yes (see discussion)* **5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?** *Yes (page 11 column 2)* **5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?** *Yes*
Howard 2014[11]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative descriptive	**4.1. Is the sampling strategy relevant to address the research question?** *Yes* **4.2. Is the sample representative of the target population?** *Yes (all interventions recorded)* **4.3. Are the measurements appropriate?** *Yes* **4.4. Is the risk of nonresponse bias low?** *Yes (data from intervention arm only)* **4.5. Is the statistical analysis appropriate to answer the research question?** *Yes*
Jeffries 2017[13]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews and focus groups)* **1.3. Are the findings adequately derived from the data?** *Yes (context-mechanism-outcome groups identified)* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of realist analysis)*
Jeffries 2018[12]	**S1. Are there clear research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (explored factors perceived to affect adoption and implementation)*

	S2. Do the collected data allow to address the research questions? *Yes*		**1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Normalisation Process Theory)*
Lane 2020[22]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (gather opinions about proposed service)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (focus groups and interviews with different staff groups at different sites)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by use of Theoretical Domains Framework)*
Madden 2022[14]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Qualitative	**1.1. Is the qualitative approach appropriate to answer the research question?** *Yes (pharmacists' experience of SMR implementation)* **1.2. Are the qualitative data collection methods adequate to address the research question?** *Yes (interviews with newly employed and established pharmacists)* **1.3. Are the findings adequately derived from the data?** *Yes* **1.4. Is the interpretation of results sufficiently substantiated by data?** *Yes (supported by relevant quotes)* **1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?** *Yes (supported by thematic analysis)*
Peek 2020[15]	**S1. Are there clear research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)*

	S2. Do the collected data allow to address the research questions? *Yes*		**3.3. Are there complete outcome data?** *Yes* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Rodgers 2022[16]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (general practices and their patients)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Can't tell (for intervention)* **3.3. Are there complete outcome data?** *No (6- and 12-month data not collected from all practices)* **3.4. Are the confounders accounted for in the design and analysis?** *No (small risk of unmeasured confounding)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (interventions not externally validated)*
Syafhan 2021[17]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative randomised controlled trial	**2.1. Is randomisation appropriately performed?** *Can't tell (method of randomisation not reported)* **2.2. Are the groups comparable at baseline?** *Yes* **2.3. Are there complete outcome data?** *No (30% lost to follow-up or withdrew)* **2.4. Are outcome assessors blinded to the intervention provided?** *Can't tell (outcome data from GP electronic records)* **2.5 Did the participants adhere to the assigned intervention?** *No (30% lost to follow-up or withdrew)*
Thayer 2021[23]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Yes (care home residents with intellectual disabilities)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (details recorded for each review and associated outcomes)* **3.3. Are there complete outcome data?** *Yes (all specified outcomes reported)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)*

			3.5. During the study period, is the intervention administered (or exposure occurred) as intended? *Yes (one-off review mainly based on records)*
Twigg 2015[24]	**S1. Are there clear research questions?** *Yes* **S2. Do the collected data allow to address the research questions?** *Yes*	Quantitative non-randomised	**3.1. Are the participants representative of the target population?** *Can't tell (no indication of attempts to recruit a representative sample)* **3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?** *Yes (data is recorded for intervention components and associated outcomes)* **3.3. Are there complete outcome data?** *Can't tell (limited response for resource use outcomes)* **3.4. Are the confounders accounted for in the design and analysis?** *No (uncontrolled before/after study)* **3.5. During the study period, is the intervention administered (or exposure occurred) as intended?** *Can't tell (approx. 30% withdrawal rate)*

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	p2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction (pp4-5)
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Methods (p6)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods (p6)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods (p7)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary file
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p7)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods (pp7-8)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods (pp7-8)
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods (pp7-8)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods (p8)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	See methods (p8)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	See methods (p8)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A (summary tables only)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods (p8)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Results (p8)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P10 and Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary table
Study characteristics	17	Cite each included study and present its characteristics.	Tables 1-4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary table
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1-4 where available and appropriate
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results (p22)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results (p22)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion (especially p27)
	23b	Discuss any limitations of the evidence included in the review.	Discussion (especially p26)
	23c	Discuss any limitations of the review processes used.	Discussion (pp27-28)
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion (pp28-29)
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Title page

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Title page
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P9
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data sharing statement (p30)

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/