# Components of pharmacist-led medication reviews and their relationship to outcomes: A systematic review and narrative synthesis.


## Abstract

**Introduction**: Pharmacist-led medication reviews are an established intervention to support patients prescribed multiple medicines or with complex medication regimes. For this systematic review (registered in PROSPERO, CRD42020173907), a medication review was defined as "a consultation between a pharmacist and a patient to review the patient's total medicines use with a view to improve patient health outcomes and minimise medicines related problems". It is not known how varying approaches to medication reviews lead to different outcomes.

**Aim**: To explore the common themes associated with positive outcomes from pharmacist-led medication reviews.

**Method:** Randomised controlled trials of pharmacist-led medication reviews in adults aged 18 and over were included. The search terms used in MEDLINE, EMBASE and Web of Science databases were "medication review", "pharmacist", "randomised controlled trial" and their synonyms, time filter 2015 to September 2023. Studies published before 2015 were identified from a previous systematic review. Risk of bias was assessed using the Cochrane risk of bias 2 tool. Descriptions of medication reviews' components, implementation and outcomes were narratively synthesised to draw out common themes. Results are presented in tables.

**Results**: Sixty-eight papers describing 50 studies met the inclusion criteria. Common themes that emerged from synthesis include collaborative working which may help reduce medicines-related problems and the number of medicines prescribed; patient involvement in goal setting and action planning which may improve patients' ability to take medicines as prescribed and help them achieve

their treatment goals; additional support and follow up, which may lead to improved blood pressure, diabetes control, quality of life and a reduction of medicines-related problems.

**Conclusion**: This systematic review identified common themes and components, e.g., goal setting, action planning, additional support and follow up, that may influence outcomes of pharmacist-led medication reviews. Researchers, health professionals and commissioners could use these for a comprehensive evaluation of medication review implementation.

## Key messages

**What is already known on this topic**

There are a substantial number of publications about medication reviews. However, the implementation of pharmacist-led medication reviews has not been explored in depth by previous authors.

**What this study adds**

This review has identified common themes underpinning the delivery of medication reviews, e.g., pharmacists' skills, experience and access to patient information, goal setting, action planning, additional support, and feedback, that may influence clinical, economic, and patient-reported outcomes.

**How this study might affect research, practice or policy**

Future research may involve stakeholders discussing the common themes underpinning the implementation of pharmacist-led medication reviews to develop a draft programme theory. Policymakers could use the conclusions of this review when updating medication review guidance.

# Introduction

Medication reviews (MRs) are a recognised intervention undertaken by healthcare professionals to support patients prescribed multiple medicines or with complex medication regimes [1]. Taking multiple medicines increases the chance of a patient experiencing adverse effects [2]. It is estimated that up to 7% of hospital admissions in the UK are due to adverse drug reactions (ADRs) [3]. Medication reviews are a recognised intervention with the aim of preventing adverse drug reactions and improving patients' experience of care. However, the evidence for the effects of medication reviews is unclear. Huiskes et al. [4] demonstrated that medication reviews undertaken by any professional in any setting had minimal effects on clinical outcomes and that evidence is lacking about their effect on economic outcomes. The implementation of medication reviews in practice was recognised as a factor which may influence outcomes, but this has not been explored further.

Many countries offer pharmacist-led medication reviews, including Australia, USA, Canada, Switzerland, Spain, and Germany [5–10]. Pharmacist-led medication reviews are an established intervention in primary care policy and practice in England [11]. Currently, the evidence for effectiveness of medication reviews is sub-optimal, and this is partly due to the lack of studies exploring which components of the medication review generate positive outcomes [12]. The Medical Research Council (MRC) produced guidance for the process evaluation of complex interventions, such as medication reviews. This framework highlights the relationships between implementation, mechanisms and context [13]. The National Institute for Health and Care Research (NIHR) and MRC Framework for evaluating complex interventions suggests investigating which components lead to the outcome(s) of interest, why and in what settings, to ensure they are acceptable, implementable, cost effective, and transferable across contexts [14]. This systematic review undertook an in-depth exploration of pharmacist-led medication

reviews to understand which components are associated with positive outcomes for patients, practitioners, and the health system.

### Aim

To explore the common themes associated with positive outcomes from pharmacist-led medication reviews.

This aim will be achieved by pursuing the following objectives in relation to medication reviews:

1. Describe their components
2. Describe their implementation
3. Describe the reported outcomes
4. Examine potential mechanisms of impact

## Method

To answer the aims and objectives a systematic review with narrative synthesis was undertaken.

### Search strategy

Based on a pragmatic approach to searching the literature, the systematic review by Huiskes was used to identify relevant papers (those focussing on pharmacist-led medication reviews) prior to 2015 [4]. The MEDLINE, EMBASE and Web of Science databases were utilised for the literature search, from 2015 to September 2023, using the same search terms used by Huiskes et al [4]. The search terms used were "medication review", "pharmacist" and "randomised controlled trial" and synonyms. The full search strategy is outlined in **supplementary material 1.** The search was supplemented during data extraction by identifying companion papers for the included studies.

## Inclusion/ Exclusion criteria

The identified papers were screened based on the following inclusion and exclusion criteria.

Population: adults 18 years and over who received a medication review delivered by a pharmacist, either alone or as part of a multi-disciplinary team, in any setting.

Intervention: medication review, which for the purpose of this review is defined as "a consultation between a pharmacist and a patient to review the patient's total medicines use with a view to improve patient health outcomes and minimise medicines related problems". Studies were excluded if the medication review was part of a wider intervention, for example, to improve diabetes care where medication review was just one part of the process.

Comparison: usual care (no medication review) or a medication review delivered by another healthcare professional.

Outcomes: studies reporting any outcomes.

Study design: randomised controlled trials and their protocol and process evaluation papers.

Time and financial constraints did not allow for translation from other languages, therefore only English language articles were included. Conference abstracts and articles where full texts were not available were excluded.

## Screening

One reviewer (MC) independently screened titles/ abstracts and full-text articles, with twenty percent of abstracts and full-texts independently reviewed by a second reviewer (HAJ). Disagreements were resolved through discussion, with a third reviewer (MJT) utilised when needed.

## Data extraction

Data was extracted from full text articles using a bespoke data collection form by one reviewer (MC). Details of the data collection form (informed by the TIDieR framework [15]), is included in **supplementary material 2**. The form was piloted with several studies. The form captured the following information: study characteristics, descriptions of intervention and comparator, details of implementation, outcomes, and mechanisms of impact. Classification of the outcomes was based upon the international core outcome set for clinical trials for medication review in multi-morbid older patients with polypharmacy and the patient relevant outcomes identified in a scoping review by Kersting et al. [16,17]. Pharmacist implementation of the medication review was mapped to the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy [18] to describe the delivery processes.

Medication review outcomes are influenced, among other things, by pharmacist and patient behaviour change (supporting medication adherence and taking medication as prescribed [19], respectively). These behaviour change components have not been recognised explicitly in the medication review literature and their design. However, they are present, and it is therefore justified to extract BCTs using the BCT Taxonomy v1 [20], as done with other clinical interventions [21–23]. We used the taxonomy to extract BCTs used by the pharmacist during the consultation to support the patient in taking their medications as directed (adherence). This allows the field to understand common and promising BCTs, as well as evidence-based BCTs which medication reviews have rarely included.

Many intervention reports do not provide clear descriptions of BCTs, so we coded any BCTs either as present in all probability (evidence not clearly reported) or present beyond all reasonable doubt (clear evidence reported for their presence) [24]. BCTs were coded in both the intervention groups (medication review) and comparison groups to understand unique BCTs included in the intervention

only. We coded BCTs in relation to a specific behaviour (supporting medication adherence) employed by one actor (pharmacist), whilst the implementation strategies apply to the whole intervention. BCTs and implementation strategies were coded independently from each other.

Mechanisms of impact are the intermediate mechanisms through which intervention activities produce intended (or unintended) effects [13]. Mechanisms of impact include:

- participant responses and interaction with the intervention (in this case, patient)
- mediators (intermediate processes which explain subsequent changes in outcomes [13]). In this review, the mediators extracted were at a participant level, where the participant was the pharmacist.
- moderators of effect (factors likely to influence intervention effectiveness [13])
- unanticipated pathways and consequences.

## Rigour

This review has been reported in accordance with the PRISMA guidelines [25] and the protocol was registered in PROSPERO (CRD42020173907). Data extraction from 20% of randomly selected studies was checked by MJT and WH. In addition to the 20% random sample, WH checked BCT extraction of a further sample of six studies to check for consistency with coding BCTs. WH has extensive expertise in identification of BCTs as co-author of the BCT Taxonomy v1 [20]. Data extraction enabled the identification of shared characteristics, relationships, and patterns. Narrative synthesis of the extracted data enabled an analysis of these relationships and patterns which were discussed regularly by the research team.

Quality assessment

Risk of bias was assessed by the first author (MC) using the Cochrane risk of bias 2 tool for randomised controlled trials [26]. Twenty percent of studies were assessed by another reviewer (MJT).

## Data synthesis

Extracted data describing medication review components, implementation and outcomes is reported in tables. These descriptions were narratively synthesised to draw out common themes. Narrative approaches are useful in generating ideas and theories, particularly around how and why an intervention might work and in what circumstances [27]. Data was interpreted by MC that could describe potential mechanisms of impact and contextual influences on medication review implementation from the results and discussion sections. In the process of data extraction, notes were taken of points that could be useful in synthesis. Confidence in the outcomes (results of the studies) included in the systematic review is an important consideration in narrative synthesis [26]. Therefore, the low risk of bias studies [28–35], with statistically significant results, were the starting point for drawing out common themes, which were added to and amended with the results from the higher risk of bias studies. The themes were inductively coded to the TIDieR framework (where, who, how, when and how much) [15], and emerging BCTs [20]. Themes were further broken down to components which reflect the physical, organisational, social dimensions of the health system context in which the medication review is implemented [14].

The GRADE framework [36] informed the overall assessment of the quality of the evidence from the studies, where it was classified as high, moderate, low, or very-low quality. Inconsistency, imprecision, and indirectness of the reported outcomes, taken holistically, influenced the overall quality of the evidence. Data was presented and discussed among the authors during a series of meetings to finalise the conclusions of this review.

# Results

## Study selection

The literature search yielded 11,946 results, with another 33 studies already identified by Huiskes et al.[4]. Deduplication reduced this to 10,947. Titles were screened and 597 abstracts were identified. Abstracts were reviewed by HAJ with substantial agreement (81% Cohen's κ =0.61). Screening of 534 abstracts reduced the total number of papers to be reviewed at full text to 246. Sixty-eight papers describing 50 individual studies were included for data extraction (see Figure 1). Interrater reliability at full text screening was 89%, Cohen's κ =0.77, indicating good agreement[37].

## Characteristics of included studies

A detailed description of the characteristics of the medication reviews can be found in **supplementary material 3**. Most studies included in this review were undertaken in Europe (23) [30,31,35,38–57], with twelve in Asia [28,32,33,58–66], eight in North America [29,67–73], and the remaining from Australia [74–77], South America [34,78] and Africa [79]. Nearly a third of studies (14) were undertaken in a hospital setting [30,38,39,41,46,48,51,56,59,60,63,67,74], with the remaining studies taking place in various primary care environments, except for six which were undertaken in outpatient departments [32,33,44,64,78,79]. Almost half of studies (22) recruited patients aged 60 years or older [30,31,34,39,40,42,43,45,46,48,52–55,65,68,73–75,77,80], with the other studies recruiting adult patients who had one or more long term conditions(s) or were taking at least four medicines. Study sample size ranged from 60 to 2637 participants.

## Quality assessment

Following the application of the Cochrane risk of Bias 2 tool [26], most studies (32) were deemed to be at high risk of bias (ROB) [41–57,60–65,69–71,73–77,79], ten studies at some ROB [38–40,58,59,67,68,72,78,81], and eight were rated low [28–35]. **Supplementary material 4** shows the risk of bias for each study in more detail. Sample sizes of the low risk of bias studies ranged from 80 to 600 participants. The domain that led to most studies being assessed at high risk was "Bias in measurement of the outcome". As pharmacists conducting the medication reviews were largely responsible for identification and measurement of the primary outcome measure i.e., medication related problems, this led to a high risk of bias in many studies.

## Content of medication review

A detailed description of the content of the medication reviews can be found in **supplementary material 3**. In summary, all 50 medication reviews sought to identify medicines related problems; 33 to address patient adherence [28–35,40–42,44–47,49,50,52,53,55–57,60–65,70,75,76,78,79], and 29 to educate patients on their medicines/ conditions [28–35,38,40,45,46,49,51,52,58–65,67,69,70,74,78,79]. In 42 studies, pharmacists aimed to resolve medicines-related problems during the medication review. In three studies [29,40,50], pharmacists could make prescription changes following the review. Follow up with patients was part of the medication review in 40 studies but follow up with prescribers following referrals occurred less frequently and was only reported in fourteen [28,29,31,35,42,51,53,55,60–62,64,73,78].

## Reporting of Behaviour Change Techniques (BCTs) in studies

The quality of intervention reports was insufficient to make a definitive judgment about BCTs. However, all studies included at least one BCT relating to intervention patients taking their medicines. The BCTs are summarised in **supplementary material 5**. The BCT "monitoring outcome(s) of behaviour by others without feedback" was present in all probability in 37 studies [28,30–35,38,39,41,42,44–50,52,53,55–60,62,64–67,72–77], in terms of identifying medicines-related problems. The BCT "monitoring of behaviour by others without feedback" was present in all probability in 23 studies where medicines were reviewed and questions asked about patients' use of medicines [29,30,35,41–46,50–53,55,60,62,64,68,70,71,75,76,79]. The BCT "information about health consequences" was present beyond reasonable doubt in six studies where patients were advised about the importance of taking their medicines as prescribed and possible consequences of non-adherence [29,47,49,56,62,78]. In five studies, goal setting in relation to behaviour was present beyond reasonable doubt [40,45,52,53,56], where an action plan or goals were established to help with patients' medicines or health.

## Medication review implementation as described in the studies

The description of the implementation of medication reviews was poorly reported. In 34 studies there was sufficient detail about the intervention to identify EPOC taxonomy domains and subcategories. Details of the EPOC taxonomy subcategories identified in each study can be found in **supplementary material 5**. The most reported EPOC subcategory was communication between providers, where a system or strategy for improving the communication between the pharmacist and other health care providers was reported [29,31,33,39,44,48,58,60–64,66,67,76,82]. Other EPOC taxonomy domains were identified in fewer studies.

Planned adaptations to the intervention were reported in eight studies [34,35,38,40,49,56,58,62]. Adaptations during the intervention were reported in eight studies; examples include adapting care plans according to patient needs and modifying the intervention based upon pharmacists' professional judgment [29,30,43,47,48,69,77,83]. Fidelity of the intervention was assessed in five studies [34,35,46,49,83]. Anderegg described non-adherence to the communication process for the latter part of the study [29]. Kempen et al. reported that 15% of control patients received unintended intervention components [46]. Graabaek et al. reported that as the staff were unaccustomed to working with the pharmacist, and the physician did not make use of the pharmacist at the start of the study [30]. The implementation rates of pharmacist recommendations was between 28.6% [58] to 86% [40].

## Description of reported outcomes

A mixture of economic, clinical, and patient-orientated outcomes were reported. Economic and clinical outcomes were most frequently reported. Healthcare utilisation was reported in 25 studies [30,31,34,35,39–41,43,45,46,48,50–56,63,70,72,73,75,76,79], medicines-relates problems/ adverse drug events/ medication appropriateness in 23 [30,32,42,44,48,52,53,55,57,58,60–67,69,71,74,77,78] , and clinical monitoring parameters in 17 [29,33,34,38,42,45,49,50,53,54,56,63,66,70,74,77,78]. Patient-orientated were reported least often with 17 studies reporting quality of life [31,33,35,39,41,43,45,53,57–59,62,65,68,73,74,77], and 14 adherence [28,32,34,48,50,56–58,62–65,78,79]. **Supplementary material 6** details all reported outcomes.

Of the eight studies that were assessed to be of low risk of bias, fourteen results were statistically significant. Two of these studies reported improvements in blood pressure in the intervention groups; mean reduction in systolic blood pressure (8.64 mm Hg; 95% CI −12.8 to −4.49) [29], achievement of hypertension treatment goals, (OR 4.37; 95% CI 2.54 to 7.51) [34]. Reduction in the number of

medicines prescribed in the intervention group was observed in two studies (mean difference-0.86; 95% CI-1.14 to -0.58 [34], mean difference of -0.87; 95% CI −1.66 to −0.08, [31]). Lim et al. and Martinez-Mardones et al. stated that medication reviews improved compliance/adherence (OR 2.52, 90% CI 1.09-5.83 [32]), OR 6.60; 95% CI 1.36 to 31.9 [34]). Statistically significant results are reported in Table 1.

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| Author (Year) | Statistically significant results | BCTs (patients taking medications as directed) | Implementation strategies | Risk of Bias |
|---|---|---|---|---|
| Alalawneh 2022 [28] | Improvement in adherence in intervention group<br>Improvement on knowledge of medicines in intervention group | *2.5 Monitoring of outcomes of behaviour by others without feedback,*<br>*2.7 Feedback on outcome of behaviour*<br>*5.1 Information about health consequences* | NR | Low |
| Anderegg 2018 [29] | Reduction in SBP in intervention group; much smaller reduction of SBP in the control group.<br>Increase in the number of medication changes in intervention group | *1.3 Goal setting (outcome), 2.1 Monitoring of behaviour by others without feedback,* **5.1 information about health consequences**<br>*11.1 Pharmacological support,* **12.5 Adding objects to the environment** | Communication between providers | Low |
| Lenaghan 2007 [31] | Reduction of medicines prescribed in intervention group compared to control | *1.7 Review outcome goal(s), 2.5 Monitoring of outcomes of behaviour by others without feedback, 5.1 Information about health consequences*<br>*12.5 Adding objects to the environment* | Communication between providers | Low |
| Lim 2004 [32] | Improved compliance in intervention group | *2.5 Monitoring of outcomes of behaviour by others without feedback*<br>**4.1 Instruction on how to perform a behaviour, 3.2 Social support (practical)**<br>*5.1 Information on health consequences, 12.5 Adding objects to the environment* | NR | Low |
| Lin 2018 [33] | Improvement in quality of life in intervention group<br>Improvement in performance in activities of daily living in intervention group<br>*Estimates reduction in medical expenditure in intervention group (3,758 TWD)* | *2.5 monitoring of outcomes of behaviour without feedback* | Role expansion or task shifting<br>Environment, Teams<br>Communication between providers | Low |
| Maritnez-Mardones (2023) [34]<br>Ahumada-Canale 2021a, 2021b [84,85] | Higher number of patients with hypertension, diabetes and high cholesterol achieving therapy goals in intervention group compared to control.<br>Reduced cardiovascular risk score for those in intervention group compared to control.<br>Reduced number of medicines prescribed in intervention group compared to control.<br>Improvement in adherence in intervention group compared to control. | *2.5 monitoring of outcomes of behaviour without feedback*<br>*2.7 Feedback on outcome of behaviour* | Educational meetings<br>Educational outreach | Low |
| Schulz 2019 Schulz 2020 Laufs 2018 [35,80,86], | Improvement in quality of life in intervention group<br>Increased adherence after 365 days in intervention group | *1.5 review behaviour goal, 2.1 Monitoring of behaviour by others without feedback, 2.5 monitoring of outcomes of behaviour, 3.1 Social support (unspecified), 5.1 Information on health consequences,* **12.5 Adding objects to the environment** | Educational material | Low |
| Aguiar 2018 [78] | Improvement in adherence in intervention group<br>Improved chance of achieving HbA1c goal in intervention group compared to control | *1.1 Goal setting (behaviour),* **2.4 Self-monitoring the outcome(s) of behaviour**<br>**5.1 Information about health consequences, 12.5 Add objects to the environment** | Environment<br>Role expansion or task shifting | Some |
| Basheti 2016[66] | Higher resolution of MRPs in intervention group than control. Improvements in blood pressure, blood glucose, triglycerides in intervention group compared to control | *2.5 monitoring of outcomes of behaviour without feedback* | Communication between providers<br>Role expansion or task shifting | Some |
| Basheti 2018 [58] | Improvement in adherence in intervention group compared to control<br>Improvement in self-care in intervention group | *2.5 monitoring of outcomes of behaviour without feedback*<br>*5.1 Information on health consequences* | Communication between providers | Some |
| Garcia 2015 [38] | Improvement in adherence in intervention group compared to control | **1.2 problem solving,** *2.5 Monitoring of outcomes of behaviour without feedback,*<br>**3.1 Social support (unspecified),** *5.1 Information about health consequences* | NR | Some |
| Jameson 1995 [67] | Change in number of medicines at follow up in intervention group compared to control.<br>Evidence of a 24% reduction of healthcare costs in intervention group | *2.5 monitoring of outcomes of behaviour without feedback*<br>*5.1 Information about health consequences* | Communication between providers | Some |
| Lisby 2018 [39] | Improvement in usual activities in intervention group | *2.5 monitoring of outcomes of behaviour without feedback* | Communication between providers | Some |
| Sakthong 2018 [59] | Improvement in post intervention quality of life in intervention group | *1.1 Goal setting (behaviour),* **1.2 Problem solving,** *2.5 monitoring of outcomes of behaviour without feedback, 2.7 Feedback on outcome of behaviour* | NR | Some |
| Williams 2004 [68] | Reduction in the number of medicines prescribed; on average 2.1 fewer drugs prescribed in the intervention group<br>Reduction in medication costs at 6 weeks; mean $38 saving in intervention group | **1.4 Action planning,** *2.1 Monitoring of behaviour by others without feedback*<br>*3.1 Social support (unspecified, 5.1 Information about health consequences*<br>*12.5 Adding objects to the environment* | Teams | Some |
| Zermansky 2002[40] | Smaller rise in number of medicines prescribed in the intervention group (number of medicines prescribed increased in both groups); Smaller rise in mean cost of medicines in intervention group (Cost of medicines increased in both groups) | **1.1 Goal setting (behaviour), 1.4 Action planning**<br>*3.1 social support (unspecified), 5.1 Information about health consequences*<br>*11.1 Pharmacological support* | Environment<br>Role expansion or task shifting<br>Communication between providers | Some |
| Aburuz 2020[60] | Reduction of MRPs at discharge in intervention group; twice as many MRPs at discharge in control group | *2.5 monitoring of outcomes of behaviour without feedback, 5.1 Information about health consequences,* **2.1 Monitoring of behaviour by others without feedback** | Environment<br>Communication between providers | High |
| Al alawneh 2019 [61] | Reduction in MRPs at follow up in intervention group, no significant change in control | *3.1 social support (unspecified)* | Communication between providers<br>Outreach services | High |
| Al-Qudah 2018, Basheti 2016 [62,81] | Significantly higher number of MRPs corrected at the end of the study in the intervention group compared to control; Improvement in medication adherence at follow up in intervention group; Improvement in self-care activity scores at follow up in intervention group | **2.1 Monitoring of behaviour by others without feedback**<br>*2.5 monitoring of outcomes of behaviour without feedback*<br>**5.1 Information about health consequences** | Communication between providers | High |

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|---|---|---|---|---|
| Briggs 2015[75] | Reduction in admission rates in intervention group | **2.1 Monitoring of behaviour by others without feedback**<br>*2.5 Monitoring of outcomes of behaviour by others without feedback* | NR | High |
| El-Refae 2017 [63] | Reduction in hospital visits in intervention group; Reduction Total cholesterol in intervention group; Improvement in self-care activities in intervention group | **3.2 Social support (practical),** *5.1 Information about health consequences*<br>*12.5 Adding objects to the environment* | Communication between providers | High |
| Erku 2017 [79] | Reduction in hospitalisation visits; number of visits in control group more than double those in intervention; Improvement in medication adherence in intervention group; 51.8% change in intervention v 17% in control | *2.1 Monitoring of behaviour by others without feedback* | NR | High |
| Freeman 2021, Foot 2017 [76,87] | Reduction in hospital re-admission/ ED presentation in intervention group<br>Estimated incremental cost per patient of the intervention = $164, benefit– cost ratio, 31:1 | *2.1 Monitoring of behaviour by others without feedback*<br>*2.5 Monitoring of outcomes of behaviour by others without feedback* | Teams; Environment; Payment methods for health workers; Educational meetings; Communication between providers | High |
| Holland 2005, 2010 [43,88], Pacini 2007 [89] | Increase in hospital readmission rate and GP home visits in intervention group<br>Reduction in medication hoarding in intervention group | *2.1 Monitoring of behaviour by others without feedback, 3.2 Social support (practical), 12.5 Adding objects to the environment, 5.1 Information about health consequences* | Educational meetings; Referral systems; Payment methods for health workers | High |
| Krska 2001 [55] | More MRPs resolved at follow up; double the number of MRPs resolved in intervention compared to control | *1.1 Goal setting (behaviour), 1.2 Problem solving, 1.4 Action planning*<br>*2.1 Monitoring of behaviour by others without feedback*<br>*2.5 Monitoring of outcomes of behaviour by others without feedback* | NR | High |
| Lea 2020 [47] | Increased overall survival in intervention group HR= 0.66, 95% CI 0.48 to 0.90, p=0.008 | *1.2 Problem solving, 2.5 Monitoring of outcomes of behaviour by others without feedback,* **5.1 Information about health consequences**<br>**12.5 Adding objects to the environment** | Teams<br>Environment | High |
| Lenssen 2018 [48] | Improvement in adherence in the intervention group; 5.7% non-adherent in intervention compared to 14% in control | *1.2 Problem solving, 2.5 Monitoring of outcomes of behaviour by others without feedback* | Communication between providers<br>Environment | High |
| Liou 2021 [65] | Reduction of MRPs at follow up; Improvement in medication adherence in intervention group; 10% in intervention compared with 8.7% in control. Participants in intervention group more willing to receive pharmacist visits; (mean, SD) Intervention = 8.9±2.2, Control =7.4±3.1, P=0.04. Improved awareness of medical problems in intervention group; (mean SD) Intervention= 3.0±4.0, Control =0.9±2.7, P=0.035 | *2.5 Monitoring of outcomes of behaviour by others without feedback*<br>**12.5 Adding objects to the environment** | Environment<br>Educational meetings | High |
| Malet-Larrea 2016[45] Jodar-Sanchez2015[83], VarasDoval 2020 [90] | Improvement in quality of life in intervention group. Reduction in number of hospital admissions; mean number of visits were double in the control than in intervention group. Reduction in health problems over 6 months in intervention group | **1.1 Goal setting (behaviour)**<br>*2.1 Monitoring of behaviour by others without feedback*<br>*2.5 Monitoring of outcomes of behaviour by others without feedback* | Educational outreach visits<br>Educational meetings | High |
| Nabergoj Makovec 2021 [57] | Reduction of MRPs at follow up. | *2.5 Monitoring of outcomes of behaviour by others without feedback*<br>**12.5 Adding objects to the environment** | Educational meetings | High |
| Ravn-Nielsen 2018[51] Rasmussen 2019 [91] | NNT for readmissions within 180 days Extended intervention =11, Basic intervention = 65 | 2.1 Monitoring of behaviour by others without feedback, **3.1 Social support (unspecified**) | Referral systems<br>Educational meetings | High |
| Shim 2018 [64] | Improvement in prescribing (medication appropriateness index) in intervention group, Improvement in adherence in intervention group; more than double the number of participants in intervention group were adherent compared to control | *1.2 Problem solving,* **2.1 Monitoring of behaviour by others without feedback**<br>*2.5 Monitoring of outcomes of behaviour by others without feedback*<br>*3.1 Social support (unspecified*) | Communication between providers | High |
| van der Heijden 2019, Ahmad 2010[52,92] | Reduction in MRPs in intervention group<br>Increase in hospital readmissions in intervention group; double the number of readmissions in intervention than control | **1.1 Goal setting (behaviour),** *1.4 Action planning,* **2.1 Monitoring of behaviour by others without feedback,** *2.5 Monitoring of outcomes of behaviour by others without feedback,* **3.1 Social support unspecified**<br>*11.1 pharmacological support, 12.5 adding objects to environment* | NR | High |
| Verdoorn 2019[53], Verdoorn 2018[93], Verdoorn 2021 [94] | Improvements in quality of life in intervention group<br>Improvement in health problems in intervention group | **1.1 Goal setting (behaviour),** *1.2 Problem solving,* **1.4 Action planning**<br>**1.5 review behaviour goals, 2.1 Monitoring of behaviour by others without feedback,** *2.5 Monitoring of outcomes of behaviour by others without feedback* | Educational meetings<br>Communication between providers | High |
| Zermansky 2006 [54] | Reduction in falls per patient in intervention group; mean 0.5 less per 6 months in intervention compared to control group. Increase in the number of drug changes in 6 months in the intervention group compared to control | *2.1 Monitoring of behaviour by others without feedback* | NR | High |
| Zillich 2014 [71] | Reduction in 60-day hospitalisations for low-risk patients in intervention group OR 3.78 (1.35, 10.57) p=0 .01 | **1.1 Goal setting (behaviour), 1.2 Problem solving, 1.4 Action planning**<br>*2.1 Monitoring of behaviour by others without feedback* | NR | High |

**Key** SBP = systolic blood pressure DBP= diastolic blood pressure GP= general practitioner ADR= adverse drug reaction MRP= medicines related problem HbA1c= glycated haemoglobin LDL=low density lipoprotein HDL= high density lipoprotein NNT= number needed to treat ADE= adverse drug event ICER= incremental cost-effectiveness ratio QALY= quality adjusted life year SMMESE= standardised mini mental state exam TWD= Taiwanese new dollars NR= not reported BCTs= Behaviour Change Techniques **BCT present beyond all reasonable doubt** *BCT present in all probability*

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## Mechanisms of impact

Potential mechanisms of impact were not easily identifiable. When exploring participant responses to, and interaction with, the intervention, data could only be extracted from one study [69], which reported that many patients declined the intervention. For the included studies, only two process evaluations enabled the identification of mediators [88,95].

Ten studies reported an unintended pathway or consequence [29,38,40,43,52,58,60–62,66]. Examples include financial or health-related barriers preventing patients attending follow-up appointments [58,61,62], and increased utilisation of healthcare practitioners due to pharmacist referrals, or patients' concern following increased patient knowledge about medication side effects [40,52]. **Supplementary material 7** provides further information about potential mechanisms of impact.

## Description of comparator groups

The comparator interventions were poorly reported, with thirteen studies providing no details. Thirty-four studies described the content of the comparator intervention: sixteen studies [30,39,40,46,47,52,53,55,58,60–63,71,78,81] sought to identify medicines-related problems, ten educated patients about their medicines/ condition(s) [35,38,52,69–71,74,78] and three focused on improving adherence [55,61,79]. Where the healthcare professionals involved in delivering care was identified, pharmacists delivered the care in nine studies [40,45,53,55,58,61–63,81], physicians in nine [30,38,39,41,44,54,73,76,79], nursing staff in five [56,65,70,71,74] and a mixture of healthcare professionals in the remaining studies [34,35,47–49,52,60,64,78].

Only ten studies reported at least one BCT relating to patients taking their medicines as directed in the comparator groups [28,44,47,56,58,60,62,64,70,81]. Where medicines-related problems were explored in the comparator group, the BCT "monitoring of outcomes of behaviour by others without

feedback" was present in all probability in six studies [28,44,47,58,60,81]. The BCTs are reported in **supplementary material 5**.

The themes underpinning medication review implementation and an explanation of how these may influence outcomes is presented in Table 2. Figure 2 illustrates the components of medication reviews.

Table 2 Themes underpinning medication review (MR) implementation.

| Themes | Explanation |
|---|---|
| Setting in which medication review is delivered | There is moderate quality evidence from low [29,31,34,35] , some [40,58,66–68] and high [45,53,54,62] risk of bias studies that medication reviews undertaken in primary care settings may have a greater impact on some outcomes, such as reduction in clinical biomarkers, number of medicines prescribed, adherence, and quality of life, whereas healthcare utilisation and mortality may not be affected. |
| | There is low quality evidence from studies with some [40,78] and a high [47,60,76] risk of bias that pharmacists with access to other healthcare professionals, such as physicians, can improve some clinical, economic, and patient-orientated outcomes, such as improved diabetes biomarkers and adherence, and reduced hospital re-admissions and medicines related problems.<br><br>There is low quality evidence from low risk of bias studies that pharmacists working collaboratively with other healthcare professionals, where their roles and responsibilities are known, may have a positive influence on outcomes[29,30], such as a reduction in prescribed medicines.[32] |
| | There is very low-quality evidence from studies with some risk of bias [58,66] that a safe, comfortable, not restricted, and professional space to conduct the medication review may improve blood pressure, blood glucose and triglyceride levels, lead to a higher resolution of medicines related problems and improve adherence and self-care activities. |
| | Three studies reported that medication reviews were only able to be delivered on specific days at specified times [30,41,75]. One low risk of bias study suggested that pharmacists lack of availability for all the operational times of the setting influenced the implementation of the intervention [29]. It is unclear how this affected outcomes. |
| Regulations and standards guiding medication review | There is low quality evidence from a low risk of bias study that medication reviews cannot be properly implemented without a protocol, and this may result in variation in delivery, which might negatively influence outcomes[29]. Furthermore, low quality evidence from low [29] and some [38] risk of bias studies that pharmacists' ability to adjust the MR content according to the patient's needs may reduce blood pressure, increase the number of medication changes, and improve adherence. |
| Recruitment of patients for medication review | Participants are often identified by another individual and referred to the pharmacist for the medication review. There is low quality evidence from low[29–31,34,35], some [67,78] and high [42,43,53,69,71,73,75,79] risk of bias studies that this may influence clinical, economic, and patient-orientated outcomes. However, it is unclear how this occurs. |
| Pharmacist skills and experience | There is moderate quality evidence from low [29,34], some[40], and high [75,76] risk of bias studies that pharmacists with greater clinical knowledge/ experience may improve blood pressure and reduce medicine costs and healthcare utilisation.<br><br>There is low quality evidence from low [29] and some [40] risk of bias studies that pharmacists having the autonomy to make some medication changes may positively influence blood pressure control and number of medicines prescribed. Furthermore, it was suggested that improved blood pressure control was likely due to implementing changes to blood pressure goals in line with new [more intensive] guidelines[29]. |

| | |
|---|---|
| Access to patient information | There is moderate quality evidence from low[28,30–32,34,35], some [38–40,59,66,78] and high [44,47,48,51,52,54,55,60–63,65] risk of bias studies that pharmacists having access to clinical and medication history for the medication review may have a positive influence on clinical, economic, and patient-orientated outcomes, such as blood pressure, number of medicines prescribed, adherence and quality of life. |
| Setting goals relating to medication taking | There is moderate quality evidence from low[30], some[40,59], and high [45,53,55,70,71] risk of bias studies that setting behaviour goals around taking their medicines, may influence outcomes such as quality of life. |
| Information about medicines and health | There is moderate quality evidence from low [29,31,35], some[66,78], and high [63] risk of bias studies that educating the patient/ carer about the reasons for taking the medicines, how medicines work, how they should be taken and the importance of healthy living may have a greater impact on some outcomes, such as improvement in clinical biomarkers, number of medicines prescribed, adherence, and quality of life. |
| Action planning for medicines use | There is low quality evidence from some [40,68] and high [52,53,55,71] risk of bias studies that developing an action plan for medicines management/ pharmaceutical care plan can have a greater impact on clinical, economic, and patient-orientated outcomes, such as an improvement in health problems, medicines related problems, number of medicines prescribed, and quality of life. |
| Social support from pharmacist and/ or other health and social care providers | There is moderate quality evidence from low [32,35], some [78], and high [49,50,63] risk of bias studies that the use of medication aids may improve adherence. However, patients may need help filling it with the correct medication[43]. |
| Follow up with patient following medication review | There is moderate quality evidence from studies with low[28,29,34,35], some [38,40,58,59,66,67,78], and high [45,48,52,53,55,57,60–65,79] risk of bias that at least one follow up appointment after the MR may result in improvements in clinical biomarkers, adherence, quality of life, a reduction of medicines related problems and increased medicine changes [36] |
| | Studies with some [58] and high [61,62] risk of bias reported that financial limitations can restrict patients' access to practitioners for follow up appointments. However, this does not appear to have impacted on outcomes. |

## Discussion

This review has outlined the common themes underpinning the implementation of pharmacist-led medication reviews and the components that may have a positive impact on outcomes. The findings can be applied at micro and macro levels. Pharmacists could evaluate their own knowledge, experience, and processes; and consider whether to include components, e.g., goal setting, action planning, education, in consultations. Commissioners could provide a framework for the delivery of medication reviews, outlining minimum level of pharmacists' clinical knowledge/training and guidance about issues to be discussed and documented.

Hikaka et al. found that pharmacists are poorly embedded in the healthcare framework and suggested that using pharmacists for their expert medicines' knowledge could free up other

healthcare professionals [96]. We identified evidence of role expansion or task shifting by pharmacists as they delivered medication reviews. In addition, there was evidence of pharmacists being added to workplace environments and participating in team -based discussions around patient care. Communication between pharmacists and physicians in any form is an essential part of the implementation of medication reviews; this was also identified by Luetsch et al. [97]. [30]

Role expansion has been observed in England where pharmacists are delivering structured medication reviews in general practice [11]. NHS England's Network Contract Directed Enhanced Service stipulates that clinical pharmacists delivering structured medication reviews should be enrolled in, or have qualified from, an approved training pathway that enables them to be a prescriber, and work with and alongside the general practice team [11]. The General Pharmaceutical Council standards for the education and training of pharmacist independent prescribers outlines four domains which must be covered by providers, one of which is collaboration. This stipulates that pharmacist must work collaboratively with others and demonstrate competence in consultation skills [98]. This additional training may influence some outcomes.

Luetsch et al. reported that recognition of pharmacists' competence and skill to perform medication reviews and pharmacist access to comprehensive clinical information can influence outcomes [97]. This supports our conclusion that pharmacist access to patients' clinical and medical history may improve clinical, economic, and patient-reported outcomes.

McCahon et al. developed a simple and pragmatic medication review model to be used by professionals across healthcare settings [99]. This Bristol medication review model [99] describes the need to establish what medicines the patient is taking, how they are taking them, whether they

understand why they are prescribed and whether the medicines prescribed are suitable for the patient. These examples support our findings, which show that educating the patient/ carer about the medicines can benefit some outcomes. The Bristol medication review model also emphasises the importance of patients' values and preferences [99]. Setting individual goals and planning with the patient demonstrates a commitment to regarding patient preferences. Our review takes this further and suggests that setting goals in relation to medication taking may improve patient outcomes.

Our review identified patient preference as a potential mechanism of impact of medication reviews. This was demonstrated by acceptability (patients declining intervention) and accessibility (financial or health barriers to follow up). Patient preference (accessibility, acceptability and convenience of location and time for the medication review and who performs it) was identified as a mechanism influencing outcomes in a realist synthesis of pharmacist-conducted medication reviews in primary care after leaving hospital [97].

Strengths and limitations

We used robust and transparent methods in reviewing the international medication review literature. Only studies published in English were included, so there is a possibility that relevant studies are missing. Whilst this review has provided a comprehensive overview of pharmacist-led medication reviews, the inclusion of all patient populations and diseases may have influenced conclusions; some components of medication reviews may be more/ less significant in different patient groups. Narrative synthesis was an appropriate approach given the heterogeneity in the included studies [27].

Medication reviews aim to “improve patient health outcomes”. We identified BCTs used in medication reviews, enabling the field to move forward in terms of making behaviour change explicit and create a point of discussion within the medication review community.

Quality assessment, evaluation of the quality of the evidence and a clear definition of the intervention, which ensured there was enough information to assess a study’s suitable for inclusion, attest the robustness of the synthesis. Most studies were assessed to be high risk of bias. This needs to be considered when interpretating the findings, as inclusion of results of studies deemed to be at high risk of bias may result in overestimating the size of the effect. This narrative synthesis has yielded some important themes, but it is a thematic summary and not a meta-analysis.

The reported outcomes were mapped to existing classifications. [16,17] The Beuscart core outcome set is concise and focussed on older patients, whereas this review includes all patients, therefore the Kersting scoping review was used to expand the classification to capture all outcomes of interest. Most studies choose to report economic or clinical outcomes, with little focus on those reported by patients. If future studies measure more patient-reported outcomes, medication reviews may be seen to have a greater impact on these [100].

## Conclusions

This systematic review explored pharmacist-led medication reviews and outlined the common themes in design, delivery and implementation that may influence outcomes. Further empirical testing is required given that the literature is often beset by poor reporting. Proposed themes include patient involvement in goal setting and action planning, and additional support and follow up; individual pharmacists can evaluate how these can be incorporated in their practice. Better exploration and elucidation of these key themes is required to obtain greater understanding of pharmacist-led medication reviews. This could involve a study exploring the effect of an “optimised”

medication review, i.e., one that contains the components identified in this review, on patient outcomes.

Figure 1 PRISMA diagram of literature search and study selection

Figure 2 Illustration of components of medication review

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