RPS Literature Search on Polypharmacy

Scope of the literature review

This literature review was conducted in June 2018 by Keele Centre for Medicines Optimisation.

Primary question: What is the available evidence from the last five years that describes healthcare interventions and/or collaboration with patients that helped to reduce inappropriate polypharmacy?

Secondary question: What are the system levers that enabled this change?

Population: members of the general population living in the community (including care home residents). No limitation on age or gender or disease severity

Interventions: any that identify/reduce inappropriate polypharmacy

Outcomes: identification of inappropriate polypharmacy, changes in numbers of medicines prescribed/records altered, morbidity, mortality, functional outcomes, falls, and cognitive function

Search duration: 2012 to 2018

Search fields: Keyword, Abstract, Title

Evidence type: Reports/grey literature at national level, systematic reviews

Language: limited to English

Databases: Pubmed (MEDLINE), NHS Evidence, CINAHLPlus, AgeLine, Academic Search Complete. (Reference lists of included articles were also checked for additional references).

Keywords: Inappropriate or problematic polypharmacy or prescribing, suboptimal prescribing, drug or medication-related problems, medicines management or optimisation, review or reconciliation, screening or assessment, implementation, leadership, facilitation, collaboration, communication

Summary of key findings

1.0 Introduction

Polypharmacy is becoming an issue of increasing importance as the size of the older population increases, and more people live with one or more long-term conditions (multimorbidity), and complex medication regimens. The 2013 report from the Kings Fund on Polypharmacy and medicines optimisation (1) summarises the definitions of polypharmacy as the prescribing of many drugs appropriately (or appropriate polypharmacy) or too many drugs problematically (or problematic polypharmacy). In many people, appropriate polypharmacy will extend life expectancy and improve quality of life. For those people receiving inappropriate polypharmacy, there is a growing body of guidance and research exploring ways in which inappropriate polypharmacy can be identified and addressed. National guidance on polypharmacy, medicines optimisation and addressing multimorbidity from the National Institute for Health and Care Excellence (NICE), and the Scottish and Welsh governments is described further below, and evidence that assesses the effectiveness of the interventions presented.

In addition, the need for collaboration and joint working between healthcare professionals has been recognised, as has the need to work with patients to achieve their health goals as per the principles of patient-centred care advocated by the 2013 Royal Pharmaceutical Society (RPS) report on Medicines Optimisation: helping patients to make the most of medicines. The King's Fund report also acknowledges that patients and professionals do not always agree on medicines usage and suggests ways of dealing with this (1), and the process of safely deprescribing medicines carries its own benefits and risks (2).

A joint report from the RPS and Royal College of General Practitioners (RCGP) (3) summarised key points from the joint RPS/RCGP Conference in 2016. The report showcased the benefits of joint working between GPs and pharmacists and offered a practical guide to the delivery of improvements in patient care. The General Practice Forward View includes a commitment to support an extra 1,500 clinical pharmacists in general practice by 2020/21.

This literature review described below, in support of the new RPS guidance on Polypharmacy, aimed to find from the evidence surrounding deprescribing and the issues of problematic polypharmacy the interventions and work with patients that showed some evidence of effectiveness, and the levers for change that enabled those interventions.

2.0 Method

2.1 Search strategy

Pubmed (MEDLINE), CINAHLPlus, AgeLine, Academic Search Complete were all searched using the keywords: (polypharmacy OR inappropriate OR problematic OR suboptimal AND prescribing or prescri*) AND systematic; AND

- Medicines management or optimisation
- Review or reconciliation
- Screening or assessment
- Faciltat* or implement*
- Leadership or collaborat* or communicat*

A grey literature search was conducted in NHS Evidence using polypharmacy as the main term and using the filters: Guidance and Policy, systematic reviews, Implementation support, practice-based information.

2.2 Study design

The population of interest was any member of the general population living in the community (including care home residents) receiving inappropriate polypharmacy as defined by the article authors. There were no restrictions on age or gender.

Systematic reviews where the majority of trials were conducted in an inpatient setting, or did not report the effectiveness of specific interventions were excluded. Only systematic reviews that described a search strategy, stated inclusion/exclusion criteria and assessed quality/limitations of the eligible trials were included (SIGN grading 1- or above).

2.3 Search results

The searches found 2,791 articles, of which 2,204 were excluded on title scan. A total of 587 article abstracts were downloaded for further examination, of which 264 were duplicates and removed. From further examination of the remaining 296 article abstracts, 89 were selected for full text retrieval. On further analysis, 66 of these articles were found not to be relevant because they did not describe an intervention to address polypharmacy in community-dwelling people or did not meet the specified SIGN grading threshold.

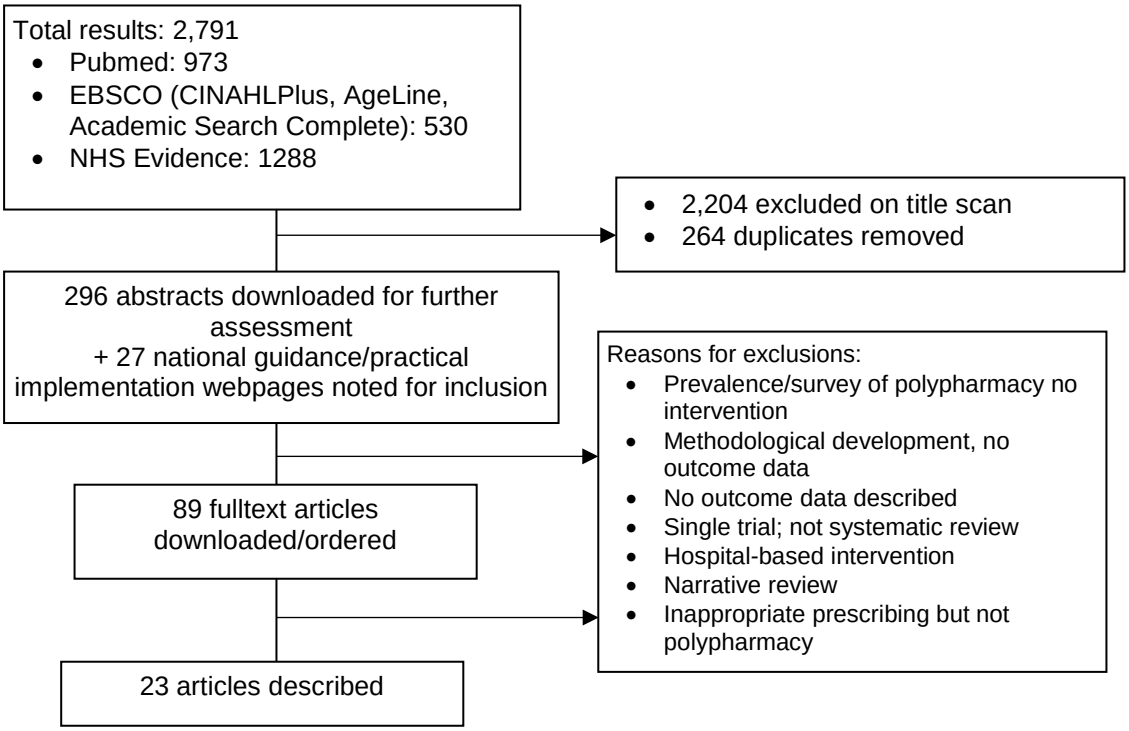

Figure 1: flow diagram of literature search and selection of articles

The search returned eight relevant articles or webpage references (4-11) that linked to national level policy and guidance on polypharmacy, multimorbidity and medicines optimisation, published by NICE (4-7;11), the Scottish government (8) and the Welsh (9) government. . These are described more fully in Section 3.1 below. Additional information and practical implementation tools were also identified on the NHS England website (Medicines optimisation) and as part of the PresQIPP polypharmacy and deprescribing webkit.(10)

Three systematic reviews (12-14) evaluated interventions to reduce inappropriate polypharmacy and reported mortality and hospitalisation rates as outcomes. One of the reviews (12) focussed on strategies (pharmacist or physician-led medication review, or via a multidisciplinary team) to reduce polypharmacy in adults over 65 taking at least four regular medications, pooling data from eighteen trials that reported all-cause mortality as an outcome measure or loss to follow up. A second review (13) was a broader look at the feasibility of deprescribing medicines in a more general context, which described a subset of twenty-one trials evaluating deprescribing to reduce polypharmacy. The third review looked at improving the quality of medication reviews in residential care for the elderly (14).

Improvements in medicines use measured using the Medicines Appropriateness Index (MAI) (15) or by other validated tool were the subject of five systematic reviews (16-20). Two updated Cochrane reviews were included (17;20). One identified twelve articles on interventions to improve appropriate polypharmacy in any setting that targeted people aged 65 years or more, with more than one long-term condition and who were receiving at least four regular medicines (17). The primary outcome measure in that review was change in the prevalence of appropriate use as measured using a validated instrument, such as the MAI or Beers criteria (21). The second review described twelve articles evaluating interventions to optimise prescribing for older people in care homes (20), ten of which described medication review as a component. Two further systematic reviews focussed on community-dwelling older adults and evaluated pharmacist-led interventions (18), and deprescribing (16). The last review looked specifically at deprescribing in older adults with an indication of frailty or disability and included thirty-six trials evaluating five interventions: pharmacist medication review (12 trials), pharmacist inclusion in a multidisciplinary team (13 trials), academic detailing (4 trials), audit and feedback (2 trials) and physician medication review (5 trials)(19).

Two systematic reviews (22;23) focussed on information technology (IT) interventions as a means of alerting prescribers to potentially inappropriate medicines at the point of ordering (CPOE) or during consultation. Such systems aim to improve medication safety by providing recommendations relating to dosing, frequency of administration, avoidance or discontinuation of medication and alerts on drug duplication, contraindications, drug interaction errors, appropriate medication orders, and warning messages. One of the reviews evaluated clinical decision support in seven studies carried out in long-term care homes (23), and the second review included studies in any outpatient setting and found ten trials in total: six evaluating CPOE with clinical decision support, two in pharmacy management IT systems, one web-based system and a telemedicine intervention (22).

Finally, three systematic reviews looked at perceived enablers and barriers to the implementation of polypharmacy reduction/ deprescribing interventions amongst prescribers (24), patients (25) and both groups (26).

There were no articles meeting the search criteria that addressed the issues of polypharmacy in populations other than people over 65 years of age e.g. children, or people receiving multiple medications for a specific condition.

3.0 Discussion

3.1 Summary of policy and guidance

A grey literature search for policy and guidance documents identified a number of relevant publications from NICE and recent guidance from the Scottish Government on Polypharmacy.

NICE publications include a Key Therapeutic Topic (KTT18)(4) that summarises the evidence surrounding multimorbidity and polypharmacy, and two Quality Standards on Multimorbidity (QS153)(5) and Medicines Optimisation (QS120)(6) to support improvements in clinical assessment, prioritising and managing healthcare. The NICE guideline on medicines optimisation (NG5)(11) gives detailed evidence-based recommendations on the use of medicines reconciliation, medication review and the use of patient decision aids to optimise the benefits of medicines to patients, including those on multiple medications. This is also covered in the NICE guidance on Multimorbidity: clinical assessment and management (NG56) (7).

Recent guidance from the Scottish Government (Polypharmacy guidance Realistic Prescribing; 2018) (8) aims to enable targeted polypharmacy management through the adoption of a 7-step patient-centred medication review process assisted by tools to prioritise patients at greater risk (Case finding indicators), and to address

issues such as anticholinergic burden and cumulative toxicity. Outcomes are assessed through improvements in metrics, such as the average number of case-finding indicators triggered per person and the proportions of patients triggering indicators, such as the number of patients aged 65 years or over prescribed three or more drugs with sedating or anticholinergic effects (excluding antiepileptics) as a proportion of all people aged 65 or over. Notably, the guidance also incorporates Sick Day Rules into the medication review process to address the need to minimise the potential for acute kidney injury. This guidance scored highest, according to AGREE II criteria, against other EU polypharmacy guidance in a 2017 systematic review of guidance to manage inappropriate polypharmacy conducted in as a part of a pan-European initiative, 'Stimulating Innovation Management of Polypharmacy and Adherence in the Elderly, SIMPATHY'(27).

Descriptions of medicines optimisation polypharmacy prescribing comparators for England and Wales are available on the NHS Business Services Information Services pages. Similarly the Polypharmacy guidance from the All Wales Medicines Strategy Group (9) advises a stepped approach to medicines review and, like the Scottish guidance, has supplied a list of commonly prescribed medicines with an estimate of effectiveness (Number needed to treat; NNT).

The PrescQIPP Polypharmacy and Deprescribing Webkit (10) offers a comprehensive range of practical implementation tools for healthcare professionals and organisations, and information relevant to the broad topic of polypharmacy and multimorbidity, including guidance on deprescribing (B176) and the Improving Medicines and Polypharmacy Appropriateness Clinical Tool (IMPACT). The PrescQIPP website also has a repository of projects from individual CCGs demonstrating good practice, tools, checklists and general local guidance. Similarly, NICE offer Shared learning case studies (28) showing how NICE guidance and standards on multimorbidity and polypharmacy have been put into practice by a range of NHS organisations.

3.2 Summary of systematic reviews of interventions

Effectiveness of interventions: mortality/hospitalisations

There was limited evidence that medication review (by a pharmacist, physician or multidisciplinary team) may reduce mortality in older patients with polypharmacy, and in older care-home residents (14), but not patient education (13). Two other reviews found no effect on all-cause mortality in older patients taking at least four medications (12;20). Controls in these studies were not well described; where detailed in data tables, they were described typically as usual care or a less detailed form of medication review or chart review. The quality of current evidence to interpret the effect of strategies to reduce polypharmacy is rather weak, with complex interventions (12), and significant variations in the types of outcomes measured (14).

Reducing number of inappropriate medications

One Cochrane review (17) specifically explored which interventions, alone or in combination, are effective in improving the appropriate use of polypharmacy and reducing medication-related problems in older people receiving at least four medications in any community or care setting (only 3 of 12 trials were with inpatients). The interventions evaluated were: medication reviews using either patient notes, or as part of a face to face consultation; patient education (patients receiving information about their prescribed medications or promotion of medication scheduling tools, for example through the use of monitored dose systems); professional education of prescribers and other healthcare professionals; computerised decision support. The review found reductions in inappropriate medication usage with intervention groups *versus* controls in six of the trials included which reported MAI scores, and reductions in levels of drugs listed in the Beer's criteria in a further two trials. Evidence of the effects of interventions on hospital admissions, and on medication-related problems was conflicting. The overall quality of evidence for all pooled outcomes was considered to be low according to GRADE criteria (29). A second Cochrane review described interventions to optimise prescribing for older people in care homes (20). The interventions evaluated were similar to the polypharmacy review but with the addition of multidisciplinary case conferencing. The review found and low quality evidence of improvements in the appropriateness of medication in the five trials that assessed appropriateness using validated tools (i.e. MAI, Beer's criteria, STOPP-START (30)) (20).

Two reviews evaluating interventions to address potentially inappropriate prescribing in older adults in the community (16;18) found pharmacist medication reviews to be effective in reducing inappropriate prescribing. One of the reviews described pharmacist-led interventions leading to recommendations to patients or their family physician (18), and the second also found evidence of reduced inappropriate prescribing with use of clinical decision support systems and multifaceted interventions (two or more techniques combined, e.g. academic detailing with audit and feedback; educational meeting with prescribing feedback) (16). In addition, one of the Cochrane reviews (20) found low-quality evidence that medication review led to improved identification and resolution of medication-related problems in seven of the ten trials that evaluated the intervention. A review focussing on unnecessary medication reduction in thirty-six trials involving older adults

with frailty or disability (19) also found that pharmacists were central to the majority of interventions, either in initiating medication reviews or participating in interdisciplinary teams. Other interventions reviewed were academic detailing to physicians accompanied by staff education, audit and feedback reports about medication overuse and physician-led medication reviews. Of the twenty-six trials reporting statistical evaluations of their intervention, twenty-two reported statistically significant reductions or differences with the intervention group *versus* a control.

Medication safety/prescribing alerts

Overall, the authors of one review commented on the paucity of research in the area of clinical decision support in long-term care, but positive findings for the use of clinical decision support in improving medication safety were found in trials of psychotropic prescribing (2 trials), prescribing in people with renal insufficiency (2 trials), and three trials that evaluated general warning alerts for potential interactions and adverse events.(23) Clinical decision support improved the quality of prescribing decisions, detected adverse drug reactions, triggered warning messages, and reduced injury risk among older adults.(23) A review encompassing IT interventions in any primary care setting found five trials evaluating CPOE with clinical decision support, with prescribing errors as the main outcome measure (22). Three of the trials reported positive outcomes in systems that compared activity to a specific list of medications or known interactions. Two other trials using warning trigger alerts found no significant decrease in medication errors or adverse drug events. There was no reduction in adverse drug events with the use of a web-based program or a telemedicine intervention (22).

3.3 Summary of enablers/barriers

Two systematic reviews looked at GP and primary care physician perspectives on managing the care of older adults in the community (24;25). Use of audit and feedback was seen as an enabler to enhance prescriber awareness of their prescribing of potentially inappropriate medications, although it was noted that prescriber beliefs at a population level did not necessarily affect practice at an individual level (24). Perceived barriers were difficulties in accessing all information required for optimal prescribing, including poor communication amongst multiple prescribers, inadequate transfer of information at care transitions, fragmented or difficult to access patient medication records and patients not always disclosing a full medical history and medications to prescribers. External factors affecting prescribers were a perceived lack of time to review and discontinue medicines, repeat prescribing, and the absence of explicit treatment plans or formal medication review. Enablers were factors such as availability of a pharmacist to carry out medication review and opportunities to review medicines use e.g. at hospital admission, change of prescriber, and specialist or scheduled review.

A second review of fourteen studies included GP (8 studies) and patient perspectives (6 studies) relating to deprescribing medicines (26). The main concerns of patients were the need for assistance and information in managing complex drug regimens and understanding the necessity of a particular medication, trust and communication with the GP, the choice to make their own decisions regarding treatment, or leave it to the doctor. System-related contributors to polypharmacy were the length of available consultation time, patient distrust of the system if they had adverse experiences, multiple prescribers and competency of prescribers. GPs reported that characteristics such as old age, impaired cognitive function, lack of adherence and education hampered effective communication and participation in decision-making about appropriate medicines. There was a perception that patients expected the GP to prescribe, or that the patient did not want to stop their medicine in case of a 'knock on effect' on doctor-patient relationship and trust. There were also difficulties in discussing the balance of life expectancy against quality of life. Additional factors included interface prescribing problems and evidence-based guidelines promoting more prescribing. Solutions that GPs were using to address perceived barriers were relaxing treatment targets, prioritising treatments, applying patient-centred strategies and using patient education. GPs thought that developing deprescribing guidelines for specific drug classes would be helpful, and that deprescribing should be a part of guidance on medicines use.

One systematic review (25) of twenty-one articles evaluated the main barriers to patient acceptance of cessation of medication and found disagreement with the need for cessation, fear of the consequences of cessation, and a lack of process in place to facilitation cessation. Enablers were an understanding of the appropriateness of cessation, a process in place to support cessation and a general dislike of medications. External influences such as family/friends, the media and experiences were all factors that could act as enablers or barriers to a patient's perception of the appropriateness of their medication.

4.0 Conclusion

There is evidence that interventions such as medication review, audit/feedback and computerised decision support reduce the use of inappropriate medication in patients over the age of 65 years in community settings.

The evidence for the effect of these interventions on clinical outcomes, such as mortality, rates of hospitalisation and medication errors, is weak.

Limitations of the systematic reviews included in this review were significant heterogeneity in outcome measures, interventions and the possibility of publication bias. Due to the nature of the interventions, there is a higher likelihood of effects of selection and performance bias. Quite often, there was insufficient outcome data to carry out meta-analyses. Grey literature searching was necessary to capture reports and guidance.

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