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The outcome of domiciliary medication reviews and their impact: a systematic review

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Abstract

Objectives Medication reviews in the domiciliary setting are becoming more prevalent internationally. Understanding the benefits of these reviews is essential to ensuring quality healthcare services. To date there has not been a systematic evaluation of the outcomes of these services and their impact on patients. A systematic review of the literature was undertaken with a view to understanding the impact of medication reviews in this setting. Controlled and uncontrolled studies were included. Outcomes were categorised according to the ECHO model. A narrative synthesis was developed.

Key findings Nineteen out of 31 papers included demonstrated an improvement in outcome. Clinical outcomes were the most commonly measured and humanistic outcomes the least commonly measured. Domiciliary medication reviews (DMRs) services are presented as providing benefit. However, it is difficult to quantify the impact of services from the published outcomes.

Summary Future work should focus on demonstrating the meaningful changes to patients that DMRs have enabled.

Introduction

The importance of medication reviews has long been acknowledged within health care.[1,2] Medication reviews can vary in levels of complexity from *ad hoc* identification of adherence problems (level 0 reviews) to full clinical reviews with access to patient notes and in conjunction with the patient (level 3 reviews).[3] Level 3 reviews are considered gold standard as they result in improved clinical outcomes through increased medicines optimisation and joint decision-making.[2]

In the United Kingdom, traditionally, medication reviews have occurred in the community pharmacy (e.g. Medicines Use Reviews and New Medicines Service) hospital (e.g. medicines reconciliation and comprehensive medication reviews) and primary care settings (e.g. clinical review in the GP surgery).[2] The impact of traditional medication reviews is reported as increasing adherence, reducing adverse drug reactions and improving patient safety.[4] Recently, comprehensive medication reviews in individual's homes, known as domiciliary medication reviews (DMRs), have become more prevalent. It is proposed that DMRs permit longer, more in-depth reviews with objectives and interventions that the professional and individual have chosen together. However, there have been no head-to-head comparisons of medication reviews in the domiciliary and traditional settings, and there is also no clear guidance or consensus on how the impact of DMR services should be evaluated.

Locally, the value of the first DMR pilot was demonstrated through the collection of activity data and a user satisfaction survey.[5] However, it was felt that this did not capture the complexity of the service; a holistic patient-centric service examining every aspect of medication management. Being able to appropriately evaluate these relatively novel services should ensure we are using resource effectively and achieving outcomes that matter to the individual. Having an in-depth understanding of the potential outcomes of DMRs could also permit examination and comparison of commonalities among services. This would allow providers and commissioners to consider whether published outcomes are generalisable to their service and whether they can, or should, target specific populations to get better outcomes or value for money.

The value of healthcare interventions can be measured by a variety of different outcomes. The validated ECHO model developed by Kozma categorises outcomes as

economic, clinical or humanistic. Economic outcomes are linked to the costs of health care, clinical outcomes are linked to events that occur because of a disease state or treatment, and humanistic outcomes are linked to the quality of life (QOL) and functional status of an individual.[6]

This systematic review will address the following research question: what is the value of DMRs? This question will be answered through the critical examination of outcome measures that are reported after DMRs. This review will provide an overview of the changes DMRs can make and whether these outcomes have economic, clinical or humanistic impact. The appropriateness and usefulness of these measures will be briefly discussed.

Methods

The systematic review followed PRISMA guidelines. A protocol for the systematic review was developed and uploaded on PROSPERO.[7] A literature search of the following databases was conducted: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (OVID), Embase (OVID), CINAHL (EBSCO), Science Citation Index (Web of Science), Proquest Dissertations and Theses Global (Proquest) and International Pharmaceutical Abstracts (OVID). The literature search was undertaken in February 2018, and all papers from inception until 06.02.2018 were considered for inclusion in the review. A combination of MeSH and free-text searching was used. The search strategy was adapted to the subject headings of databases. The search strategy for MEDLINE is described in Appendix S1.

Reference lists of relevant papers and systematic reviews were considered to ensure all relevant articles had been identified. Published papers and popular journals were hand-searched to identify additional papers that were not discovered from literature databases. Grey literature was sought by searching the National Institute for Clinical Excellence (NICE) Evidence Search, The Kings Fund and other targeted resources to try and find further relevant studies. Only papers with a full text available in English were included in the review.

Inclusion criteria

Studies of empirical design, where a DMR was the intervention and there was information on its effect, were included. Study participants were deemed eligible if they were over 18 years old and resided in their own home. No restriction was placed on the type of professional conducting the DMR. The following definition of medication review was taken: 'A structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste' (Room for Review, 2002[3]).

Exclusion criteria

Participants were excluded if they were <18 years old or if they did not reside in their own home, for example care home residents. Papers which described DMRs that targeted a single clinical condition were also excluded as they do not involve a comprehensive review of every drug, a requirement of a level 3 medication review.[2]

Data selection

Papers were extracted using the comprehensive search strategy described above. Title and abstracts were reviewed by two reviewers (PM & RC) to determine whether papers meet the inclusion criteria. Full texts of the abstracts selected for inclusion were reviewed separately by the two reviewers. If there was disagreement among the two reviewers as to which papers should be included, a discussion was had. If a consensus could not be reached a third reviewer (BC), read the paper and cast a deciding vote. Duplicate papers were excluded.

Data extraction

A data collection tool was developed for the studies which captured the following domains: year of publication, country study was conducted within, number of participants, demographics of participants, study design, the intervention schedule and follow-up (if any), how participants were targeted and identified and details of the DMR intervention. The data collection form was piloted on five studies.

Quality assessment

For randomised control trials (RCTs), bias was assessed using the Cochrane Risk of Bias Assessment tool as described in chapter 8 of the Cochrane Handbook v5.1.[8] Bias in observational studies was assessed using the Joanna Briggs Institutes Checklists for cohort and prevalence (no comparator arm) studies.[9]

Synthesis of results

As the reporting of inferential statistics was limited, there was no scope for meta-analysis or pooling of statistical results. Studies are described in a narrative synthesis. Outcomes were categorised according to the Kozma

definitions for economic, clinical and humanistic outcomes. Some outcomes did not fully meet the definitions for each category, in these instances the research team discussed and agreed the best fit for each outcome.

Results

Overview

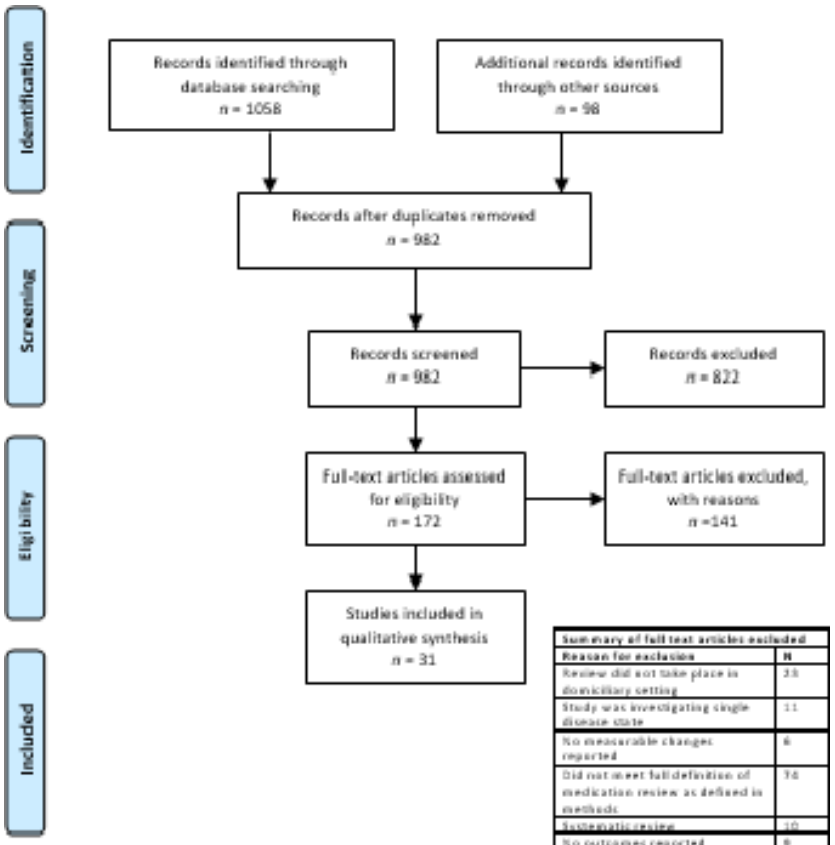
A total of 1058 articles (Figure 1) were found from database searching, and an additional 98 articles were found from other sources, including hand searching. 174 duplicate articles were removed. The abstracts of the remaining articles were reviewed and 822 were excluded as they did not meet the inclusion criteria. The main reason for exclusion at this point was that articles did not describe medication reviews that had happened in the home setting.

The full text of 172 articles was reviewed and a further 141 were excluded. The most common reason for exclusion of a paper was that the medication review described in the paper did not meet the definition of a comprehensive medication review. Examples of this include papers not involving a medication review at all, but simply describing drug taking behaviour[10] and retrospective chart reviews for clinical appropriateness without consultation with the patient.[11] Other reasons for exclusion included medication reviews not performed in the home environment, and no reported outcomes.

After this process, 31 papers were included in the systematic review analysis. These comprised 30 published in peer-reviewed journals and one university report describing a study. 31 papers described 28 individual studies, with one RCT generating two papers[12,13] and another RCT generating three papers.[14–16]

Although databases were searched from inception, the included articles were published from 1996 to 2017, with the majority being published after 2000 (n = 28).

An overview of the included studies is provided in the Table S1.



Summary of full text articles excluded	
Reason for exclusion	N
Review did not take place in domiciliary setting	33
Study was investigating single disease state	11
No measurable changes reported	6
Did not meet full definition of medication review as defined in methods	76
Systematic review	10
No outcomes reported	0
Setting unclear	6
No English translation available	1
Study on patients < 18 years old	1
Total	141

Figure 1 PRISMA flow chart describing article selection.

Study design

Studies were categorised as RCTs, cohort or prevalence studies. Most of the papers described prevalence studies (n = 16), randomised controlled trials were the second most common type of study (n = 12 papers, describing 10 RCTs), and papers describing cohort studies were the least common (n = 3).

Bias within studies

For RCTs, the risk of bias due to randomisation methods could not be assessed for two studies as information on randomisation methods used was not provided. Lenaghan[17] did not provide sufficient details for assessment; the authors simply stated that randomisation was carried out by a third party. Similarly, Lowe[18] stated only that a third party carried out randomisation without expanding on the methods used. It is difficult to blind participants for this type of study and this does not automatically introduce a risk of bias. The HOMER study,[14–16] POLYMED study[17] and RCT conducted by Nissen[19] were considered to have high risk of performance bias as participants were unblinded and outcomes reported were linked to the behaviour of participants.

Frequently, the professional conducting the intervention also measured the outcomes within studies. The potential for bias varies according to the outcomes recorded and whether the professional affected these outcomes. The level of bias is lower for outcome measures that the professional was unlikely to have been able to affect, for example hospital readmission and death rates and higher for measures such as change in adherence rates. We could not comment on whether bias exists due to selective reporting as protocols could not be located for any of the RCTs.

In the two cohort studies Bellone[20] and Cheen,[21] there were substantial differences between the baseline demographics of the control and intervention groups. Only two of the prevalence papers[22,23] conducted sample size calculations before carrying out their interventions. For most papers, statistical analysis was limited to the presentation of descriptive statistics, means, medians etc. In general, prevalence papers did not provide enough information to adequately assess the bias risk for the above categories.

For both cohort and prevalence studies but particularly prevalence studies, the potential for bias comes from the issue that most of the papers are describing observational outcomes from established clinical services. They were not set up as rigorous scientific studies and did not provide enough details of methodologies to fully assess the risk of bias. Overall, many of the papers were considered to have high risk of bias due to study designs. An overview of the bias within studies is depicted in Tables S3–S5.

Countries providing DMR services

The 28 studies included in the systematic review came from six countries; the UK has published the most evidence (n = 9), followed by Australia (n = 8), the United States (n = 7), Singapore (n = 2), and Canada (n = 1) and Denmark (n = 1).

Professional providing DMR service

Pharmacists conducted all the DMRs in the 28 studies.

Most papers published in Australia involved the nationally commissioned Home Medicines Review (HMR) service. In the Australian studies included, reviews were conducted by consultant pharmacists who may be attached to community, GP practices or work independently of both settings. In the remaining studies, the pharmacists were community pharmacists, hospital pharmacists, including a consultant pharmacist, or they were described as study pharmacists without detail of which sector they had experience of working within.

The link between the professional experience and the DMR services' outcomes was only explored for the HOMER trial.[15] The authors found that professional characteristics – number of years qualified, experience of medication reviews, obtainment of a higher degree and a hospital pharmacist background (versus community pharmacy) – made no difference to the study's primary outcome (admission rate). An exploration of the characteristics of the professionals involved in DMR studies and the impact on outcomes is beyond the scope of this systematic review.

Eligibility criteria for DMR services

Eligibility criteria of the target population varied between studies. Frequently, individuals over 65 years of age were targeted. Minimum number of regular medications prescribed, the minimum number of chronic medications prescribed and a previous recent hospital admission and use of another healthcare service were also used as eligibility criteria.

Outcomes

From the 31 papers included in the systematic review, an improvement in outcomes was observed in 19 papers and

a combination of improvement in some outcomes and no difference in others in eight papers. There was no difference in outcomes in three papers, a worsening of outcomes in one paper and a combination of worse outcomes and no difference in outcomes in one paper. An overview of outcomes is summarised in the Table S2. Outcomes from studies were categorised as either clinical, economic or humanistic.

Most outcomes reported in the included studies were clinical outcomes. The majority of articles that demonstrated benefit focused on clinical outcomes. Some articles presented only outcomes from a specific domain, while others presented a combination of outcomes. Several articles also presented results that were not actually outcomes, but rather process measures including number of visits or time taken to conduct the review and reporting of drug-related problems (DRPs), without discussion on how the intervention affected the DRPs.

Excluded outcomes

Outcomes were excluded if they were deemed to be process measures. These measures are an indication of what is involved with service provision but do not provide an objective measure of the outcomes of the service.

Outcomes were excluded if it was unclear they were a result of the DMR. For example, an outcome of 'number of drug-related problems', presented for the intervention group only would not be included, but if the number of DRPs was provided before and after the DMR, then that was deemed suitable for inclusion.

Economic outcomes

An outcome was considered economic if the authors provided a monetary value associated with the outcome. Economic outcomes included the following:

- Cost saving to social services resulting from reduced need for services.
- Difference in cost of prescribed medication.
- Cost saving to health services resulting from difference in rate of hospital admissions, emergency department attendances or primary care appointments.

Black and Glaves[24] estimated a £460 000 annual saving to social services through a reduction in care calls as a result of the DMR helping participants regain the ability to take their medications independently. The authors state this saving comes from 24 care packages with four calls per day no longer being required over a 1-year period.

Three studies[16,23,25] looked at the difference in healthcare costs because of their intervention using composite measures such as hospital admission costs and cost associated with using other healthcare services, for example primary care appointments. Ong et al.[23] showed a reduction in costs because of the DMR intervention. Pacini et al.[16[and Sorensen et al.[25] were able to demonstrate marginal cost reductions for their intervention arms, but these differences were not found to be statistically significant.

Dilks[26] estimated that the Exeter Cluster Pharmacy team produced a combined annual saving of £100 000 to both the local health and social care systems. Costs were extrapolated from estimates of hospital admission avoidance estimates using the NPSA[27] and Rio[28] risk scoring tools.

Krska et al.[12] investigated the cost of medications as a result of their pharmaceutical care plan intervention but found that there was no difference in the monthly costs of medication between the two arms.

Clinical outcomes

Clinical outcomes were the most commonly reported. There were a wide range of clinical outcomes reported within studies. The most commonly reported were rates of healthcare services usage and changes in markers of inappropriate prescribing.

Four studies whose intervention population received a DMR after an admission looked at readmission rates at 1, 2, 3 and 6 months postdischarge. One study showed no significant difference between intervention and control groups.[29] Three studies showed a statistically significant reduced readmission rate in intervention patients.[20,30].

Several papers whose study populations were community-residing looked at hospital admissions as an outcome. Four studies examined hospital admissions over a 6-month period, with one showing increased admission rate following intervention,[14] two showing no difference[17,25] and one showing reduced admission rate following intervention.[23] Olesen et al. looked at a longer time period, with no significant difference in hospitalisation rate seen at 2 years postintervention.[31]

Two studies reported potential avoidance of hospital admissions, with Krska[13] reporting that 10 out of 17 (59%) PCI-related admissions were avoidable. Dilks et al.[26] reported a projection of 109 admissions which could be avoided each year due to a home medication review intervention.

Other use of health resources was explored. Three studies showed a reduction in the number of emergency department visits.[21,23,29] Sorensen[25] showed no difference in GP visits or non-admission hospital services.

Several papers explored measures of inappropriate prescribing. These included potentially inappropriate medicines,[2432] medication appropriateness index score,[33]

problems related to medications taken[21,23,30,34–36] risk of medication-related harm,[26] pharmaceutical care issues[12]and adverse drug event rate.[25] All studies reported improvements in their chosen measures of inappropriate prescribing. Castelino[32] used the dug burden index to show a reduction in the complexity of prescribing, and Lenaghan[17] demonstrated a reduction in the average number of medications prescribed. Hsia[22] showed a significant reduction in medication discrepancies before and after intervention.

Many studies reported a measure of rate of acceptance of interventions or implementation of interventions by the primary prescriber. Between 35% and 95.8% of recommendations were accepted or implemented by the prescriber.[12,14,19,26,29,30,35,37–39] Similarly, Naylor and Oxley,[40] and Quirke[41] reported that 48% and 84% of patients' medication, respectively, changed as a result of the intervention.

Adherence was frequently used as an outcome. This was measured in various ways including presence of inappropriate medications in the home,[15,22] patient self-reports of adherence or understanding of medications or illness,[18,41,42] or changes in adherence as measured by researchers.[18,30,31] All studies reported improvements in their chosen measures of adherence. Steele[34] looked at a range of specific inappropriate prescribing measures linked to insurance performance payments. Improvements were shown for adherence to hypertension medications, but not other measures, for example presence of high-risk medications.

Mortality, measured at time points from 90 days months to 2 years, was used as an outcome measure in five studies.[14,17,21,30,31] No significant difference in mortality rates was demonstrated in any of these studies.

Other broad measures of clinical status included overall use of health and social care services,[12] severity of illness[25] and care home.[17] No significant difference was noted after intervention in any study.

Humanistic outcomes

Outcomes which affected participants' functional status or QOL, as outlined in the ECHO model,[6] were interpreted as humanistic outcomes. Coleman et al.[43] measured participants' increased confidence in managing their medications and managing illness. They took before and after intervention measures from participant feedback questionnaires, reporting that confidence increased by 50% for managing medications and 34% for managing illness.

The most common humanistic outcome presented in the papers was QOL measures. The HOMER[14] and POLYMED[17] trials used the EQ-5D scale[44] to measure the difference in QOL scores of their study participants. In addition, the HOMER trial also used the visual analogue scale.[44]

Neither study was able to show a significant difference in QOL between intervention and control arms because of their DMR intervention.

Sorensen et al.,[25] Krska et al.[12] and Nissen[19] captured QOL scores using the SF-36 scale.[45] Again, none of these studies was able to achieve a difference in QOL of score between intervention and control arms because of their DMR interventions.

Two studies, Nissen et al.[19] and Pacini et al.,[16] chose to measure the quality-adjusted life year (QALY).

Nissen et al.[19] found no difference in QALY between control and intervention arms. Pacini et al.[16] calculated the QALY for the DMR intervention described in the HOMER trial,[14] and they found that cost per QALY gained was £54, 454; meaning the intervention was unlikely to be considered cost-effective. The NICE threshold for cost-effectiveness is usually set between £20 000 and £30 000 per QALY gained.[46]

Discussion

To our knowledge, this is the first systematic review examining the outcomes resulting from DMRs. Most of the outcomes presented in the literature were clinical outcomes rather than economic or humanistic. A shift away from economic outcomes which purely present monetary values is expected as healthcare services focus on quality.[47] However, not presenting humanistic outcomes is unexpected. There is a large heterogeneity of outcomes reported, and the impact across outcomes varies.

A limitation of the systematic review was difficult in identifying MeSH terms to capture DMR evidence. This was counteracted by choosing broad search terms which returned many results, the inclusion of free-text terms and a rigorous screening process to ensure only relevant results were included in the review. Another potential limitation is DMRs with a single morbidity review were excluded, as it was felt the narrower focus of reviews would limit the generalisability of results. If they had been included, this may have increased the scope of the review.

The ECHO theoretical model was developed over 25 years, partly to demonstrate the limitations of evaluating pharmaceutical interventions through traditional clinical models and outcomes.[6] Capture and reporting of patient-related outcomes has been shown to enable the evaluation and improvement of modern healthcare services.[48] Despite the call for humanistic outcomes, the DMR body of evidence still appears to focus on clinical outcomes. For DMR services, this is most frequently presented through a reduction in appropriate prescribing and the number of interventions made that were

accepted. Clinical outcomes are important in patient-centred reviews. However, the impact of these outcomes and the level of patient involvement are not always clear.

There is a large heterogeneity in the evidence, including how DMR interventions were carried out, the participants targeted, and the outcomes presented. This limited the comparisons which could be made across studies. However, the heterogeneity in the published studies represents the 'real-world' and should not be discounted.

The initial number of search results returned indicated a growing body of evidence describing medication reviews in the domiciliary setting. However, the review process revealed only a small number of papers which met the inclusion criteria of describing a comprehensive medication review and presenting outcomes which demonstrated measurable differences because of the DMR intervention.

Flaws in the evidence stem from the issue that many of the included studies describe the outcomes of services which are already operating and were not designed as controlled studies.

Bias is a limitation of these studies. For all clinical outcomes, prevalence studies are highly prone to bias due to regression to the mean which may limit their validity. For example, an increase in use of health services by a patient due to ill health may reduce over time due to resolution of the underlying problem, regardless of any interventions provided. Therefore, simply measuring the change in use of health services over time, without a comparator group, could give misleading results. Patients targeted for DMR services may also be identified at the same time as having potential to benefit from other support services so it can be challenging to isolate the effect of the DMR alone. Well-designed controlled studies can help to minimise the effect of regression to the mean but may still be prone to confounding effects of other services offered at the same time as a DMR.

Not all papers defined the level of statistical significance they are aiming for, others did but then did not explicitly state in the results whether results were significant, leading to the possibility of misinterpreting results as significant when they were not.

DMRs are anticipated to be a better medication review than traditional settings. DMRs are likely to be less cost-effective than those performed in other settings due to travel time required by healthcare professionals to reach patients' homes, but the literature suggests they are more in-depth and can provide better outcomes. The current published evidence does not yet back this assertion up. Even if it can be demonstrated that DMRs are beneficial, further research is needed to quantify the added benefit they bring over medication reviews in traditional healthcare settings. We will now look at the economic, clinical and humanistic outcomes presented by the included papers.

Economic outcomes

By focusing on economic savings, authors are ascribing the value of the DMR service in monetary terms. For example, they may focus on the cost saving stopping a medication represents without considering the wider impact of a reduced pill burden.

Dilks et al.[26] estimated cost savings to health and social care services as a result of the DMR intervention. This is an important domain to investigate, considering the known overlap between the use of these services for the multimorbid older patient. It is particularly relevant in the UK where the position of Secretary of State for Health has also been given responsibility for national oversight of the provision of social care. One study looked at drug costs[12]; this may have a direct impact on patients in health systems where patients are required to pay or contribute towards the cost of medications used (e.g. United States, although this paper was a UK study).

Most of the papers describe newly set up services which were likely required to demonstrate their effectiveness to those funding such services. However, there is a risk that a pressure to provide cost savings to prove the worth of a DMR will mean professionals focus on interventions that provide economic benefit, rather than holistic interventions aiming to resolve issues that are relevant to the service user.

Papers did not generally provide a cost associated with providing a DMR service and not all accounted for the cost of a DMR service in their economic analysis. Black and Glaves,[24] Ong,[23] and Krska[12] reported cost analyses without accounting for the cost of providing services necessary to achieve these cost savings. However, Pacini,[16] Sorensen[25] and Dilks[26] did account for the cost of their services in their economic evaluations. Although the cost of running a service in different locations and countries will vary, which will limit its usefulness as a measure, it should be included in cost analyses so readers can see a truer picture of the economic value of a service.

The economic outcomes that are provided are basic measures which do not consider all cost implications included with service provision. Quantifying outcomes, which will generally have been multifactorial, particularly in the elderly population is extremely difficult.[49] Considering the basic nature of the economic outcome presented, they cannot be focused on as demonstrating the value of a DMR service.

Clinical outcomes

Kozma defines clinical indicators as separate from clinical outcomes. Clinical indicators are 'measurements of a patient's physical and biomedical status used to infer the

degree of disease',[6] for example blood pressure, spirometry. 'Medicine-focussed' measures such as measures of appropriate prescribing can be considered clinical indicators rather than clinical outcomes per se. They show there is potential to make a difference in clinical outcomes but do not demonstrate a difference themselves, whereas clinical outcomes are 'medical events that occur as a result of disease or treatment' such as stroke, respiratory exacerbation, or in the context of non-disease-specific medication reviews, events such as adverse drug reactions, hospitalisation, or death. For the purposes of this systematic review, we have reported outcomes that are considered as clinical indicators under the umbrella of clinical outcomes, as that is the domain in which they best fit, however, there is an argument that such measures do not represent true clinical outcomes. Nevertheless, they are commonly used in these papers, likely because they are relatively easy to measure by services.

The papers included in this systematic review were aimed at patients with a broad range of clinical conditions. Therefore, non-disease-specific clinical outcomes would be expected to be the most appropriate to measure impact, for example hospital occupancy, utilisation of health services, or all-cause morbidity or mortality.

.Outcomes related to hospital occupancy (e.g. admission or readmission rates, number of inpatient bed days) are relatively simple to objective measure, as well as being very meaningful outcomes to patients. The time period these are measured over should be carefully considered, using too short a time period would cause challenges in having a sufficiently powered study, due to relatively low frequency of hospital admissions. However, using too long a time period could risk changes in admission rates not being attributable to the original intervention. Hospital occupancy measures are also highly susceptible to confounding due to patients eligible for DMRs commonly being offered other health and social care interventions which could also affect hospitalisation rates.

As discussed earlier, using extrapolated figures for preventability of admissions or admission avoidance can be problematic due to the wide range of confounding factors. However, they may be useful ways of quantifying the benefit of services which are difficult to evaluate because of risk of bias and ethical problems in randomising patients. If such measures are to be used, it is key to ensure that appropriately validated tools are used for estimating prevented admissions.

For 'medicine-focussed' outcomes, such as appropriate prescribing, number of new medications and number of high-risk medications, all studies appeared to show benefit. It would be expected that improved access to pharmacists performing comprehensive medication review would almost inevitably improve such measures, but whether these are significant to patients is arguable. Similarly, for measures related to adherence, all studies showed improvement, but this may not translate to clinically meaningful outcomes. There is some evidence to show that improvement in such measures (such as reduced drug burden index) can result in improved patient outcomes,[50] but most of the studies included here did not demonstrate this in their populations. However, although medicine-focussed outcomes may be limited in their clinical significance, they can be more directly attributed to the DMR and so are less prone to confounding of results by other services offered to patients.

Humanistic outcomes

Humanistic outcomes should demonstrate the impact of an intervention to an individual. As DMR services are intended to be patient-centric, it is reasonable to assume that studies would include humanistic outcomes. This is the case for only a minority of the studies discussed in this review. The validated QOL measures regularly used in the literature are too broad and rarely focus on medication-related domains but rather broader health measures. However, medications are generally a sign of multimorbid patients, which in turn suggests a complex healthcare status. Given this complexity, there is potential for DMRs to have a wide-reaching impact so there is an argument that QOL measures could be used cover this regardless of what intervention is made. While an overall improvement in QOL is too ambitious for a medication review, this does not mean that humanistic outcomes should not be considered at all, and consideration should be made as to what benefits can realistically be achieved from the patient's perspective. The increased confidence measure used by Coleman et al.[43] is more specific to the DMR intervention. However, it comes with the healthcare professional decided assumption that lack of confidence managing medications is a problem that service users will want tackled. If services are truly patient-centric, future work should also explore the opinions of patients and other relevant stakeholders on what they hope to gain from a DMR and their perceived benefit of the medication review.

Excluded outcomes

Studies reported outcomes that were excluded from this systematic review, including process measures and outcomes that did not demonstrate a measurable difference. Although these were not appropriate for inclusion in this systematic review, this does not necessarily mean that they were not useful measures for the individual services. However, until studies can report a measurable difference, the generalisability and usefulness to other services is limited.

Conclusion

This review shows that DMRs can have a positive impact on the cost of health and social care provision, hospital admission and readmission rates, emergency department and other outpatient service visits, inappropriate prescribing and individuals' confidence with managing complex therapies. However despite many services heralding their interventions as patient-centric, the wider impact of the DMR outcome on the individual is not always clear. Future research studies should focus on capturing longer term measures or identifying proxy measures that can be to demonstrate impact in the short term.

Capturing outcomes for established services which have not been set up as research studies can be difficult. Future prevalence studies should try to present data on the measurable difference (s) that have occurred because of the medication review rather than incomplete outcomes. Authors should also consider about moving from drug focused proxy outcomes like DRPs to robust outcome measures that demonstrate meaningful benefit to patients.

Declarations

Conflict of interest

The authors have no conflict of interest to declare.

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Authors' contributions

Patricia McCormick was the lead and corresponding author, wrote protocol, conducted literature search, selected papers and main contributor to the manuscript. Rebecca Chennells was the second author, conducted literature search, selected papers and contributed to the manuscript. Dr Bridget Coleman was the contributing author, reviewed first draft of the manuscript and suggested amendments, third reviewer for paper selection when consensus could not be reached, PhD supervisor for PM. Professor Ian Bates was the contributing author, intellectually contributed to the design and content of the systematic review and reviewed draft of the manuscript.

Ethical approval

Ethical approval was not required as the systematic review involved creating a narrative synthesis around anonymised data that had already been published by other authors/ researchers.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Search strategy for MEDLINE.

Table S1. Summary of included studies.

Table S2. Summary of included studies: Summary of study outcomes.

Table S3. Summary of included studies: Summary of bias in prevalence studies, assessed against JBI critical appraisal checklist for prevalence studies.

Table S4. Summary of included studies: Summary of bias in randomised control trials, assessed against cochrane risk of bias assessment tool v5.1.

Table S5. Summary of included studies: Summary of bias in cohort studies, assessed against JBI critical appraisal checklist for cohort studies.