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Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis

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We set out to determine the effects of pharmacist-led medication review in older people by means of a systematic review and meta-analysis covering 11 electronic databases. Randomized controlled trials in any setting, concerning older people (mean age > 60 years), were considered, aimed at optimizing drug regimens and improving patient outcomes. Our primary outcome was emergency hospital admission (all cause). Secondary outcomes were mortality and numbers of drugs prescribed. We also recorded data on drug knowledge, adherence and adverse drug reactions. We retrieved 32 studies which fitted the inclusion criteria. Meta-analysis of 17 trials revealed no significant effect on all-cause admission, relative risk (RR) of 0.99 [95% confidence interval (CI) 0.87, 1.14, $P = 0.92$], with moderate heterogeneity ($I^2 = 49.5$, $P = 0.01$). Meta-analysis of mortality data from 22 trials found no significant benefit, with a RR of mortality of 0.96 (95% CI 0.82, 1.13, $P = 0.62$), with no heterogeneity ($I^2 = 0\%$). Pharmacist-led medication review may slightly decrease numbers of drugs prescribed (weighted mean difference = −0.48, 95% CI −0.89, −0.07), but significant heterogeneity was found ($I^2 = 85.9\%$, $P < 0.001$). Results for additional outcomes could not be pooled, but suggested that interventions could improve knowledge and adherence. Pharmacist-led medication review interventions do not have any effect on reducing mortality or hospital admission in older people, and can not be assumed to provide substantial clinical benefit. Such interventions may improve drug knowledge and adherence, but there are insufficient data to know whether quality of life is improved.

Introduction

Older people are often affected by multiple ailments, and it is no surprise that they end up taking numerous medications. The complexity and toxicity of some drug regimens means that care must be taken to promote adherence, minimize harm and overcome problems with storage and stock-piling. Therefore, medication review by a pharmacist may have important benefits for older people.

Medication review is a structured evaluation of a patient's medicines, aimed at reaching agreement with the patient about drug therapy, optimizing the impact of medicines, and minimizing the number of medication-related problems. However, medication review is a relatively new intervention and we do not know whether such reviews have a definite impact on important outcomes such as reducing hospital admissions and mortality. Much of the research has so far tended to focus on prescribing outcomes rather than hospital admissions [1], but an Australian study of home-based medication review has demonstrated a reduction in hospital admissions of 25%, and also a reduction in out-of-hospital deaths [2]. A comprehensive overview of related research would help to determine if these findings were reproducible, and generalizable to other settings.

However, existing literature reviews in this area have concentrated on pharmacists' roles, rather than investigating key questions as to whether these new interventions actually have any worthwhile impact on important patient outcomes [3]. One Cochrane review of outpatient

pharmacist roles, which reviewed trials up to March 1999, had great difficulty drawing conclusions due to the limited quality of the research available at that time [4]. More recently, a systematic review of clinical pharmacists and inpatient medical care concluded that there was generally improved care and no evidence of harm, but the authors did not attempt to pool the results statistically [5]. Another meta-analysis looked at medication review in the primary care setting and identified only weak evidence for an effect on admissions [6]. We therefore aimed systematically to evaluate and quantify the effects of medication review by pharmacists on substantive clinical outcomes (namely, hospital admissions and mortality) for older people across all care settings. We also aimed to evaluate, as secondary outcomes, the effects of medication review on qualitative outcomes such as quality of life and patient satisfaction.

Methods

Searching

Our search strategy identified research on medication review interventions involving pharmacists. Interventions were identified using a broad range of search terms and Medical Subject Headings (MeSH), including: medicine/medication review, drug review, medicine management, drug adherence/compliance/concordance, and pharmaceutical care planning. We developed our search with reference to the indexing of previously identified studies (full search available from the authors). The following databases were searched from their inception to 1 September 2005: MEDLINE, EMBASE, Cumulative index to Nursing and Allied Health Literature (CINAHL), Allied and Complementary Medicine (AMED), Cochrane Controlled Trials Register, Web of Science (including a citation search of key papers), Pharmline, International Pharmaceutical Abstracts, the Royal Pharmaceutical Society's Electronic Pharmacy Information Coverage (EPIC) database, Cochrane Database of Systematic Reviews, and Database of Abstracts of Reviews of Effects (DARE). Reference lists of included articles and relevant review articles were searched.

Study selection

All titles retrieved by the literature search were reviewed by one of six investigators. Titles needed to appear potentially relevant to the study area. Pairs of investigators assessed abstracts independently against five criteria: (i) intervention involved pharmacist-led review of patient's medication; (ii) intervention delivered primarily by a pharmacist; (iii) randomized controlled trial; (iv) mainly included older people (mean age of subjects > 60 years); and (v) encompassed patients with a range of diseases (more than one diagnostic category). Studies could be carried out in any setting (hospital, clinic, etc.), but needed to have a minimum follow-up period of 1 month and be reported in English. Full papers from potential studies were assessed independently by the two investigators for their suitability for inclusion. Differences were resolved by discussion with reference to a third reviewer if necessary.

Validity assessment

Many quality scales have been created to judge trials. Juni has recommended assessing trial quality by assessing three key components: concealment of allocation, use of intention-to-treat (ITT) analysis, and blinding of outcome assessment [7]. As blinding of outcome assessors is not particularly relevant to the end-points of hospital admissions or deaths, we therefore assessed whether studies confirmed outcome data by using at least two sources (e.g. hospital data and self-report). In addition, trial quality was assessed against criteria recommended by the York Centre for Reviews Dissemination [8]: explicit statement of inclusion criteria; baseline comparability between groups; a clearly defined primary outcome; and sample size calculation reported. The review team also considered the following criteria important in reference to this study area: length of follow-up (where = 6 months was considered adequate), >80% of patients retained in the trial, and reporting the training or selection of pharmacists. This gave a total of 10 quality criteria against which studies were assessed.

Data abstraction

We extracted data on a previously piloted data extraction form. Second reviewers checked extracted data. Data included type of participants, intervention details, outcomes and trial quality characteristics.

Study characteristics

Classification of interventions Interventions had to be principally delivered by a pharmacist. Interventions were excluded which were delivered by combinations of health professionals (e.g. physician, nurses) where the pharmacist was only partly involved. Interventions needed to be targeted at patients and not health professionals, but could involve reviewing a patient's records. All forms of medication review for checking and optimizing the patients' drug regimens (i.e. ability to make recommendations on altering the regimen) were considered, provided that the interventions were not limited simply to increasing patients' knowledge and/or adherence. Studies were categorized by: the predominant setting of review; type of pharmacist involved; number of pharmacists involved; access to patient medical records; intervention components; contact between pharmacist and prescriber; ability of pharmacist to enact recommendations; and the extent of contact of the pharmacist with the patient (based on number of review opportunities).

Outcomes The primary outcome was proportion of patients with one or more hospital emergency admission (all-cause). Secondary outcomes were all-cause mortality and mean drugs prescribed. Outcome data were extracted at the study's prespecified last follow-up point. Data on

quality of life, patient satisfaction, drug-related problems, drug knowledge, adherence, adverse drug reactions, storage problems, removal of unnecessary drugs and cost data were also extracted. The latter included extracting the form of economic evaluation undertaken (e.g. cost-effectiveness analysis). Formal pooling was not possible for these additional outcomes due to the diversity of scales used. Nevertheless, informal pooling of results was undertaken in terms of number of studies showing a significant positive effect, a nonsignificant positive effect, no effect or a negative effect.

Quantitative data synthesis

We included all trials reporting appropriate data in the meta-analyses if interventions were compared with usual care. Authors of trials were contacted to provide additional data where needed if published after 2000. It was assumed that additional result data were unlikely to be available from articles published prior to this cut-off. For data on 'proportion admitted' and 'mortality' the effect of the intervention was reported as a relative risk. For 'mean drugs' a weighted mean difference was calculated. Meta-analyses were carried out using random effects methods using RevMan version 4.2.8. Funnel plots were used to assess possible publication bias.

The robustness of the findings in relation to admission and mortality were investigated in the following sensitivity analyses. First, we investigated reasons for any heterogeneity found and repeated analyses using fixed effects methods. We then explored the effect of excluding poorer quality studies. This was investigated in two ways: (i) comparing those demonstrating, or not, components recommended by Juni [7]; and (ii) removing those achieving $\leq$50% vs. those achieving >50% of the 10 criteria above. Finally, the effect of hospital or specialist pharmacists was compared against community pharmacists; and the effect of the studies with higher levels of patient contact (defined as three or more medication review opportunities) compared against less intense interventions.

Results

Search results and study characteristics

A total of 17 272 titles were identified, yielding 889 potentially relevant studies, of which 32 fitted the inclusion criteria (Figure 1). The first identified trial was published in 1990, but few trials were published in the following decade. Since 2000 numbers have increased rapidly, with almost two-thirds ($n = 22$) of identified trials published since then. The majority of trials were conducted in either the UK ($n = 13$, 41%) or USA ($n = 10$, 31%); four were conducted in Australia, three in Canada, one across several European countries and one in Singapore. The mean age of subjects in the studies varied between 61 and 85 years (average across trials was 71 years), with the proportion of male subjects varying from 20% to 99% (the latter recruited from a Veterans hospital [9]). Only one study limited inclusion to specific diagnoses (either chronic obstructive pulmonary disease or hypertension) [10].

Trial quality

For the three key quality components, only 18 (56%) clearly described a form of concealed allocation, 15 (47%) definitely or probably used an ITT analysis and 12 (38%) used some form of data checking. In total, five studies (16%) satisfied all three key quality components together [9, 11–14], three of which were published since 2001. When trials were considered against all 10 quality criteria, the majority (17/32) met at least six. Quality issues often lacking were reporting a sample size calculation and defining a primary outcome.

Interventions (Table 1)

The majority of interventions were delivered in either hospital ($n = 8$, 25%) or a clinic/primary care setting ($n = 13$, 41%). Three were delivered in a community pharmacy, seven in the patient's own home and one in a nursing home. Pharmacists were described as hospital or clinical pharmacists in a third of trials ($n = 11$), community pharmacists in a third of trials ($n = 10$), specialist or research pharmacists in nine trials, whereas one trial used a mixture. Sixteen trials (50%) used a single pharmacist to deliver their intervention, thus limiting generalizability.

In 23 trials (72%) intervention pharmacists had access to patient medical notes (either hospital or primary care records), whereas in three trials pharmacists had some form of detailed referral information. Information in the remaining trials was limited to either a discharge letter (two trials), repeat prescribing data (three trials), or patient self-report. Pharmacists delivered medication counselling, advice on adherence, checked drug benefit and adverse events, and aimed to optimize medication in >60% of the trials. Contact with the physician was considered close (i.e. face-to-face) in over half of trials ($n = 17$), telephone contact was used in four trials, and mail in seven trials (not described in four trials). Pharmacists were generally unable ($n = 19$, 59%) or only partly able to enact their own recommendations ($n = 10$, 36%). Only in two trials (6%) were pharmacists considered to be able to enact fully their recommendations [15, 16]. Overall, we found that the pharmacists generally had one or two review visits with the patients, but that there were seven trials where patients could be reviewed on three or more occasions (usually in person, but sometimes through regular telephone calls).

Effect on all-cause admission (Figure 2)

Seventeen trials, including a total of >9900 patients, provided data on this outcome. Meta-analysis suggested that pharmacist-led medication review has no effect on all-cause admission, relative risk (RR) of 0.99 [95% confidence interval (CI) 0.87, 1.14, $P = 0.91$]. However, overall results were conflicting, with four trials providing significant or

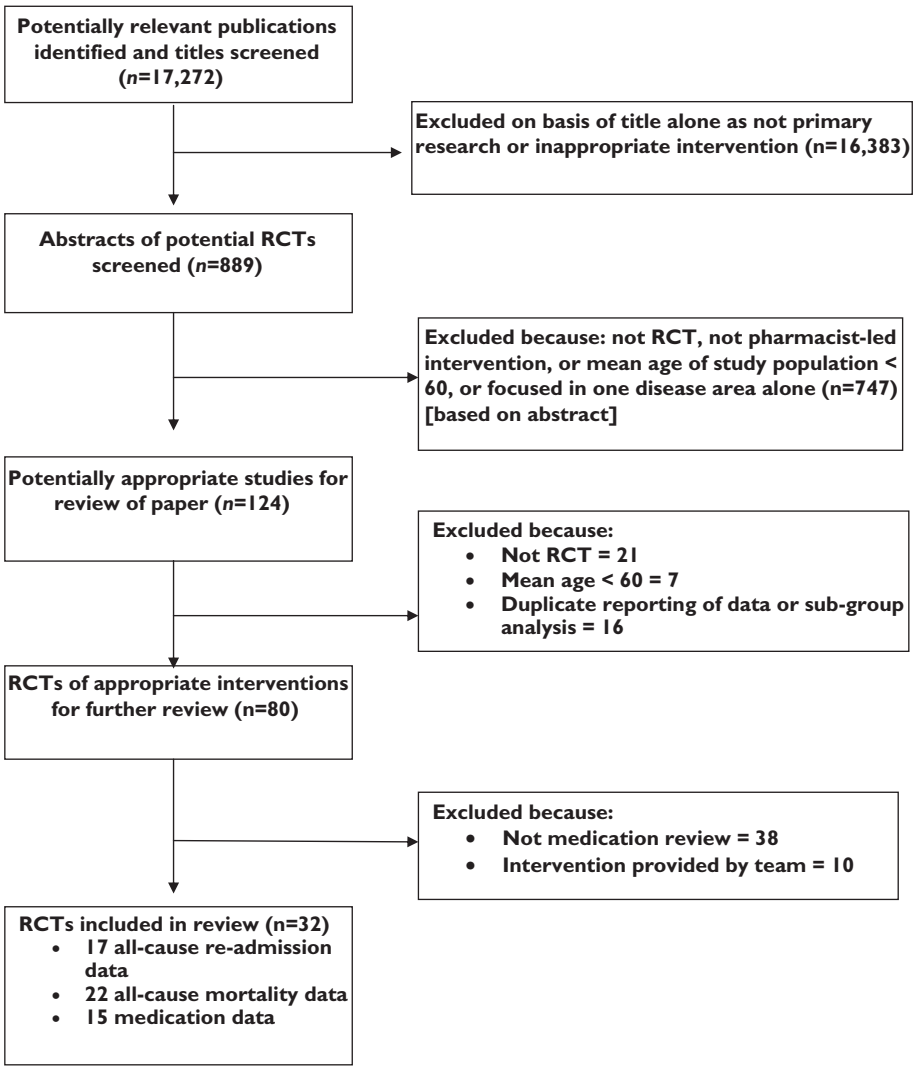

Figure 1

Flowchart describing study selection and excluded studies

borderline significant results in favour of the intervention [17–20], whereas others provided evidence favouring the control [13, 21]. This variation in findings can be seen as moderate heterogeneity on statistical testing ($P = 0.01$, $I^2 = 49.5$).

Effect on all-cause mortality (Figure 3)

Twenty-two trials, which included a total of >11 700 patients, provided data on mortality. Meta-analysis suggested that pharmacist-led medication review has no effect on mortality (RR = 0.96, 95% CI 0.82, 1.13, $P = 0.65$). No heterogeneity was detected between trials ($I^2 = 0\%$).

Effect on prescribing (Figure 4)

Fifteen trials provided data on prescribing. Meta-analysis suggested that these interventions may reduce numbers of drugs prescribed (weighted mean difference = –0.48, 95% CI –0.89, –0.07). However, as with admissions, heterogeneity was identified, although in this case it was very marked ($P < 0.001$, $I^2 = 85.9\%$) with five positive trials [9, 20, 22–24] and one negative trial [25].

Effect on additional outcomes (Table 2)

Interventions appeared to have a positive effect on intermediate outcomes such as numbers of drug-related problems, knowledge, adherence, improving storage and reducing unnecessary drugs. Equally, both patient satisfaction and adverse drug reactions generally, but not always, were improved by these interventions. However, despite these positive effects, only one-third of those trials that measured quality of life found a benefit and these were

Table 1

Description of studies and interventions

Study author	Date	Country	No. of patients	Mean age, years	% male	Type of pharmacist	No. of pharmacists	Intervention	Patient data	Ability to enact advice	Contact with prescriber	Setting	Extent of patient contact
Begley [1]	1997	UK	222	82	39.4	Research pharmacist	Unclear	Home visits and counselling by a pharmacist after hospital discharge	Discharge letter	Unable to enact	Unclear	Own home	Four detailed visits over a year
Bernsten [18]	2001	Europe	2454	74	42.4	Community pharmacist	104	Community pharmacy assessment of drug-related problems and implementation of a pharmaceutical care plan	Repeat prescribing data	Unable to enact	Unclear	Pharmacy	Unclear
Bolas [34]	2004	Northern Ireland	243	74	39.5	Hospital/ clinical pharmacist	1	Full history, preparation of discharge letter. Medication review (stated in abstract but not method).	Full notes	Unable to enact	Close contact	Hospital	Inpatient ward visit plus discharge plan
Bond [17]	2000	UK	3074	66	41.6	Community pharmacist	62	Pharmacist-controlled repeat prescription system where pharmacist checked if medication needed. Review of side-effects and interactions	Repeat prescribing data	Unable to enact	Contact by letter	Pharmacy	Limited contact, mainly review of repeat scripts
Carter [35, 36]	1998	USA	1054	66.7	96.3	Hospital/ clinical pharmacist	>4	Medication assessment and adherence, change of nonformulary to formulary drugs, and education	Full notes	Partly enact	Close contact	Primary care or clinic	Detailed enquiry, mean 3.5 visits over a year
Furniss [37]	2000	UK	330	81.2	27	Research pharmacist	1	Medication review with patient	Drug chart in nursing home	Unable to enact	Unclear	Nursing home	Detailed review, with second brief visit at 8 months
Gourley [10]	1998	USA	231	68.05	97.8	Hospital/ clinical pharmacist	45	Pharmacists involvement in healthcare team in the management of patient's drug therapy	Full notes	Partly enact	Unclear	Hospital	Clinical, review, at least 5 visits over 6 months
Graffen [38]	2004	Australia	402	77.7	38.8	Research pharmacist	1	Clinic-based medication review	Full notes	Unable to enact	Close contact	Primary care or clinic	One visit with brief enquiry
Granas [14]	1999	UK	500	65	38	Community pharmacist	Probably 1	Community pharmacist identified a drug-related problem and this was then discussed with pt's GP	Full notes	Unable to enact	Close contact	Primary care or clinic	Review of repeat prescription only
Grymonpre [39]	2001	USA	135	77	20.74	Hospital/ clinical pharmacist	1	Home medication history taken by 'lay person' and reviewed by a pharmacy consultant	Lay person report	Unable to enact	Contact by letter	Primary care or clinic	Single visit over a year
Hanlon [9]	1996	USA	208	69.8	99	Hospital/ clinical pharmacist	1	Monitored drug therapy, patient outcomes, medication use & drug-related problems	Full notes	Unable to enact	Close contact	Primary care or clinic	At least two visits and option for multiple visits over a year

Table 1

Continued

Study author	Date	Country	No. of patients	Mean age, years	% male	Type of pharmacist	No. of pharmacists	Intervention	Patient data	Ability to enact advice	Contact with prescriber	Setting	Extent of patient contact
Holland [13]	2005	UK	872	85.4	37.6	Mixture	22	2 home visits to check adherence, ability to self-medicate, evaluate patients and carer, remove out of date drugs, report ADRs to GP, and need for interventions such as compliance aid	Discharge letter	Unable to enact	Contact by letter	Own home	Two visits over 6 months
Jameson [15]	1995	USA	64	60.5	20	Specialist pharmacist	Probably 1	Pharmacist performed a chart review and medication history then interviewed pt on current regimen and side-effects. A new regimen was developed by pharmacist and physician, which pharmacist then explained to the pt with additional info on drug therapy	Full notes	Fully enact	Close contact	Primary care or clinic	Two visits over 6 months
Kassam [25, 40]	2001	Canada	363	73.5	33.1	Community pharmacist	>4	Interview and follow-up to identify drug-related problems	Repeat prescribing data	Unable to enact	Unclear	Pharmacy	At least two visits over a year
Krska [41]	2001	UK	381	75.1	39.5	Hospital/ clinical pharmacist	1–5	Detailed profile of pt formed from med notes by pharmacist who then interviewed pt in own home about use of and response to meds and use of health and soc. services. Care plan drawn up, given to GP; pharmacist agreed actions assisted by practice staff	Full notes	Partly enact	Contact by letter	Own home	One visit over 3 months
Lenaghan [24]	2004	UK	136	84.3	34.3	Community pharmacist	1	Home based medication review	Full notes	Partly enact	Close contact	Own home	Two visits over 6 months
Lim [16]	2004	Singapore	136	80	35	Hospital/ clinical pharmacist	Probably 1	Each patient was evaluated with the aim of simplifying regimen, improving effectiveness and decreasing ADRs. Recommendation discussed with doctor and those accepted were implemented	Full notes	Fully enact	Unclear	Hospital	One visit plus follow-up at two months
Lipton [22, 42]	1992	USA	706	74.5	49	Hospital/ clinical pharmacist	2	Clinical pharmacist reviews of hospital records and drug regimens of participants and consultation with these patients and their physicians	Full notes	Unclear	Close contact	Hospital	Five visits in 3 months
Lowe [43]	2000	UK	181	76.25	33	Hospital/ clinical pharmacist	1	Assessment and rationalizing of medication, med education and knowledge and compliance assessed at the end of the study period	Full notes	Partly enact	Close contact	Primary care or clinic	Three visits in 7 weeks
Mackie [44]	2001	UK	3025	67	36.6	Research pharmacist	4	Problems identified during patient interview in GP/home, discussed with GP and enacted.	Full notes	Partly enact	Contact by letter	Primary care or clinic	One visit over 40 weeks

McMullin [45]	1999	USA	259	61	30	Specialist pharmacist	6	Review to identify cost saving interventions e.g. removing unnecessary drugs, modifying route of administration, or use of cheaper agents	Full notes	Unable to enact	Contact via telephone	Hospital	Ward review only
Naunton [19]	2003	Australia	136	75.5	37.5	Research pharmacist	1	Medication review and counselling by home visit	Full notes	Partly enact	Contact via telephone	Own home	One visit over 3 months
Nazareth [12]	2001	UK	362	84	36	Community pharmacist	34	Hospital interview with initial medication assessment and rationalization, check ability to self-medicate, provide advice. Then patient visit by a pharmacist to check discrepancies, understanding, adherence	Full notes	Partly enact	Contact by letter	Hospital	Two visits over 6 months
Sellors [46]	2001	Canada	132	76	35	Community pharmacist	1	Clinic based medication review, then telephone interviews	Full notes	Unable to enact	Close contact	Primary care or clinic	One visit and several telephone calls over 6 months
Sellors [11]	2003	Canada	889	74	47	Community pharmacist	24	Clinic based medication review and telephone interview and recommendation to physician	Full notes	Unable to enact	Close contact	Primary care or clinic	One visit plus 1–2 telephone calls over 5 months
Sidel [47]	1990	USA	284	65	33	Unclear	Unclear	Explanations and contact physician	Survey by nonmedical staff	Unable to enact	Contact via telephone	Own home	Two home visits over 6 months
Smith [48]	1997	UK	68	77.5	Not stated	Hospital/ clinical pharmacist	1–5	Medication review in hospital with discharge care plan and access to telephone helpline	Full notes	Unable to enact	Contact by letter	Hospital	One pre-discharge visit, 1 week follow-up
Sorensen [27]	2004	Australia	400	71.8	36.3	Community pharmacist	32	Home visit and medication review by pharmacist and team conferences with GP and implementation at next patient/GP visit	Home visit and GP's report	Unable to enact	Close contact	Own home	One visit over 6 months
Stowasser [49]	2002	Australia	240	66	55	Hospital/ clinical pharmacist	Unclear	Medication review plus special discharge summary	Full notes	Unable to enact	Close contact	Hospital	One hospital visit, plus follow-up at 30 days
Taylor [20]	2003	USA	81	65.6	31.9	Community pharmacist	4	Rural education and drug information programme	Full notes	Unable to enact	Close contact	Primary care or clinic	Brief enquiry, number of visits not described
Williams [23]	2004	USA	140	73	43	Specialist pharmacist	1	Medication review	Full notes	Partly enact	Close contact	Primary care or clinic	One detailed review, with 6 weeks' follow-up
Zermansky [50]	2001	UK	1188	73.5	44	Specialist pharmacist	1	Record current drugs, medical problems, perform patient interview, confirms drug still needed, ADRs, consider costs, assess adherence & feedback to GP + assessing implementing agreed changes	Full notes	Partly enact	Close contact	Primary care or clinic	One review over 12 months

ADRs, adverse drug reactions.

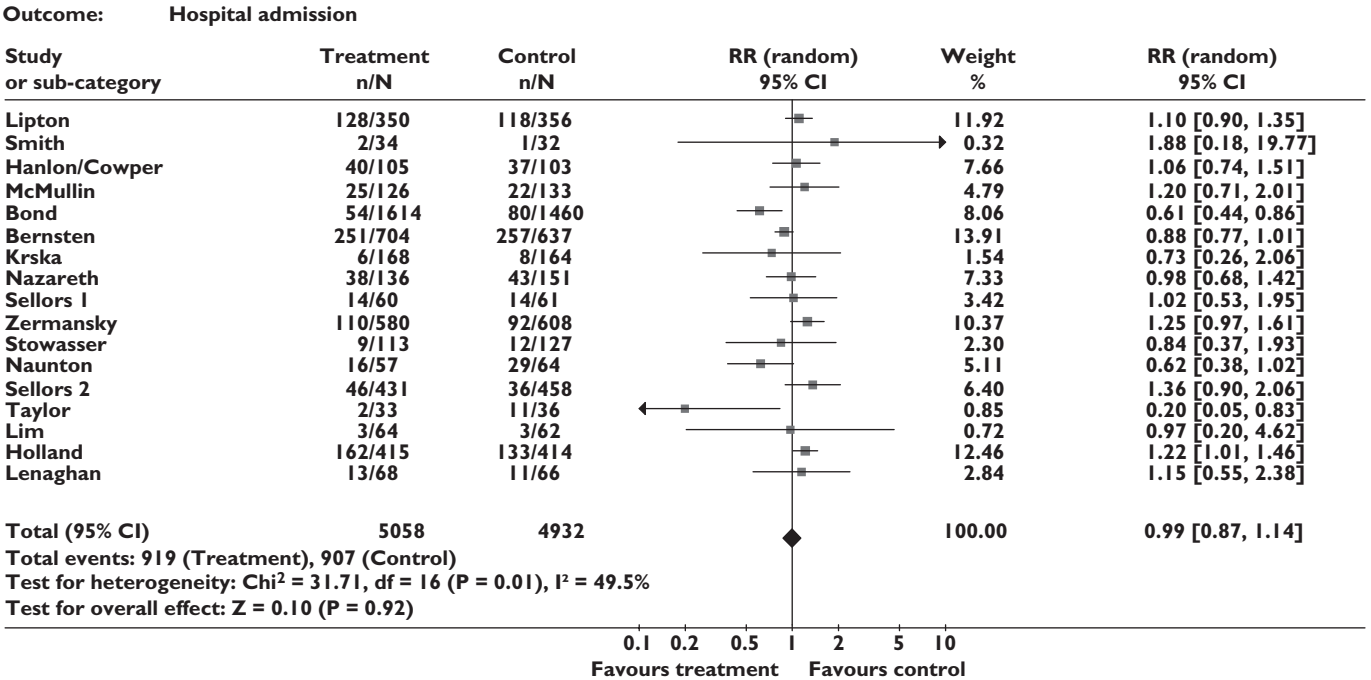

Figure 2
Meta-analysis showing relative risk for all-cause admission

not statistically significant. Finally, 14 trials collected data on cost, of which only three performed formal economic evaluations [13, 26, 27], the remainder being simple cost analyses focusing on prescribing costs. The cost analyses appeared promising, with nine of the 11 studies yielding a positive or nonsignificantly positive outcome. The cost effectiveness analyses used differing comparators: cost per gain in medication appropriateness index [26], and cost per reduction in adverse drug effects [27]. Only one study calculated an incremental cost per quality adjusted life year (QALY) and this found it to be very high [28].

Sensitivity analyses

Table 3 describes the various sensitivity analyses conducted on the primary outcome (all-cause admissions). The overall effect was very similar across all sensitivity analyses, with the exception that those studies which appeared to be of lower research quality appeared to provide more effective interventions than higher quality studies, although the CIs overlapped. Table 3 also describes the same sensitivity analyses conducted on mortality data. Again, the overall effect appeared reasonably similar across all sensitivity analyses, with the exception that those studies that did not appear to use concealed allocation for randomization appeared to have a more favourable effect on mortality (RR = 0.65, 95% CI 0.43, 0.97, $P = 0.03$). Finally, there was no evidence of publication bias evident from inspection of funnel plots (available from the authors).

Discussion

Main study findings

This systematic review has identified a large and rapidly growing body of trial evidence investigating the effectiveness of pharmacist-led medication review. This evidence is of increasingly high quality, suggesting that researchers in this area have responded to earlier criticism [4, 29]. However, our review has not identified any clear effect on either hospital admission or mortality. Importantly, this lack of effect did not seem to be related to type of pharmacist performing the review, or the intensity of their review.

Our review has identified that these forms of intervention may be able to reduce numbers of prescribed drugs slightly, and would appear to have positive effects on a wide range of intermediate outcomes, such as drug knowledge, adherence and drug storage. Despite this, few studies identified any important effect on quality of life, and those that suggested positive effects were not statistically significant.

Figure 3

Meta-analysis showing relative risk for all-cause mortality

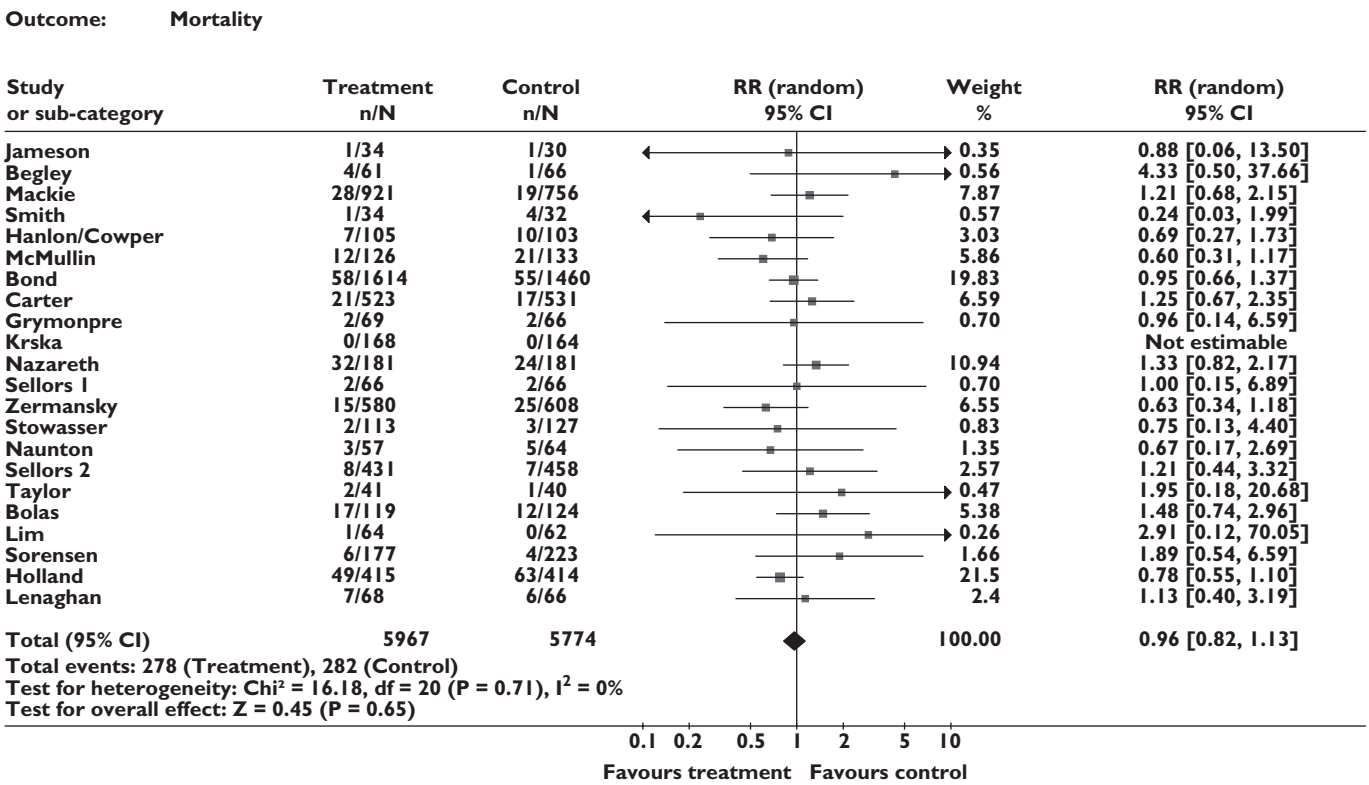

Figure 4

Meta-analysis showing weighted mean difference for number of drugs prescribed

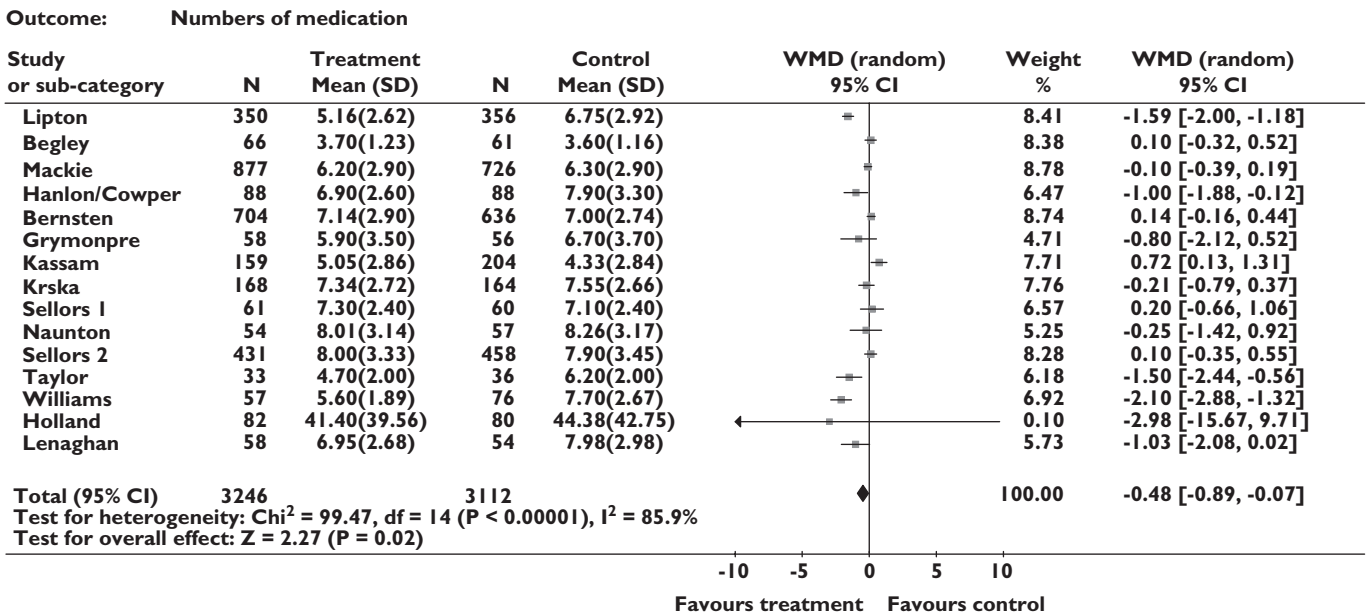

Table 2

Qualitative pooling of secondary outcomes

	No. of trials reporting outcome compared with control	No. reporting a significant positive effect (%)	No. reporting a nonsignificant positive effect (%)	No. reporting no effect (%)	No. reporting either a nonsignificant or a significant negative effect (%)
Quality of life	12	0	4 (33)	8 (66)	0
Patient satisfaction	4	2 (50)	1 (25)	0	1 (25)
Drug-related problems	4	4 (100)	0	0	0
Knowledge	11	6 (55)	2 (18)	3 (27)	0
Adherence	14	7 (50)	4 (29)	3 (21)	0
Adverse drug reactions	9	1 (11)	3 (33)	3 (33)	2 (22)
Storage problems	3	2 (66)	0	1 (33)	0
Unnecessary drugs	7	5 (71)	2 (29)	0	0
Cost analysis*	14	4 (29)	6 (43)	2 (14)	2 (14)

*Three studies reported some form of cost-effectiveness analysis.

Strengths and weaknesses of the study

This study searched all key databases relevant to this study area. The database search was supplemented by checking study references, review articles and conducting a citation search of identified studies. In addition, authors of included studies were contacted where additional data were required. Finally, conducting this review across a team of researchers allowed data extraction to be checked and decisions agreed. We acknowledge that there may be unpublished data that we have not been able to retrieve, but given the number of studies already in our meta-analysis, the results are likely to be significantly changed only if the unpublished studies consisted of several large-scale randomized trials. Although nonrandomized studies may provide additional information, we excluded such studies due to their susceptibility to bias.

The main focus of this study was to quantify the direct impact of medication review on hard outcomes such as hospital admissions and death. As such, we did not evaluate interventions which were designed solely to improve knowledge or medication adherence. It is possible that interventions of this nature may have substantial qualitative effects on older patients, and that such outcomes may be better evaluated using descriptive methods, rather than the statistical techniques used here.

The review was to some extent limited by reporting of the primary outcome. In total, only 17 of the 32 studies provided data on this outcome. Some authors reported total admissions (as opposed to proportion admitted or not), which could not be entered into the meta-analysis, or reported that there was no difference observed but omitted numerical data in their paper. Efforts to contact these authors added four additional data points. As a result, data on the primary outcome were provided for almost 10 000 patients.

The meta-analysis of our primary outcome (all-cause admission) demonstrated moderate heterogeneity, suggesting that some differences existed between the studies included in that analysis. Nevertheless, it should be stressed that our sensitivity analysis (Table 3) did not identify changes to our main finding of no effect, with the exception that poorer quality studies seemed to yield greater effect than higher quality studies, which is not an unusual finding. Only a small proportion of studies fulfilled all the quality criteria, thus indicating that some of the studies may have been susceptible to bias.

We have also attempted to evaluate other patient-related measures such as medication-related problems, adherence and quality of life, given that global outcomes such as hospital admissions may not relate specifically to the interventions delivered, or particular patient's needs. However, these other outcomes are not consistently reported in the trials (Table 2), thus limiting our ability to draw any robust conclusions on the effectiveness of the intervention on such outcomes.

Heterogeneity in the results for all-cause admission may also have arisen from factors that are difficult to quantify in a precise way. The baseline risk for medication problems of the patients may have differed amongst the trials, as may have the care that the patients' received from other sources or teams within that particular healthcare system. Differences in the delivery of the pharmacist-led medication review and care settings of the trials may have masked findings of beneficial effects in certain situations. However, it is also important to note that there was no heterogeneity in the mortality measure.

It is somewhat surprising that the number of medication review opportunities with the patient did not appear to relate closely to the effectiveness of the intervention. However, this may simply reflect that there are multiple other complex factors at play here, which prevent this analysis from identifying the key ingredients of a 'successful' intervention. It should be noted that few studies appeared to be particularly intensive – thus, the CIs on the

Table 3

Sensitivity analysis on primary outcome (admission) and mortality

	Admission No. of patients (no. of trials)	Relative risk (95% CI)	*P*-value for overall effect	I^2-value for heterogeneity (%)	Mortality No. of patients (no. of trials)	Relative risk (95% CI)	*P*-value overall effect	I^2-value for heterogeneity (%)
Random *vs.* fixed effects								
Random effects	9990 (17)	0.99 (0.87, 1.14)	0.92	49.5	11 741 (21)	0.96 (0.82, 1.13)	0.65	0
Fixed effects	9990 (17)	1.00 (0.92, 1.08)	0.95	49.5	11 741 (21)	0.97 (0.82, 1.13)	0.66	0
Removing outliers								
Base case	9990 (17)	0.99 (0.87, 1.14)	0.92	49.5	–	–	–	–
Removing extreme trials*	5831 (12)	1.02 (0.93, 1.11)	0.74	0	NA	–	–	–
Quality component								
1. Concealed allocation	5542 (7)	1.02 (0.82, 1.27)	0.84	57.5	9 264 (13)	1.04 (0.87, 1.24)	0.66	0
No clear concealment	4448 (10)	0.97 (0.87, 1.14)	0.92	45.5	2 477 (8)	0.65 (0.43, 0.97)	0.03	0
2. Intention to treat (ITT)	7326 (10)	1.06 (0.90, 1.26)	0.47	43.9	9 721 (12)	0.95 (0.80, 1.13)	0.57	2.4
Unclear if ITT used	2664 (7)	0.89 (0.72, 1.10)	0.29	44.6	2 020 (9)	1.08 (0.68, 1.72)	0.74	0
3. Data cross-checked	2877 (9)	1.09 (0.95, 1.26)	0.21	4.3	2 973 (9)	0.90 (0.70, 1.16)	0.42	0
No clear cross-check	7103 (8)	0.94 (0.76, 1.17)	0.59	65.5	8 768 (12)	1.01 (0.82, 1.25)	0.93	0
Overall quality score								
High score (>5 out of 10)	7894 (11)	1.07 (0.93, 1.23)	0.37	37.4	10 540 (13)	0.97 (0.82, 1.16)	0.76	0
Low score (≤5 out of 10)	2096 (6)	0.83 (0.62, 1.11)	0.20	36.5	1 201 (8)	0.96 (0.59, 1.43)	0.70	6.5
Extent of patient contact								
Three or more opportunities	1035 (3)	1.09 (0.92, 1.29)	0.33	0	1 521 (4)	1.11 (0.68, 1.82)	0.67	0
Less than three opportunities	8834 (13)	1.00 (0.84, 1.19)	0.77	46	10 220 (18)	0.95 (0.80, 1.12)	0.53	0
Type of pharmacist								
Hospital/clinical	3246 (9)	1.08 (0.95, 1.23)	0.23	0	5 840 (13)	0.94 (0.73, 1.21)	0.61	0
Community/other	6744 (8)	0.95 (0.76, 1.19)	0.66	68.5	5 901 (8)	0.98 (0.80, 1.21)	0.65	0

*Removing Smith [48], Bond [17], Taylor [20], Naunton [19] & Holland [13]; NA, not applicable.

estimates were broad. Equally, authors did not always provide full details of their interventions, thus making it difficult for us to distinguish successfully between more intense and less intense interventions.

Prescribing data were also infrequently reported by studies, despite drugs being the focus of all interventions. Only a third of studies could be included in the meta-analysis of these data, and, to a greater extent than for admissions, trial results appeared very heterogeneous.

Findings in comparison with other studies

The findings from this review agree with the pooled result of randomized trials included in the earlier review by Royal in primary care [6]. However, other pharmacist interventions with similar components have been effective particularly when pharmacists form part of a team [2, 30, 31]. It is interesting to note that no trial evidence currently exists on the benefit, or otherwise, of general practitioners reviewing older patients' medication, despite extensive guidance recommending its provision [32] and it is now part of their current contract in the UK. Equally, more focused patient review interventions delivered by specialist personnel have been found to be highly effective in conditions such as heart failure [33].

Conclusion

This review emphasizes that pharmacist-led medication review interventions can not be assumed to reduce hospital admissions or mortality rates in older people. These interventions may improve drug knowledge and drug adherence, but insufficient data exist to know whether the latter affects patients' quality of life positively. It should be stressed that no trial has as yet been of a sufficient size to identify a small but important gain in quality of life. The inability to demonstrate consistent benefit may stem from the wide variations in the delivery of care and patient selection in the existing trials, and it may be possible to develop higher quality research into potentially effective interventions. This would ideally involve multicentre, collaborative trials with well-defined medication review components and clearly specified, clinically relevant outcome measures.

Our findings have major implications on the provision of healthcare for older patients. Medication review is a time-consuming process for both the health professional and the patient, but is it worth the time and trouble if there is no clear benefit on hospital admissions and deaths? Delivering a medication review service for an expanding population of older people is also likely to be resource-intensive, Indeed, increasing investment is being made in providing such services (e.g. medication usage reviews in the UK) in spite of the lack of a clear evidence base demonstrating positive effect, and in the face of the potential for increasing health service costs [13]. Although improvements in patient knowledge and adherence are laudable objectives, those who are directly involved in the care of older people may justifiably feel that money is better spent on cost-effective interventions that have a definite effect on reducing hospital admissions and deaths.

Competing interests

Y.K.L. is on the Editorial Board of the British Journal of Clinical Pharmacology, but has had no involvement in the handling and review process of the manuscript while under consideration by the journal. There are no other conflicts of interest to declare.

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