Do randomised controlled trials relevant to pharmacy meet best practice standards for quality conduct and reporting? A systematic review.

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ABSTRACT

Background: Evidence-based pharmacy practice requires a dependable evidence base. Randomised controlled trials (RCTs) are the gold standard of high quality primary research, and tools exist to assist researchers in conducting and reporting high quality RCTs. This review aimed to explore whether RCTs relevant to pharmacy are conducted and reported in line with Cochrane risk of bias and CONSORT standards respectively.

Methods: A Medline search identified potential papers. After screening of titles, abstracts and full texts, the 50 most recent papers were reviewed and assessment of bias according to Cochrane domains and compliance with CONSORT checklist items was recorded. Each domain of the Cochrane tool, CONSORT checklist item, and each article was given a percentage score, reported as median and interquartile range (IQR). Correlation between quality of conduct, quality of reporting, country of origin, and journal impact factor was conducted using the R^2 statistic.

Results: The median domain score for risk of bias by paper according to the Cochrane risk of bias tool was 53.0% (IQR 38.5-68.5), while the median compliance score by paper for the CONSORT checklist was 64.0% (IQR 36.0%-94.0%). The median Cochrane domain, and median CONSORT item completion scores respectively were 50.0% (IQR 33.3%-66.7%) and

59.5% (IQR 52.0%-70.3%). The highest risk of bias was associated with allocation concealment and blinding, and the least well reported items were randomisation details, sequence generation and allocation concealment. A positive relationship between conduct and reporting of RCTs was found ($R^2 = 0.75$), while no correlation was found between quality of conduct or quality of reporting and journal impact factor, correlation coefficients ($R^2=0.06$ and $R^2=0.05$ respectively).

Conclusion(s): This review identified that issues related to randomisation and blinding are often inadequately conducted or not comprehensively reported by researchers conducting pharmacy relevant RCTs, providing useful information for education and future research.

Keywords: RCT, Systematic Review, Pharmaceutical Care, Other

INTRODUCTION

Evidence-based pharmacy practice requires a dependable evidence base.[1] As the gold standard of high quality primary research,[2,3] the evidence from randomised controlled trials (RCTs) is the usual basis for meta-analysis and systematic review, which informs policy and practice.[4,5] However, when evidence from high quality RCTs is not available, decisions are based on expert consensus.[3,6]

In the global context, pharmacists have been acknowledged by the public as accessible and trusted health professionals,[7,8] and they are therefore uniquely placed to provide health related interventions to patients. However, systematic reviews of pharmacist led interventions often grade the quality of the research evidence base as low.[9-11]

For evidence obtained from RCTs to be graded as high, the studies must be conducted robustly, and reported in a clear and transparent manner.[2,12] There are many tools available to assist researchers in conducting and reporting high quality RCTs. CONSORT is a comprehensive and

widely acknowledged checklist, which, if followed, facilitates the reporting of transparent and high quality RCT publications.[2] In order to meet the requirements of the CONSORT checklist satisfactorily, the planning and conduct of the study has to have included the topic of each checklist item. However, the CONSORT checklist per se is *not* intended for use in assessment of quality of RCT methodology.[2]

When using evidence from RCTs to inform practice change, it is important to recognise the limitations of the original research which might affect the validity of the findings. For example, poorly conducted studies often lead to results which favour the intervention. The Cochrane collaboration's tool for assessing risk of bias in randomised trials[13] (the Cochrane risk of bias tool) comprises six domains against which an RCT is judged as having a high, low or unclear risk of bias. Therefore, assessing any study against a combination of the Cochrane risk of bias tool and the CONSORT reporting checklist highlights potential areas of weakness and allows the study findings to be interpreted in the context of any caveats. It is considered likely that studies which have been well reported, are developed with current standards of good research practice in mind, and therefore these studies are likely to have equivalently lower biases when assessed against the Cochrane tool. Finally, if research findings are to influence practice and policy, they need to be in the public domain, and authors are dependent on acceptance by academic journals for this to occur. It is therefore imperative that for journals to accept papers they prioritise studies conducted in an appropriate manner, and that the most highly regarded, higher impact factor journals only accept stronger papers.

This review aimed to explore whether RCTs relevant to pharmacy are conducted and reported in line with Cochrane and CONSORT standards respectively. The objectives of this review of published RCTs relevant to pharmacy were:

- to describe the quality of conduct using the Cochrane tool,
- to describe the quality of reporting using the CONSORT checklist,
- to identify if there is a relationship between quality of conduct and quality of reporting in RCTs, and
- to explore the relationship between journal impact factor, quality of conduct and quality of reporting of RCTs.

METHODS

This review is reported following relevant items of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (The PRISMA Statement).[14]

Eligibility criteria

Eligible papers included those: reporting the results of an RCT relevant to pharmacy (i.e. studies involving interventions implemented by a pharmacist or pharmacy technician, or interventions occurring in any pharmacy setting). Comparators included usual care or non-pharmacy interventions, and outcomes were any measure of change. Inclusion and exclusion criteria are listed in *Table 1*.

Information sources

The Medline database was used to identify eligible papers for inclusion in analysis. A single database was used due to time constraints.

Search

The Cochrane highly sensitive search strategy for identifying RCTs in Medline[15] was used to identify papers. Relevant medical subject headings (MeSH) terms along with text terms were

used, as shown in *Table 2*. The filter "English language only" was applied to the search. The search was conducted on the 30th of November 2017.

Sample size

The target sample was the most recent 50 eligible papers identified by Medline. This sample size was selected a priori for the following reasons. Firstly, only the most recently published papers would allow the current quality of conduct and reporting of pharmacy relevant RCTs to be assessed. This recognised that standards in conducting and reporting RCTs across the wider discipline of health services research are continually improving. Secondly, it was decided by consensus that 50 papers would balance being a large enough sample to provide generalisable results, yet, not too large that the data extraction could not be performed thoroughly by a single researcher in the given time frame.

Data collection process

The most recent 200 papers identified by the Medline search were screened to identify eligible papers. This process was chosen with the intention of screening a further 200 papers, if 50 eligible papers were not identified from the most recent 200 papers.

The most recent 50 eligible papers were screened by title and duplicate papers were removed. Inclusion and exclusion criteria were applied during title screening and remaining papers were screened by abstract against the eligibility criteria. Where there was uncertainty about eligibility, the researcher (AR) consulted a second researcher (CB) and a decision was reached

by consensus. If, following full text evaluation, a paper was excluded due to ineligibility, the next most recent eligible paper was included.

Data items

The 50 eligible papers were reviewed and data extracted by one researcher (AR) to assess the risk of bias and identify compliance with best practice reporting standards for RCTs using the Cochrane risk of bias and CONSORT tools respectively. Each paper was read by the researcher and received a coded numerical value denoting its risk of bias in each of the domains of the Cochrane risk of bias tool (1= low risk of bias, 2= high risk of bias, 3= unclear risk of bias). Each paper additionally received a coded numerical value denoting its compliance with each item of the CONSORT checklist (1= yes, 2= no, 3= unclear, 4= not applicable, 5= partially complete). As a quality assurance measure of the validity of the data extraction a second researcher (DP) independently extracted data and coded a random sample of ten papers (20%).

A data matrix was assembled in Microsoft Excel 2016 using the domains of the Cochrane risk of bias tool and the items of the CONSORT checklist. Each researcher independently entered data to their version of the matrix at the time of full text evaluation. Supporting information found along with each tool[2,13] was used to assist the researcher in assigning codes to the papers. Additionally, publication and study information were recorded, including a summary of the evidence from the paper, journal and year of publication, country of origin and authors and their respective institutions. For the sample of ten papers where there was duplicate extraction, matrices were compared and a consensus agreed if needed.

Summary measures

To enable comparison between papers based on risk of bias and quality of reporting, each paper was given a score. The Cochrane risk of bias score was the percentage of the domains classified as "low risk of bias". The CONSORT score was the percentage of checklist items which were classified as "yes". Adjusted CONSORT scores were calculated for each paper by removing the "not applicable" responses from the denominator prior to calculating the percentage of "yes" responses. There was no need to adjust Cochrane risk of bias scores as there was no numerical code denoting "not applicable".

Additionally, each domain of the Cochrane risk of bias tool and each item of the CONSORT checklist were given a percentage score based on the number of papers which received a "low risk of bias" or "yes" code for that domain or item divided by the total number of papers. Adjusted CONSORT scores were calculated by determining the number of "not applicable" responses for each item, and removing these from the denominator before calculating the percentage of "yes" responses. This allowed identification of those items least well conducted or reported.

Analysis and synthesis of results

Analysis of results was completed in two parts. Firstly, each domain of the Cochrane risk of bias tool and item of the CONSORT checklist were assessed for frequency of each possible coded response. Domains of the tool and items of the checklist were ranked based on the frequency of "low risk of bias" and "yes" responses to determine the highest to lowest scoring areas of each tool, based on the percentage of these responses. If the data were normally distributed, mean +/- standard deviation (SD) was used to describe the data, while if the data were not normally distributed the median and interquartile range (IQR) were used. The median or mean "low risk of bias" responses for Cochrane risk of bias and "yes" responses for

CONSORT were calculated to facilitate interpretation of how well domains and items of the tools were completed.

Secondly, papers were ranked based on their individual Cochrane risk of bias and CONSORT scores. The median and IQR or mean +/- SD of the papers' Cochrane risk of bias and CONSORT percentage scores were calculated to enable interpretation of the spread of the data. A scatter plot was created by pairing each individual paper's Cochrane risk of bias score with its CONSORT score, to identify if there was correlation between quality of conduct with low risk of bias and reporting. A second scatter plot was created by pairing each individual paper's adjusted CONSORT risk of bias score with its Cochrane score.

The papers were also classified by the journal in which they were published. The median percentage scores and IQR or mean +/- SD for each journal was calculated to determine the spread of the data and facilitate interpretation. The median or mean score of each journal (for Cochrane risk of bias, CONSORT and adjusted CONSORT) was plotted against the journal's current impact factor to explore any correlations. All data analysis was completed on Microsoft Excel 2016 for Macintosh.

RESULTS

Papers included in analysis

The Medline search identified 1517 papers. The most recent 200 papers were screened by title; after removing duplicates (50) and those ineligible (27), 123 remained. A further 66 papers were excluded following the abstract screening, leaving 57 eligible papers for data extraction (*Figure 1).* Two papers from the most recent 50 were ineligible and were replaced by the next two most recent papers.

For the 20% random sample of papers that had independent duplicate data extraction consensus was reached for all items. .

Overview of papers

The largest number of papers was from North America (*n*=20), followed by Asia and Europe (both *n*=12), Australasia (*n*=4), and South America and Africa (both *n*=1). The papers covered a range of clinical (*n*=25), medication management/use (*n*=17), public health (*n*=6) and continuing professional development (CPD) (*n*=2) topics (*Table 3).* A summary of the papers can be found in Supplemental material 1.

Quality of reporting and risk of bias

The papers' median domain score for risk of bias according to the Cochrane risk of bias tool was 53.0% (IQR 38.5-68.5). There was a high risk of bias due to inadequate allocation concealment and blinding (66% and 56% of papers respectively). Conversely, 70% of papers were assessed as a low risk of bias score for selective outcome reporting. For other sources of bias, 38% of papers were assessed as high risk or unclear risk, and 24% as low risk (Table 4).

The median level of compliance by paper with the items of the CONSORT reporting checklist for RCTs was 64.0% (IQR 36.0%-94.0%). All papers met item 2a (scientific background and rationale), and none met item 7b (when applicable, explanation of any interim analyses and stopping guidelines). After adjusting for 'not applicable' items (5 items had >80% of papers coded as 'not applicable'), fifteen checklist items were completed by at least 90% of papers (2a, 2b, 3b, 4a, 4b, 5, 6a, 6b, 11b, 12a, 15, 16, 20, 22 and 25) and six for less than 50% of papers (3a,7b,8b,9,10,24). The median level of compliance was 84.0% (IQR 60.0-96.0%). Percentage

scores for each item of the CONSORT checklist are displayed in *Table 5*. Items least well reported were related to randomisation and blinding (8a,8b,9,10).

Quality of reporting and risk of bias of individual papers

The median Cochrane risk of bias score by individual paper was 50.0% (IQR 33.3-66.7). Only one paper[16] met all criteria of the Cochrane tool and two papers[17,41] did not meet any. The median CONSORT score was 59.5% (IQR 52.0%-70.3%) with three papers[18-20] meeting 83.8% of the criteria and one meeting only 29.7% [21]. The median adjusted CONSORT score was 72.4% (IQR 61.8%-83.9%), with the highest score of 96.9% achieved by one paper,[20] and the lowest (35.5%) by one paper[21] (see Supplemental Material 2 and Supplemental Material 3).

Additional analyses

There was a correlation between Cochrane and CONSORT scores, ($y = 1.5165x - 39.197$, $R^2 = 0.72$), as shown in *Figure 2*. The same correlation was observed using adjusted CONSORT scores ($y = 1.4292x - 49.735$, $R^2 = 0.75$).

Considering only those continents with more than one paper included in analysis, Australasia (*n*=4) was the continent with the highest median Cochrane, CONSORT and adjusted CONSORT scores, of 75.0%, (IQR 62.5-85.4%), 68.9% (IQR 65.5-72.9%) and 82.3% (IQR 78.8-86.3%) respectively, and North America (*n*=20) was the continent with the lowest Cochrane, CONSORT and adjusted CONSORT scores, of 45.8% (IQR 33.3-66.7%), 56.7% (IQR 51.4-70.9%) and 66.2% (IQR 60.5-82.3%) respectively. The median percentage scores classified by continent are displayed in *Supplemental material 5*.

There was no correlation between Cochrane scores and journal impact factor or CONSORT scores and journal impact factor, with correlation coefficients of $R^2=0.05$ and $R^2=0.06$,

respectively. Additionally, there was no correlation between journals' adjusted median CONSORT score and journal impact factor (R^2=0.04).

Supplemental material 4 summarises journal impact factor with median Cochrane, CONSORT, and adjusted CONSORT scores. The journal with the highest impact factor, The Journal of the American College of Cardiology (impact factor 19.9), had Cochrane, CONSORT and adjusted CONSORT scores of 75.0%, 72.9%, and 81.8% respectively. There were several journals with an impact factor of 0 (*n*=5). Of these, BMC Public Health was the journal with the most consistent high results with median Cochrane, CONSORT and adjusted CONSORT scores of 91.7%, 83.8% and 93.9% respectively.

DISCUSSION

This review showed that of 50 RCTs relevant to pharmacy, only one met all the quality standards in every domain of the Cochrane risk of bias tool, and approximately one quarter met only two out of six domains. The criterion for low risk of bias in allocation concealment was met by the fewest number of papers, with only a third complying, and under half complied with the criterion for blinding of participants, personnel and outcome assessors. Conversely, selective outcome reporting, i.e. reporting all outcomes originally specified, was the domain for which most papers were assessed as meeting the criterion. Similarly, no paper reported on all the items required by the CONSORT checklist, although one reported 96.9% of items.

There was good correlation between the Cochrane and CONSORT scores of individual papers. There was no relationship found between quality of conduct and reporting of RCTs relevant to pharmacy and journal impact factor. For example, the journal with the highest impact factor, The Journal of the American College of Cardiology (impact factor 19.9) had lower scores for

both the Cochrane risk of bias tool and the CONSORT checklist than BMC Public Health (impact factor 0).

A strength of this review is its novelty and relevance to improving the research evidence base for pharmacy. It was conducted systematically and reported according to the PRISMA statement.[14] Further, the use of adjusted scores for CONSORT gave a more accurate representation of quality. This is especially important given that trials in health services research may not always find every item relevant. Indeed, the issue of blinding can be more difficult to achieve in this context, than perhaps a more traditional drug trial. Recognising and acknowledging the implications of the potential biases this introduces is therefore particularly important.

There are some limitations to the review. Firstly, the sample size of 50 papers is relatively small, and therefore the results of this review may not be generalisable to all pharmacy relevant RCTs. However, the sample is diverse, covering many topics, settings, countries and journals.

Secondly, only one data base was searched due to time restrictions. However, Medline is one of the most comprehensive databases for this category of paper and previous systematic reviews in this field have found that adding in other databases such as Embase and CINAHL do not greatly increase the number of unique titles for screening. Further, due to lack of time and resource we did not conduct independent duplicate data extraction and coding. As a quality assurance measure, a second researcher extracted and coded data from a random 20% of papers, and after discussion there were no disagreements.

Further, it has been assumed that each domain of the Cochrane tool and each item of the CONSORT checklist are of equal weight. Ideally, a formal consensus, such as a Delphi survey, would have been conducted to weight the items and domains, and ultimately develop a validated score. Finally, the review has focussed on the study setting not the researchers per se. It is recognised that research teams are heterogeneous in their academic affiliations and individual disciplines making it hard to tailor the key messages for improvement appropriately.

The findings of this review have multiple implications for future research. Jull *et.al*[22] conducted a comparable review in nursing journals. As in this review, it was found that allocation concealment was the domain of the Cochrane tool least likely to be assessed as low risk of bias (20.5%).[22] The results from Jull *et.al*'s review in combination with the results of the current review suggest that evidence from future RCTs in health services (e.g. pharmacy and nursing) could be more robust if more attention was paid to allocation concealment during the design of the trial.

Another similar review carried out with RCTs in anti-arrhythmic drugs by Camm *et.al* found that the mean compliance score to the CONSORT checklist was 15.4 out of 25 items, 61.8% (SD 3.05, range 9-22.5), calculated using similar methods to the current review.[23] The review by Camm *et.al* revealed relatively low percentages of RCTs were compliant with items 8a, 8b, 9 and 10 of the CONSORT checklist, with scores of 25.4%, 18.6%, 13.6% and 6.8% respectively.[23] Although higher numerically, the results of these items for the current review are similar, in that they are relatively low. Interestingly, Camm *et.al* found that there was a significant correlation ($R=0.45$, $p<0.001$) between CONSORT score and journal impact factor, contrary to the results of the current review. This might be because the current review focussed on pharmacy relevant RCTs, the majority of which have been published in low impact

pharmacy and medical journals. Camm *et.al* focussed their review on RCTs involving anti-arrhythmic drugs, which may have been published in higher impact medical journals.

A review assessing the quality of reporting of RCTs according to CONSORT carried out in otorhinolaryngologic medicine by Peters *et.al* [24] found that RCTs reported in general medical journals had a significantly higher compliance to CONSORT reporting than those published in ear, nose and throat (ENT) specific journals ($p<0.001$). These findings were hypothesised to be due to higher impact general medical journals requesting RCTs to be reported in accordance to CONSORT. Implications to be drawn from Peters *et.al* and the current review are that for the quality of reporting of RCTs to improve, endorsement from journals and research funding bodies of CONSORT reporting and other recognised guidelines appropriate to other study designs may be necessary. Lower impact, more specialised journals in areas of health and medical research, such as pharmacy and otorhinolaryngologic medicine could potentially increase their impact factor by encouraging reporting according to CONSORT and only accepting complete and transparent RCT reports. Interestingly, Peters *et.al's* findings additionally supported the results of the current review and the review by Camm *et.al*, that items 8a, 8b, 9 and 10 of the CONSORT checklist are inadequately reported in both specialty ENT journals and general medical journals.

Overall, conclusions to be drawn from the current review and previous systematic reviews of the quality of conduct and reporting of RCTs in health services research[22-24] include the requirement for researchers conducting RCTs to focus on including details of randomisation, sequence generation and allocation concealment (items 8a to 10 of CONSORT). These areas were found in the current review and in previous reviews to have been inadequately reported in many RCTs and, when they have been reported, they have been conducted poorly according to

the sequence generation and allocation concealment domains of the Cochrane tool. Additionally, it can be concluded that although the current review found no correlation between journal impact factor and quality of conduct and reporting, this finding was not supported by the results of previous reviews. Future reviews considering the quality of conduct and reporting of RCTs relevant to pharmacy should consider ascertaining whether journals in which the RCTs are published require the use of CONSORT when reporting RCTs, as well as the impact factor of the journal to identify if there is a correlation between endorsement of CONSORT and adherence to the recommendations. Future lines of enquiry could also include exploring associations with other potential predictors of research quality such as funding type (eg Research Council or commercial or none), or reporting of earlier feasibility and piloting. Qualitative work could also be conducted to understand the reason for the deficiencies and introduce interventions to address them. For example, is it lack of expertise and expert advice, lack of funding and/or lack of time?

CONCLUSION

The results of this review have identified areas of pharmacy related research which are either not conducted to the highest standard or where the reporting is inadequate, suggesting an aspect of an RCT was either not completed or reporting made it difficult to judge whether it was completed well. These are mostly associated with randomisation and blinding. It therefore highlights the need for identifying ways in which to update researchers on the standards expected to allow pharmacy research findings to have the greatest validity and therefore impact. We especially commend all researchers to access and apply the relevant research guidelines which exist.

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Table 1. *Inclusion and exclusion criteria*

Inclusion	Exclusion
1. Results of RCT reported 2. Relevant to pharmacy 3. Recently published (2015-2017) 4. English language papers 5. Available online	1. Published RCT protocols 2. Pilot studies 3. Pharmacokinetic studies 4. Interventions in which the pharmacist's only role is blinding 5. Interventions involving a pharmacy student 6. Non-English language papers 7. Papers not available online 8. Conference abstracts

Table 2. *Search terms used to identify records on Medline database. Terms within columns were combined with the Boolean operator "OR", terms across columns were combined with the Boolean operator "AND".*

The Cochrane highly sensitive search strategy for identifying randomised controlled trials in Medline	Search terms used for identifying RCTs relevant to pharmacy
1. Randomi?ed controlled trial.pt. 2. Controlled clinical trial.pt. 3. Randomi?ed.ab. 4. Placebo.ab. 5. Drug therapy.fs. 6. Randomly.ab. 7. Trial.ab. 8. Groups.ab. 9. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 10. Animals.mh NOT humans.mh 11. 9 NOT 10	1. Pharmacist OR pharmacy OR pharmacists OR pharmacies OR pharmacy technician OR chemist 2. *Pharmacists/ 3. Pharmacy OR pharmacies OR pharmacist OR pharmacy technician.mp [mp = title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 4. 1 OR 2 OR 3

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Table 3. *Description of papers* *

CONSORT score (%) median (IQR)	59.5 (52.0-70.3)	
Adjusted CONSORT score (%) median (IQR)	72.4 (IQR 61.8-83.9).	
Cochrane score (%) median (IQR)	50.0 (33.3-66.7)	
Continent *n* (%)	Africa	1 (2)
	Asia	12 (24)
	Australasia	4 (8)
	Europe	12 (24)
	North America	20 (40)
	South America	1 (2)
Journal *n* (%)	Addiction	2 (4)
	American Journal of Kidney Disease	2 (4)
	Basic and Clinical Pharmacology and Toxicology	1 (2)
	BioMed Research International	1 (2)
	BioMed Central Health Services Research	4 (8)
	BioMed Central Nephrology	1 (2)
	BioMed Central Public Health	1 (2)
	British Journal of Clinical Pharmacy	1 (2)
	The Consultant Pharmacist	1 (2)
	Drug and Alcohol Dependence	1 (2)
	Drugs & Aging	1 (2)
	Health and Quality of Life Outcomes	1 (2)
	Hypertension	1 (2)
	International Journal of Clinical Pharmacy	7 (14)
	International Journal of Cardiology	1 (2)
	Journal of the American Society of Hypertension	2 (4)
	Journal of General Internal Medicine	1 (2)
	Journal of Medical Systems	1 (2)
	Journal of Pharmaceutical Sciences	1 (2)
	Journal of Clinical Pharmacy and Therapeutics	2 (4)
	Journal of Hospital Medicine	1 (2)
	Journal of Managed Care and Specialty Pharmacy	2 (4)
	Journal of Pharmacy Practice	1 (2)
	Journal of the American College of Cardiology	1 (2)
	The Medical Journal of Australia	1 (2)
	Patient Education and Counselling	1 (2)
	The Permanente Journal	1 (2)
	Pharmacotherapy	2 (4)
	PLOS One	1 (2)
	Population Health Management	1 (2)
	Process Evaluation and Measurement	1 (2)
	Research in Social and Administrative Pharmacy	1 (2)
	Telemedicine and e-Health	1 (2)
	The Diabetes Educator	1 (2)
	The Journal of Clinical Hypertension	1 (2)
Topic of trial *n* (%)	Clinical	25 (50)
	Diabetes	*5 (10)*

	Hypertension	*5 (10)*
	*CVD**	*3 (6)*
	Respiratory disease	*3 (6)*
	*CKD***	*3 (6)*
	Oncology	*3 (6)*
	Osteoporosis	*1 (2)*
	Gout	*1 (2)*
	Iron-overload	*1 (2)*
Medication management/use		17 (34)
Public health		6 (12)
	Smoking cessation	*4 (8)*
	*Sexual health/HIV^*	*1 (2)*
	Alcohol	*1 (2)*
CPD^^		2 (4)

*CVD = Cardiovascular disease, **CKD= Chronic kidney disease, ^HIV= Human immunodeficiency virus, ^^CPD = Continuing professional development
*D**ata were not normally distributed, therefore median and IQR** reported

Table 4. *Number and percentages of papers assessed at different levels of risk for each domain of the Cochrane tool*

Domain of the Cochrane tool	**Domain completion rank (/6)**	**Low risk of bias *n* (%)**	**High risk of bias *n* (%)**	**Unclear risk of bias *n* (%)**
Sequence generation:	3	23 (46)	25 (50)	2 (4)
Allocation concealment:	5	16 (32)	32 (64)	2 (4)
Blinding:	4	20 (40)	28 (56)	2 (4)
Incomplete outcome data:	2	33 (66)	2 (4)	15 (30)
Selective outcome reporting:	1	41 (82)	2 (4)	7 (14)
Other sources of bias:	6	12 (24)	19 (38)	19 (38)

Table 5. *Number and percentage of papers complying with each item on the CONSORT checklist.*

CONSORT checklist item	Item completion rank (/37)	Yes *n* (%)	No *n* (%)	Unclear *n* (%)	Not applicable *n* (%)	Partially complete *n* (%)
1a: Identification as a randomised trial in the title	=24	32 (64)	18 (36)	0 (0)	0 (0)	0 (0)
1b: Structured summary of trial design, methods, results, and conclusions	19	41 (82)	1 (2)	0 (0)	0 (0)	8 (16)
2a: Scientific background and explanation of rationale	=1	50 (100)	0 (0)	0 (0)	0 (0)	0 (0)
2b: Specific objectives or hypotheses	=5	49 (98)	0 (0)	1 (2)	0 (0)	0 (0)
3a: Description of trial design (such as parallel, factorial) including allocation ratio	=31	18 (36)	0 (0)	0 (0)	0 (0)	32 (64)
3b: Important changes to methods after trial commencement (such as eligibility criteria), with reasons	=1	3 (100)*	0 (0)	0 (0)	47 (0)	0 (0)
4a: Eligibility criteria for participants	=9	48 (96)	2 (4)	0 (0)	0 (0)	0 (0)
4b: Settings and locations where the data were collected	=5	49 (98)	1 (2)	0 (0)	0 (0)	0 (0)
5: The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	=11	47 (94)	0 (0)	1 (2)	0 (0)	2 (4)
6a: Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	=11	47 (94)	0 (0)	3 (6)	0 (0)	0 (0)
6b: Any changes to trial outcomes after the trial commenced, with reasons	=1	1 (100)*	0 (0)	0 (0)	49 (0)	0 (0)
7a: How sample size was determined	27	30 (60)	19 (38)	0 (0)	0 (0)	1 (2)
7b: When applicable, explanation of any interim analyses and stopping guidelines	36	0 (0)	1 (2)	0 (0)	49 (98)	0 (0)
8a: Method used to generate the random allocation sequence	28	28 (56)	21 (42)	1 (2)	0 (0)	0 (0)
8b: Type of randomisation; details of any restriction (such as blocking and block size)	=31	18 (36)	27 (54)	1 (2)	0 (0)	4 (8)
9: Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	33	15 (30)	35 (70)	0 (0)	0 (0)	0 (0)
10: Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	30	22 (44)	27 (54)	0 (0)	0 (0)	1 (2)
11a: If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	29	26 (52)	24 (48)	0 (0)	0 (0)	0 (0)
11b: If relevant, description of the similarity of interventions	=1	8 (100)*	0 (0)	0 (0)	42 (84)	0 (0)
12a: Statistical methods used to compare groups for primary and secondary outcomes	=5	49 (98)	0 (0)	0 (0)	0 (0)	1 (2)
12b: Methods for additional analyses, such as subgroup analyses and adjusted analyses	17	30 (85.7)*	4 (8)	1 (2)	15 (30)	0 (0)
13a: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	21	40 (80)	8 (16)	0 (0)	0 (0)	2 (4)
13b: For each group, losses and exclusions after randomisation, together with reasons	26	29 (60.4)*	14 (28)	2 (4)	2 (4)	3 (6)
14a: Dates defining the periods of recruitment and follow-up	15	44 (88)	6 (12)	0 (0)	0 (0)	0 (0)

14b: Why the trial ended or was stopped	35	2 (4)	48 (96)	0 (0)	0 (0)	0 (0)
15: A table showing baseline demographic and clinical characteristics for each group	=9	48 (96)	2 (4)	0 (0)	0 (0)	0 (0)
16: For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	13	46 (92)	1 (2)	3 (6)	0 (0)	0 (0)
17a: For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	18	42 (84)	1 (2)	3 (6)	0 (0)	4 (8)
17b: For binary outcomes, presentation of both absolute and relative effect sizes is recommended	22	19 (76)*	2 (4)	2 (4)	25 (50)	2 (4)
18: Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	20	30 (81.1)*	4 (8)	2 (4)	13 (26)	1 (2)
19: All important harms or unintended effects in each group	23	2 (66.7)*	0 (0)	0 (0)	47 (94	1 (2)
20: Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	=5	49 (98)	1 (2)	0 (0)	0 (0)	0 (0)
21: Generalisability (external validity, applicability) of the trial findings	16	43 (86)	3 (6)	4 (8)	0 (0)	0 (0)
22: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	=5	49 (98)	0 (0)	0 (0)	0 (0)	1 (2)
23: Registration number and name of trial registry	=24	32 (64)	0 (0)	0 (0)	0 (0)	18 (36)
24: Where the full trial protocol can be accessed, if available	34	6 (12)	41 (82)	0 (0)	0 (0)	3 (6)
25: Sources of funding and other support (such as supply of drugs), role of funders	14	45 (90)	4 (8)	0 (0)	0 (0)	1 (2)

**The % completion of these items was adjusted to remove the "not applicable" responses to provide a more accurate picture of "yes" percentage scores.*

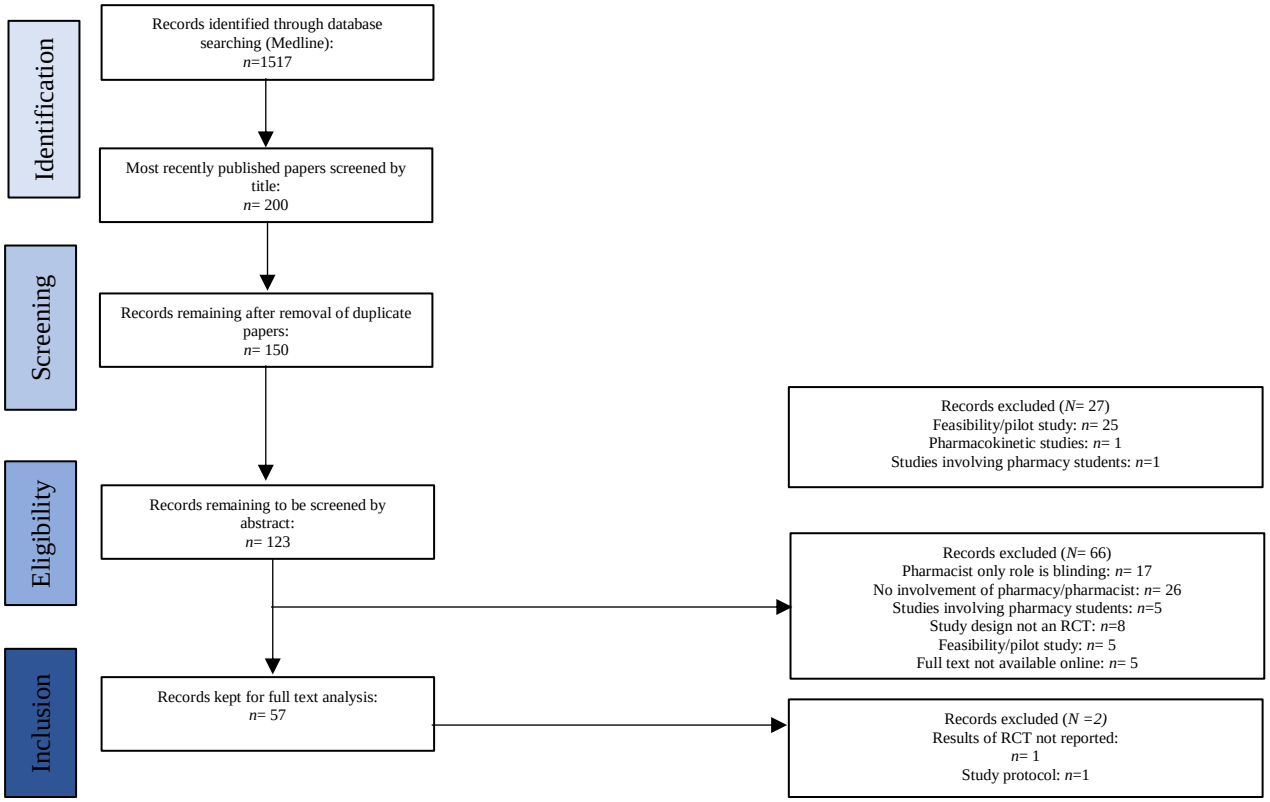

Figure 1: *Inclusion process for records identified through database searching. Of the 57 eligible full texts, the most recent 50 records were included.*

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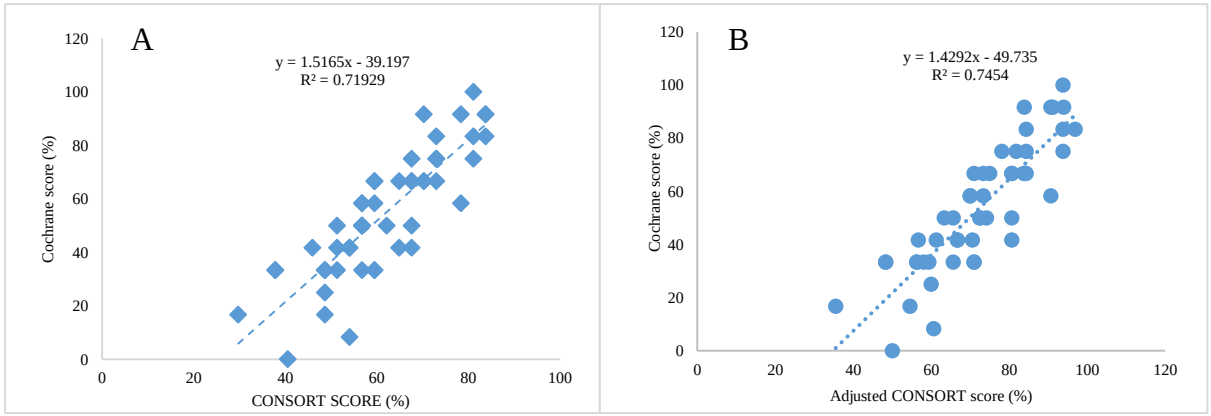

Figure 2. *Panel A shows the correlation between Cochrane and CONSORT scores of individual papers. Panel B shows correlation between Cochrane and adjusted CONSORT of individual papers. NOTE: there are fewer data points than papers, as some data points represent more than one paper.*

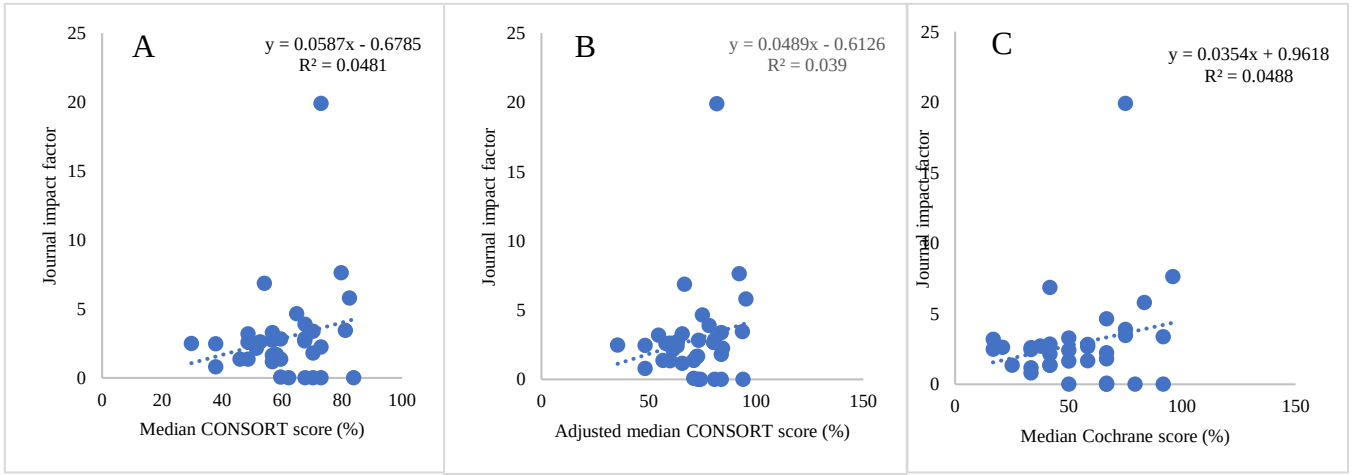

Figure 3*. The relationship between journal impact factor and median CONSORT, median adjusted CONSORT and median Cochrane scores, in panels A, B and C respectively.*

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SUPPLEMENTARY Materials

Supplemental material 1 . *Summary of article characteristics and findings*

Article ID	Author, year	Country	Aims/objectives	Methods	Findings
1.	Treibich, 2017[25]	France	Identify benefits of dispensing exact pill numbers	Experimental group counted out medication by unit, control group received existing pharmaceutical company box sizes	Beneficial to environment (less wasted), medication adherence and public health to dispense exact number of pills.
2.	Lalonde, 2017[26]	Canada	Assess impact of ProFiL program on medication adherence in patients with CKD	Intervention group pharmacists received 90-minute web-based training program about medication use in CKD, control group - usual care	ProFiL trained pharmacists lead to fewer drug related problems in patients with CKD
3.	Tong, 2017[27]	Australia	Determine if pharmacist-completed medication management plans reduce rate of medication errors in discharge summaries	Intervention group received pharmacist medication management plans, control group standard medical discharge summaries	Significant reduction in medication errors in medication management plans completed by pharmacists
4.	Periasamy, 2017[28]	Malaysia	Develop, implement and evaluate pharmacist led chemotherapy counselling on quality of life	Intervention group received counselling "Managing patients on chemotherapy" from pharmacist.	Managing patients on chemotherapy and repetitive counselling from pharmacists was shown to increase quality of life in oncology patients
5.	Manfrin, 2017[18]	UK	Evaluate the Italian Medicines Use review (I-MUR) using asthma patients	Structured, face-to-face asthma education from pharmacist	I-MUR demonstrated effectiveness and cost-effectiveness
6.	Houle, 2017[29]	Canada	Explore the needs of community pharmacies to provide medication management services	Intervention pharmacies received external task-focused facilitation, control group usual practice	External facilitation seems to be feasible and acceptable to support community pharmacy medication management services
7.	El Hajj, 2017[19]	Qatar	Test the effect of a structured face-to-face pharmacist intervention to aid smoking cessation	Intervention group received structured support from pharmacist at 2-4 week intervals, control group received brief unstructured smoking cessation advice	There was no statistically significant difference in smoking abstinence rates at 12 months between groups
8.	Bahnasawy, 2016[30]	Egypt	Evaluate the occurrence of drug related problems in paediatric beta-thalassaemia major patients	Control group received standard medical care, intervention group received standard medical care plus clinical pharmacy services	There was a decline in the number of drug related problems in the intervention group from baseline to follow up
9.	Axtell, 2017[31]	USA	To compare the effectiveness of 4 different instructional interventions in correct inhaler technique	Subjects assigned to one of four interventions: 1. Read MDI instructions, 2. Watch CDC video demonstrating MDI technique, 3. Watch a youtube video demonstrating MDI technique, 4. Receive direct instruction of MDI technique from pharmacist.	A 2-minute pharmacist counselling session is more effective than other interventions in correctly teaching inhaler technique.
10.	Kane-Gill, 2016[32]	USA	Assess the importance and performance of consultant pharmacist services to detect and manage adverse drug events (ADEs) among nursing home residents	Clinical pharmacy services including academic detailing to physicians, response to drug alerts, and provision of structured recommendations about ADE management were provided in the intervention	Clinical pharmacy led intervention can improve physician's assessment of importance and performance of clinical pharmacy services
11.	Gong, 2016[33]	USA	To evaluate enhance pharmacy care program of pharmacist telephone counselling for smoking cessation	Intervention group patients received 3 telephone counselling sessions from specialist pharmacists, control group received usual care	Pharmacist telephone counselling to encourage smoking cessation can increase adherence to prescription smoking cessation medications

12.	Spoelstra, 2016[34]	USA	Evaluate the acceptability of Text message support in adult cancer patients	Intervention patients received text messages according to their medication regimen, control group received usual care	Adult cancer patients were likely to enrol into text message support
13.	Anderegg, 2016[35]	USA	Evaluate if pharmacist intervention can minimise healthcare disparities in high-risk racial and socioeconomic hypertensive patients	Patients in intervention group received structured interview with pharmacist, control group received usual care	Pharmacist intervention reduced racial and socioeconomic disparities in the treatment of hypertension
14.	Qudah, 2016[36]	Jordan	Evaluate the clinical pharmacist's role in the management of blood pressure in haemodialysis patients	Intervention arm patients received physician-pharmacist collaborative care, control group received standard medical care	Collaborative pharmacist-physician care improved rate of blood pressure control in haemodialysis patients
15.	Malet-Larrea, 2016[37]	Spain	Assess impact of medication review with follow up provided in community pharmacy to aged polypharmacy patients on the number of medication related hospital admissions	Intervention group pharmacies provided comprehensive medication review, control group delivered usual care	Medication review and follow up delivered by community pharmacists might be effective in reducing medication related admissions
16.	Tong, 2016[38]	Australia	Evaluate the effectiveness of a partnered pharmacist charting model completed at the time of admission to reduce medication errors	Intervention patients received partnered pharmacist charting, control group received standard medical care	Partnering between medical staff and pharmacists to jointly chart initial medications on admission significantly reduced inpatient medication errors
17.	Messerli, 2016[39]	Switzerland	Investigating the impact of Polymedication check (PMC) on polypharmacy patients	Intervention group received a PMC at baseline and after 28 weeks, control group only received PMC at 28 weeks.	Through the PMC the pharmacist was able to identify a significant number of Drug related problems
18.	Geurts, 2016[40]	The Netherlands	To determine whether a clinical medication review followed by a pharmaceutical care plan reduces the number of potential drug related problems and pharmaceutical care issues	Intervention patients received a clinical medication review, followed by development of a pharmaceutical care plan. Control group received care as usual	The integrated use of clinical medication review and pharmaceutical care plan development facilitates the detection of and decrease in drug related problems
19.	Smith, 2016[41]	USA	Compare physician-pharmacist collaborative model to usual hypertension care	Intervention group received collaborative physician-pharmacist care, control group received usual hypertension care	Team based care in the primary care setting may be effective at treating treatment resistant hypertension
20.	Tsuyuki, 2016[42]	Canada	Evaluate the effectiveness of a community pharmacy-based case finding and intervention on cardiovascular risk	Usual care group received usual pharmacist care, intervention group received medication therapy management review from their pharmacist and CVD risk assessment and education	The results demonstrated a significant reduction in risk for CVD events in intervention patients
21.	Basheti, 2016[43]	Jordan	Identificaiton of treatment related problems through a medication management review	All patients visited in their home for medication management review, pharmacist sent letter to GP of intervention group patients with receommendations regarding treatment	Home based medication management review decreased the total number of treatment related probelsm and improved self-reported adherence
22.	Lim, 2016[44]	Malaysia	Assess the clinical outcomes of patients managed by pharmacists in Diabetes Medication Therapy Adherence Clinic (DTMAC)	Intervention group received usual care plus DTMAC, including 8 follow up visits. Control group received usual care	Pharmacist managed DTMAC significantly improved glycaemic control and lipid profile of diabetic patients
23.	Bell, 2016[45]	USA	Determine the effect of a tailored, pharmacist-delivered health literacy intervention on unplanned healthcare utilisation	Intervention group received pharmacist assisted medication reconciliation, inpatient pharmacist counselling, adherence aids and individualised telephone follow up after discharge	The intervention did not reduce unplanned health care utilisation

24.	Goldfien, 2016[46]	USA	To determine whether a pharmacist staffed gout management program is more effective in achieving target serum uric acid levels in gout patients	Intervention group received management by a clinical pharmacist following protocol, control group received management of their gout from their usual treating physician	A structured pharmacist staffed program was more effective than usual care for achieving target serum uric acid levels
25.	Meulendijk, 2016[47]	The Netherlands	To determine if having a group of users perform a similar task over a prolonged period of time leads to improvements in efficiency in that task	Independent physician-pharmacist teams conducted medication reviews using supported software	The amount of time users needed to perform similar tasks decreased significantly as they gained experience over time
26.	Phatak, 2016[48]	USA	Assess the impact of pharmacist involvement in transitions of care measured by decreased medication errors	The control group received standard hospital care. The intervention group received face-to-face medication reconciliation, patient specific pharmaceutical care plan, discharge counselling and 3 post-discharge phonecalls	It was demonstrated that pharmacist involvement in hospital discharge transitions of care had a positive impact on decreasing inpatient readmissions and ED visits
27.	Basheti, 2016[49]	Jordan	To assess the impact of a medication management review service on treatment related problems and certain clinical outcomes in outpatients	The clinical pharmacist conducted baseline assessment in both patient groups, reccomendations regarding treatment related problems were only forwarded to the physician of intervention group patients	The medication management review service resulted in significantly lower number of treatment related problems and improved clincial outcomes
28.	Blackburn, 2016[16]	Canada	To test a brief intervention for preventing statin nonadherence among community pharmacy patrons	Intervention pharmacists attended a 2.5 hour training addressing barriers to statin adherence and screened for new statin users to assess their compliance	The intervention was ineffective for improving patient adherence to statin therapies in community pharmacies
29.	Ishani, 2016[50]	USA	To determine whether an intervention consisting of telehealth with interprofessional team case management could be effectively implemented and improve the combined end point of death, hospitalisation, ED visits or admission to nursing home in patients with CKD	Intervention patients received care from an interprofessional team using a telehealth device, control patients received usual care	Telehealth by an interprofessional team is a feasible care delivery strategy in patients with CKD. There was no statistically significant evidence of the interventions superiority on health outcomes over usual care
30.	Roblek, 2016[51]	Slovenia	To determine if interventions by clinical pharmacists can reduce the prevalence of clinically relevant drug drug interactions during hospitalisation of patients with heart failure	All attending physicians received standard advice about pharmacologic therapy, those in the intervention group also received alerts about clinically relevant DDIs	Pharmacist intervention significantly reduces the number of patietns with clinically relevant DDIs, but not clinical endpoints 6 months from discharge
31.	Suhaj, 2016[52]	India	Evaluate the effectiveness of clinical pharmacist intervention on health related quality of life (HRQoL) in patients with COPD	The intervention pharmacist emphasised importance of medication compliance, smoking cessation, simple ecercise, proper use of inhalers, need for timely follow up. Control group received usual care	Pharmacist intervention improved HRQoL of patients with COPD.
32.	O'Sullivan, 2016[53]	Ireland	To design a structured pharmacist review of medications supported by software for reducing adverse drug reactions in older hospitalised patients	Intervention patients received the clinical decision software supported structured pharmacist review of medications within 48h of admission, control group received care as usual	The intervention significantly reduced incidence of adverse drug reactions in acutely hospitalised older people
33.	Thomas, 2016[54]	Australia	Evaluate the effectiveness of a pharmacist-led multi-component smoking cessation program	Pharmacist-led behavioural counselling and/or pharmacotherapy provided during hospital stay, on discharge and one month post discharge was provided to the intervention group, control group received routine hospital care	The intervention did not improve sustained abstinence rates at either 6 or 12 months post intervention

34.	Chen, 2016[55]	Taiwan	To evaluate the effects of pharmaceutical care on glycaemic control of ambulatory older patients with type 2 diabetes	Control group received standard care, intervention group received pharmaceutical care from a certified diabetes educator pharmacist who identified and resolved drug related problems	The intervention improved long-term safe control of blood sugar levels for ambulatory older adults with type 2 diabetes
35.	Wang, 2015[21]	China	Evaluate the efficacy of pharmaceutical intervention on chemotherapy knowledge, attitude and practice (KAP) and quality of life (QoL) in cancer patients	Intervention group patients were given information booklets and 30 minute face-to-face medication education and psychological counselling by clinical pharmacists twice weekly for 2 months	The intervention significantly improved KAP and QoL in adult cancer patietns over control.
37.	Dhital, 2015[20]	UK	To evaluate the effectiveness of a brief intervention delivered by community pharmacists to reduce hazardous or harmful drinking	Control group patients received a leaflet about the harms of drinking, intervention group patients received a brief motivational discussion (10mins) from a pharmacist who had received a half-day training in delivering the intervention	The brief motivation discussion appeared to have no effect in reducing hazardous or harmful alcohol consumption
38.	Donyai, 2015[56]	UK	Test the outcome of training people to use CPD framework through distance learning material	The control group received information in the mail about new CPD requirements, the intervention group received the CPD framework and associated training	The intervention was shown to improve participant's CPD behaviour
39.	Tso, 2015[57]	USA	Evaluate the impact of conducting a pharmacist-led telephone outreach program to improve osteoporosis managemnet in elderly women after experiencing fractures	The patients were split into 3 groups: baseline intervention consisting of patient education mailing, baseline intervention plus a live outbound intervention call to patients by pharmacist, and baseline intervention plus pharmacist call to patients health providers to recommend initiation of osteoporosis therapy and/or BMD test	Pharmacist calls did not improve osteoporosis management over mail and fax notifications
40.	Basger, 2015[58]	Australia	Examine the effects of applying a validated prescribing appropriateness criteria set during medication review in patients >65 at time of discharge from hospital	Control group patients received usual care, intervention received discharge medication counselling and review from a clinical pharmacist	The intervention did not increase the number of prescribing appropriateness criteria met nor significantly improve HRQoL
42.	Obarcanin, 2015[59]	Germany	Evaluate the impact of pharmaceutical care in adolescents with T1DM provided by pharmacists in collaboration with physicians on important clinical outcomes	Intervention group received structured monthly pharmaceutical care visits plus supplementary visits as needed for 6 months, control group received usual diabetic care	The findings suggest that multi-disciplinary pharmacuetical management may add value in adolescent patients with T1DM
43.	Carter, 2015[60]	USA	To evaluate the sustained hypertension control following pharmacist intervention in veterans	All patients received intensive pharmacist intervention for the first 6 months, at which point the patients were stratified based on BP control and randomised to continue the intervention for 24 months or cease the intervention	The findings suggest that once BP control is achieved following pharmacist intervenion patients can be referred back to their primary care provider
44.	Kooy, 2015[61]	The Netherlands	Assess effects of pharmacists' counselling by telephone on patients satisfaction with counselling and information and beliefs about medicines for newly prescribed medicines	Control patients received usual care, intervention patients received telephone counselling to address barriers to adherent behaviour	Telephone counselling by pharmacists improved satisfaction with counselling and satisfaction with information
45.	Jahangard-Rafsanjani,2015[62]	Iran	Investigate the efficacy of a community-pharmacist delivered diabetes support program for patients receiving specialty medical care	The pharmacist trained patietns in the intervention group for 5 months including 5 follow up visits and 5 phone calls. Control group received care as usual	The intervention improved self-care activity, medication adherence and BMI in patients receiving specialty medical care
46.	Upadhyay, 2015[17]	Malaysia	Determine the baseline satisfaction level of newly diagnosed diabetics and to	Intervention group received pharmaceutical care, control group patients received usual care from	The intervention significantly improved the satisfaction level of diabetics in the test group

			explore the impact of pharmaceutical care intervention on patient's satisfaction during their follow ups	physicians/nurses. Outcomes measuresd at baseline, 3, 6, 9 and 12 months.	
47.	Cooney, 2015[63]	USA	To evaluate the effect of a pharmacist based quality improvement program on outcomes for patients with CKD and adherence to CKD guidelines in primary care setting	Intervention patients received a phone-based pharmacist intervention, pharmacist-physician collaboration and patient education	The intervention did not improve BP control in patients with CKD, however it did improve guideline adherence
48.	Adams, 2015[64]	USA	To determine whether brief, structured telephonic tobacco cessation counselling delivered by clinical pharmacists impacted tobacco cessation attempts compared to usual care	Control group received usual care, the intervention group received brief, structured telephone tobacco cessation counselling	It was found that the brief structured telephone intervention may not adequately affect patient motivation to impact tobacco cessation attempts
49.	Javadi, 2015[65]	Iran	Compare the efficacy of two types of continuing pharmacy education on selected reproductive health topics	Intervention group received small group training with simulated patients, while control group received the CPE in didactic lecture format	There were no significant differences observed between satisfaction and attitude scores of the two groups
50.	Gums, 2015[66]	USA	To describe medication adherence and medication intensification in a physician-pharmacist collaborative management (PPCM) model compared to usual care	Control group received usual care, intervention group received a structured pharmacist interview and created a care plan	The PPCM model increased medication intensification, however no significant change in medication adherence was detected
51.	Lewis, 2015[67]	USA	To examine the impact of a pharmacy-randomised intervention to reduce injection risk amongst people who inject drugs	Intervention pharmacies received in depth harm reduction training and recurited syringe customers into the study and provided additional services, primary control pharmacies recruited syringe customers into the study but did not provide additional services, secondary control did not recruit	The findings suggest that expanded pharmacy services for people who inject drugs can ecnourage sterile syringe use and decrease injection risk
52.	Becerra-Camargo, 2015[68]	Colombia	To measure the impact of pharmacist-acquired medication history during admission to an ED	All patients had standardised, comprehensive medication history interview focusing on the patient's current home medication regimen prior to being seen by the Dr	It was found that involving a pharmacist and drawing up a history of complete medicaiton could contribute towards reducing the risk of potential adverse drug events

Note: Papers 36 and 41 were excluded due to ineligibility.

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Supplemental material 2 . *Cochrane domain scores for each article.*

	Sequence generation	Allocation concealment	Blinding of participants, personnel and outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
1. Treibich, 2017						
2. Lalonde, 2017						
3. Tong, 2017						
4. Periasamy, 2017						
5. Manfrin, 2017						
6. Houle, 2017						
7. El Hajj, 2017						
8. Bahnasawy, 2016						
9. Axtell, 2016						
10. Kane-Gill, 2016						
11. Gong, 2016						
12. Spoelstra, 2016						
13. Anderegg, 2016						
14. Qudah, 2016						
15. Malet-Larrea, 2016						
16. Tong, 2016						
17. Messerli, 2016						
18. Geurts, 2016						
19. Smith, 2016						
20. Tsuyuki, 2016						
21. Basheti, 2016						
22. Lim, 2016						
23. Bell, 2016						
24. Goldfien, 2016						
25. Meulendijk, 2016						
26. Phatak, 2016						
27. Basheti, 2016						
28. Blackburn, 2016						
29. Ishani, 2016						
30. Roblek, 2015						
31. Suhaj, 2015						
32. O'Sullivan, 2015						
33. Thomas, 2015						
34. Chen, 2015						
35. Wang, 2015						
37. Dhital, 2015						
38. Donyai, 2015						
39. Tso, 2015						
40. Basger, 2015						
42. Obarcanin, 2015						
43. Carter, 2015						
44. Kooy, 2015						
45. Jahangard-Rafsanjani, 2015						
46. Upadhyay, 2015						
47. Cooney, 2015						
48. Adams, 2015						
49. Javadi, 2015						
50. Gums, 2015						
51. Lewis, 2015						
52. Becerra-Camargo, 2015						

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Supplemental material 3. *CONSORT item scores for each article.*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	37	38	39	40	42	43	44	45	46	47	48	49	50	51	52
1a: Identification as a randomised trial in the title	2	1	1	1	1	1	1	2	2	2	1	2	2	2	2	1	1	2	2	1	1	2	1	1	2	2	1	1	1	1	1	1	1	1	2	1	2	2	1	1	2	1	1	1	1	1	1	2	1	1
1b: Structured summary of trial design, methods, results, and conclusions	5	1	1	1	1	1	1	5	1	1	1	5	2	1	1	1	1	1	5	1	5	5	1	1	5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1
2a: Scientific background and explanation of rationale	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2b: Specific objectives or hypotheses	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3a: Description of trial design (such as parallel, factorial) including allocation ratio																																																		
3b: Important changes to methods after trial commencement (such as eligibility criteria), with reasons	4	4	4	4	1	1	4	4	4	4	1	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
4a: Eligibility criteria for participants	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1
4b: Settings and locations where the data were collected	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5: The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	1	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6a: Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3	1	1	1	1	3	1	1	1	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6b: Any changes to trial outcomes after the trial commenced, with reasons	4	4	4	4	1	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
7a: How sample size was determined	2	1	1	1	1	2	1	2	1	2	1	2	2	2	2	1	1	1	2	1	1	1	1	2	2	5	1	1	1	1	1	1	1	1	2	1	2	1	1	2	2	2	1	1	1	1	1	2	2	2
7b: When applicable, explanation of any interim analyses and stopping guidelines	4	4	4	4	4	4	4	2	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
8a: Method used to generate the random allocation sequence	1	1	1	1	1	2	1	1	1	2	2	2	2	1	1	2	2	1	2	1	1	2	1	2	2	1	1	1	1	2	2	2	1	1	1	1	2	2	2	1	1	2	3	2	1	1	1	2	2	1
8b: Type of randomisation; details of any restriction (such as blocking and block size)	1	1	1	2	1	2	1	2	2	2	2	2	1	3	1	1	1	2	5	5	2	2	1	5	2	2	2	1	1	2	2	2	1	2	2	1	1	2	2	2	1	1	1	2	5	2	2	2	2	2
9: Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	2	1	2	2	2	2	1	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	1	2	2	2	2	1	1	2	1	2	1	1	2	1	2	2	1	1	1	2	1	2	2	2	2	2	2	2
10: Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	1	1	1	2	1	2	1	2	2	2	2	2	1	1	1	2	1	1	2	2	2	2	1	2	2	1	2	1	1	2	5	1	1	1	2	1	2	2	2	1	2	2	1	2	2	2	1	2	2	1
11a: If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	2	1	1	1	1	2	1	2	2	2	2	2	2	1	1	1	1	2	2	1	1	1	1	2	2	1	2	1	1	1	2	2	1	2	2	1	1	2	1	2	2	1	2	2	1	1	1	2	2	1
11b: If relevant, description of the similarity of interventions	4	4	4	4	4	4	1	1	1	4	4	4	4	1	4	4	4	4	1	4	1	4	4	4	4	4	4	4	4	1	4	4	4	4	4	4	4	1	4	4	4	4	4	4	4	4	4	4	4	4
12a: Statistical methods used to compare groups for primary and secondary outcomes	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12b: Methods for additional analyses, such as subgroup analyses and adjusted analyses	4	1	1	1	1	4	1	1	1	4	1	1	1	4	2	4	1	4	1	1	2	1	1	4	4	4	4	1	1	1	4	4	1	2	2	1	1	4	1	1	1	1	1	4	1	4	1	1	3	1
13a: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	1	1	1	1	1	2	1	1	2	2	1	1	1	5	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	2	1	5	1	1	1	1	1	1	2	1	1	2	2	1	1

13b: For each group, losses and exclusions after randomisation, together with reasons	2	1	4	1	1	2	1	2	2	2	1	1	1	5	2	1	5	2	3	1	1	1	1	3	2	1	1	1	1	4	1	1	1	2	2	1	2	1	1	1	1	1	1	2	1	1	2	2	5	1
14a: Dates defining the periods of recruitment and follow-up	1	1	1	1	1	1	1	1	1	2	2	1	1	1	1	1	1	1	2	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1
14b: Why the trial ended or was stopped	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
15: A table showing baseline demographic and clinical characteristics for each group	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1
16: For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	1	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	3	1	1	1	1	1	1	3	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1	1	1	1	1
17a: For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	5	1	1	1	1	1	1	5	1	1	1	1	1	1	1	3	3	1	1	1	1	1	3	1	1	5	1	5	1	1	1	1
17b: For binary outcomes, presentation of both absolute and relative effect sizes is recommended	4	1	1	4	1	4	1	4	4	4	1	4	4	4	1	5	4	4	1	1	4	2	5	1	4	1	3	1	1	4	4	1	1	4	4	1	2	3	4	4	4	1	4	4	4	4	4	1	1	1
18: Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	1	2	2	1	1	4	1	1	1	4	1	4	4	4	1	4	1	1	1	1	4	4	1	4	4	1	4	1	1	1	4	1	5	3	2	1	1	2	1	1	1	1	1	3	1	4	1	1	1	1
19: All important harms or unintended effects in each group	4	4	4	4	4	4	4	4	4	4	1	4	4	4	4	4	1	4	4	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
20: Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
21: Generalisability (external validity, applicability) of the trial findings	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	3	1	1	1	1	2	1	1	2	1	1	1	1	3	1	1	3	1	3	1	1
22: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1
23: Registration number and name of trial registry	1	1	1	1	1	5	1	5	5	5	5	5	1	5	1	5	1	5	1	1	1	5	1	1	1	5	5	1	1	1	1	1	1	1	5	1	5	5	1	1	1	1	1	5	1	5	5	1	1	1
24: Where the full trial protocol can be accessed, if available	2	2	2	5	1	2	1	5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	5	2	2	2	2	2	2	1	2	2	1	2	2	2	2	2	1	2	2	2	2	2	2	2	1
25: Sources of funding and other support (such as supply of drugs), role of funders	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	5	1	1	1	1	1	1	1	1	1	1	1	1
1 = yes, 2= no, 3= unclear, 4= not applicable, 5=partially complete																																																			

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Supplemental material 4. *Journals of analysed RCTs, their impact factors and median CONSORT and Cochrane scores.*

Journal (n)	Impact factor	Median Cochrane score (%)	Median CONSORT score (%)	Median adjusted CONSORT score (%)
Addiction (2)	5.8	83.3	82.4	95.3
American Journal of Kidney Disease (2)	7.6	95.8	79.7	92.2
Basic and Clinical Pharmacology and Toxicology (1)	3.2	16.7	48.6	54.5
BioMed Research International (1)	2.5	16.7	29.7	35.5
BioMed Central Health Services Research (4)	0	79.2	72.9	72.9
BioMed Central Nephrology (1)	0	66.7	70.3	83.9
BioMed Central Public Health (1)	0	91.7	83.8	93.9
British Journal of Clinical Pharmacy (1)	3.9	75.0	67.6	78.1
The Consultant Pharmacist (1)	0.8	33.3	37.8	48.3
Drug and Alcohol Dependence (1)	3.3	50.0	56.8	65.6
Drugs & Aging (1)	2.8	41.7	67.6	80.6
Health and Quality of Life Outcomes(1)	0	66.7	67.6	80.6
Hypertension (1)	6.9	41.7	54.1	66.7
International Journal of Clinical Pharmacy (7)	1.3	41.7	59.5	70.9
International Journal of Cardiology (1)	4.6	66.7	64.9	75.0
Journal of the American Society of Hypertension (2)	2.6	20.8	52.7	59.9
Journal of General Internal Medicine (1)	3.4	75.0	81.1	93.8
Journal of Medical Systems (1)	2.5	33.3	37.8	48.3
Journal of Pharmaceutical Sciences (1)	2.6	33.3	48.7	58.1
Journal of Clinical Pharmacy and Therapeutics (2)	1.7	58.3	58.1	72.9
Journal of Hospital Medicine (1)	2.1	41.7	51.4	61.3
Journal of Managed Care and Specialty Pharmacy (1)	2.7	37.5	56.7	63.4
Journal of Pharmacy Practice (1)	1.2	33.3	56.7	65.6
Journal of the American College of Cardiology (1)	19.9	75.0	72.9	81.8
The Medical Journal of Australia (1)	3.4	91.7	70.3	83.8
Patient Education and Counselling (1)	2.2	66.7	72.9	84.4
The Permanente Journal (1)	1.3	25.0	48.7	60.0
Pharmacotherapy (2)	2.7	58.3	67.6	80.3
PLOS One (1)	2.8	58.3	59.5	73.3
Population Health Management (1)	1.6	50.0	56.8	72.4
Process Evaluation and Measurement (1)	0	50.0	62.2	74.2

Research in Social and Administrative Pharmacy (1)	2.4	50.0	51.4	63.3
Telemedicine and e-Health (1)	1.4	41.7	45.9	56.7
The Diabetes Educator (1)	1.8	66.7	70.3	83.9
The Journal of Clinical Hypertension (1)	0.1	66.7	59.5	70.9

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