Association of Pharmacist Interventions with Adverse Drug Events and Potential Adverse Drug Events

Kelly WN¹, Ho MJ¹, Smith T², Bullers K³, David W. Bates⁴, and Kumar A²

¹University of South Florida Taneja College of Pharmacy
²University of South Florida Morsani College of Medicine
³USF Health Shimberg Health Sciences Library
⁴Brigham and Women’s Hospital Channing Division of Network Medicine

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Abstract

Background: Adverse drug events (ADEs) are a frequent cause of injury in patients. Our aim was to assess pharmacist interventions and their association with ADEs and potential adverse drug events (PADE). Methods: The search criteria: a published RCT, evidence of a pharmacist intervention, a comparison control group, and measurement of ADEs or PADEs. The information sources included MEDLINE, Embase, and two other databases through September 19, 2022. The risk of bias was assessed using the Cochrane tool for RCTs. A random-effects model for pooled studies was employed. Results: Fifteen references meeting inclusion criteria were discovered. For ADEs, the pooled results showed a statistically significant benefit of pharmacist intervention in comparison to the control group (RR = 0.86; [95% CI 0.80-0.94]; P = 0.0005. The heterogeneity was insignificant (P = 0.72; I² = 0%). Patients receiving a pharmacist intervention were 14% less likely for ADE than those who did not receive a pharmacist intervention. The estimated number of patients needed to prevent one ADE across all patient locations was 33. For PADEs, the pooled results did not show a statistically significant benefit for pharmacist intervention in comparison to the control group (RR = 0.79; [95% CI 0.47 – 1.32]; P =0.37. There was substantial heterogeneity in the pooled studies (P = 0.01; I² = 77%). However, there was a statistically significant subgroup difference (P = 0.005) for the intervention type. Conclusions: To our knowledge, this is the first systematic review and meta-analysis of RCTs seeking to understand the association of pharmacist interventions with ADEs and PADEs. The risk of having an ADE is reduced by a seventh for patients receiving a pharmacist care intervention versus no such intervention. This fraction could be higher for certain high-risk patients. The estimated number of patients needed to be followed across all patient locations to prevent one preventable ADE across all patient locations is 33. Also, a subgroup analysis of pharmacist intervention focus suggests that further research is necessary to fully understand the impact of TOC pharmacist intervention on PADEs. If validated, these findings have potential to significantly reduce drug-related morbidity and related healthcare costs.
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Conclusions: To our knowledge, this is the first systematic review and meta-analysis of RCTs seeking to understand the association of pharmacist interventions with ADEs and PADEs. The risk of having an ADE is reduced by a seventh for patients receiving a pharmacist care intervention versus no such intervention. This fraction could be higher for certain high-risk patients. The estimated number of patients needed to be followed across all patient locations to prevent one preventable ADE across all patient locations is 33. Also, a subgroup analysis of pharmacist intervention focus suggests that further research is necessary to fully understand the impact of TOC pharmacist intervention on PADEs. If validated, these findings have potential to significantly reduce drug-related morbidity and related healthcare costs.

KEY WORDS:
ADEs, PADES, pharmacist interventions, drug safety

Key Points:

- Adverse drug events (ADEs) are still the most frequent cause of harm in hospitals and occur in ambulatory patients.
- This is the first known systematic review and meta-analysis of the association of pharmacist interventions with ADEs and PADEs.
The study shows the risk of having a preventable ADE is reduced 14% for patients with a pharmacist care intervention versus no intervention.

More research is needed to validate or refute these findings. However, until then, using pharmacists to prevent ADEs and PADEs should be undertaken to prevent harm to patients.

1 | INTRODUCTION

Any injury resulting from medical intervention related to a drug is called an adverse drug event (ADE). Each year, about 4.3 million people in the United States visit an outpatient clinic or emergency room for ADEs, and 350,000 are admitted to the hospital. The incidence of ADEs varies by patient age, location, and the intensity of therapy. In early studies among hospitalized patients, an estimated 6.5% of patients experience an ADE with an almost 2-fold increased risk of death in this population. For intensive care patients, the ADE incidence is 40.8%. The incidence of ADEs in older ambulatory patients is about 5%. What distinguishes ADEs from reports on the incidence of medication errors, adverse drug reactions, medication-related problems and drug interactions is injury. The severity of ADEs in hospitalized patients varies with 1% fatal, 12.0-18.5% life-threatening, 30.0-33.3% serious, and 48.2-57% significant.

ADEs are costly. The total estimated cost of drug-related morbidity and mortality in the United States in 2000 (excluding malpractice costs and just for the ambulatory environment) was $717B each year. One study found an ADE increased hospital stay by 2.2 days and costs $3,244. In one study, a PADE increased hospital stay by 4.6 days and costs $5,857. These estimates were conservative as they do not include the costs of injuries to patients or malpractice costs. However, not all ADEs are preventable. Rates vary by patient location: hospital 28.0; ICU 31.4%; ambulatory (older patients) 27.6%.

A key priority of pharmacy practice is to prevent medication harm. Therefore, the primary objective of this investigation was to assess the association of pharmacist interventions (versus no pharmacist care intervention) with ADEs and PADEs. The secondary objective was to investigate if these associations varied by disease category, length of follow up, the intervention focus, patient risk, or by patient or pharmacist intervention location.

2 | METHODS

2.1 | Protocol

We performed a systematic review and meta-analysis (SR/MA) of randomized controlled trials (RCTs) published according to the methods outlined a priori in the protocol registered with PROSPERO (CRD 420234630087). We report this study according to the Preferred Reporting Items for SR/MA guidelines (PRISMA).

2.2 | Eligibility criteria

For inclusion in the systematic review, studies had to meet the following criteria: (1) a published RCT, (2) evidence of pharmacist only intervention in any setting in the study group, (3) a comparison control group providing usual care or usual pharmacist care, and (4) measurement of ADEs or PADEs. An ADE was adverse drug “incidents” or “events” from medical intervention resulting in injury. A PADE was an ADE intercepted before injury occurred.

2.3 | Information sources and search

We conducted searches in MEDLINE via Ovid, the Cochrane Library for clinical trials in CENTRAL, Embase via Elsevier and International Pharmaceutical Abstracts (IPA) via Ovid were conducted from inception through September 19th, 2022. A health librarian [KB] developed and conducted the search with the process peer-reviewed by another health librarian. The search strings included MeSH, Emtree, and IPA subject terms and synonyms for key terms. The “randomized controlled trial strategy” filters for Embase and Medline, designed by information specialists at the BMJ Knowledge Centre, was applied. The filter was modified as warranted to accommodate the specific databases. No other filters or limits, like patient location or language were applied to the search.
Search results were exported to an EndNote library and deduplicated using the SR-Accelerator Deduplicator developed by the Institute for Evidence-Based Healthcare and Bond University. The automated deduplication results were reviewed, and manual deduplication performed in EndNote. The deduplicated data was uploaded into Rayyan for screening and review.

Following the study selection process, a backwards citation analysis and a forwards citation analysis of the final studies selected for inclusion was conducted on November 11, 2022. This step maximized our chances of identifying all relevant studies and was conducted using the SR-Accelerator SpiderCite tool. Extracting references from the available SR/MA supplemented the search. (Appendix 1).

2.4 | Study selection

Two co-authors (WK and MJH) reviewed the results of the search independently using Rayyan. After applying exclusion criteria, each researcher determined which studies to include in the analysis with the final studies included reached by consensus.

2.5 | Data collection process

Using the Rayyan tool, two authors (WNK and MJH) reviewed (independently) the titles and abstracts identified by the systematic review with differing results resolved by consensus. Data on study characteristics were extracted by WNK and MJH and collected using a pretested standardized form with instructions according to the Cochrane Handbook for Systematic Reviews of Interventions. Differences in the data extraction were settled by mutual agreement.

2.6 | Data items

The selected characteristics of each study included: the primary author, patient country, follow-up period, population studied, information on the intervention, adherence, the adherence measurement method, quality-of-life scores, and the quality-of-life measurement method. The terms “counseling,” “education,” “pharmaceutical care,” or medication management/review” were used to identify the pharmacist care interventions, while the term “transitions” and “reconciliation” were used to identify a TOC management intervention. A subgroup analysis included seven covariates:

- The intervention focus:
  - pharmacist care (like counseling for proper use and adherence)
  - drug regimen review and recommendations to the prescriber for medication-related problems
  - transition of care (TOC) management – a check for missing or duplicate therapy

- Patient location = inpatient, inpatient then outpatient, or outpatient

- Intervention location = hospital or outpatient (clinic, group practice, pharmacy, or home)
  - Mean age category = <65 or ≥65 years old
  - Patient risks (elderly, multiple medications, high co-morbidity, recent hospitalization) = <3 low or ≥3 high
  - Primary disease studied = mixed or specific
  - Follow up = <6 months or ≥6 months

An MS Excel spreadsheet contained the consensus data. Studies meeting the inclusion criteria were in two groups: cluster RCTs (groups of subjects randomized, such as by pharmacies) and participant RCTs (individuals randomized) to assess the effect of the intervention by a group of pharmacists versus individual pharmacists.

2.7 | Risk of bias in individual studies

Two investigators (WK, MJH) assessed the data independently with differences resolved by consensus. We summarized the overall quality of evidence using the Grading of Recommendations and Evaluation (GRADE)
2.8 | Summary measures

We summarized ADEs and PADEs as risk ratios (RR) with 95% confidence intervals (CIs). The data analyst pooled the data using Review Manager software version 5.3 (Cochrane Collaboration), and subgroup analyses were performed on ADEs and PADEs with each covariate.

2.9 | Synthesis of results

A data analyst (TS) performed the synthesis of results. A random-effects model using the DerSimonian-Laird approach to pooled studies for all analyses was employed. The analyst evaluated the heterogeneity among pooled studies using Chi-square and $I^2$ statistics. An $I^2 > 50\%$ suggested substantial heterogeneity. A chi-square test with the significance level set at $P < 0.01$ indicated statistically significant heterogeneity.

3 | RESULTS

3.1 | Search Results and Study Characteristics

The search identified 837 references, of which fifteen met inclusion criteria for the systematic review. All fifteen had extractable data for the meta-analysis. Figure 1 displays the flow of study selection through the SR/MA. Ten studies were from the United States, and twelve studies included mostly older patients with various diseases. Twelve studies reviewed ADEs, one study PADEs; and two studies ADEs and PADEs. Table 1 lists the characteristics of the included studies. In ten RCTs, pharmacist care was the focus, while five focused on TOC management.

Table 1.

Selected characteristics of included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population Studied</th>
<th>Patient Location</th>
<th>Follow Up (mo.)</th>
<th>N</th>
<th>Mean Age</th>
<th>Male %</th>
<th>Primary Disease Risks</th>
<th>Location Focus</th>
<th>Location Structure</th>
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<td>OP</td>
<td>PC</td>
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<td>Oman</td>
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<td>57</td>
<td>42</td>
<td>Mixed</td>
<td>Low</td>
<td>IP/OP</td>
<td>TOC</td>
</tr>
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<td>96</td>
<td>Mixed</td>
<td>High</td>
<td>IP/OP</td>
<td>TOC</td>
</tr>
<tr>
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<td>Australia</td>
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<td>110</td>
<td>83</td>
<td>39</td>
<td>Mixed</td>
<td>High</td>
<td>IP/OP</td>
<td>TOC</td>
</tr>
<tr>
<td>Farris 21</td>
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<td>630</td>
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<td>Low</td>
<td>IP/OP</td>
<td>TOC</td>
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<tr>
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<td>361</td>
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<td>51</td>
<td>Mixed</td>
<td>High</td>
<td>OP</td>
<td>PC</td>
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<td>70</td>
<td>99</td>
<td>Mixed</td>
<td>High</td>
<td>OP</td>
<td>PC</td>
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<tr>
<td>Jost 24</td>
<td>Slovenia</td>
<td>LOS</td>
<td>120</td>
<td>72</td>
<td>55</td>
<td>Mixed</td>
<td>Low</td>
<td>IP</td>
<td>TOC</td>
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<td>Kripalani 25</td>
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<td>862</td>
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<td>59</td>
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<td>Low</td>
<td>IP/OP</td>
<td>PC</td>
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<td>Phatak 26</td>
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<td>IP/OP</td>
<td>PC</td>
</tr>
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<td>Low</td>
<td>IP/OP</td>
<td>PC</td>
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<tr>
<td>Surepill SG 29</td>
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<td>1094</td>
<td>?</td>
<td>57</td>
<td>Mixed</td>
<td>Low</td>
<td>IP</td>
<td>PC</td>
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</table>
3.2 | ADEs

An ADE necessitated injury. The mean incidence of ADEs in included studies across all patient locations was 21%. The pooled results showed a statistically significant reduction in ADEs associated with pharmacist intervention in comparison to the control group (RR = 0.86; [95% CI 0.80-0.94]; P = 0.0005. (Figure 2). The observed heterogeneity was insignificant (P = 0.72; I^2 = 0%). The risks of having an ADE are reduced by 14% in patients receiving a pharmacist care intervention. There was no statistically significant subgroup effect for the secondary objective. Only two RCTs reported severity of the ADEs prevented by pharmacist interventions. In one, 18.1% of ADEs were serious or life-threatening, and in the other, 26.6% were severe or life-threatening.

3.3 | PADEs

To discover the likelihood of a PADE potentially being an ADE, all studies used a panel of experts, and sometimes inter-rater reliability assessment. The mean incidence of PADEs in included studies was 10.7%. The pooled results for PADEs did not show a statistically significant benefit for pharmacist intervention in comparison to the control group (RR = 0.79; [95% CI 0.47 - 1.32]; P =0.37. (Figure 3). There was substantial heterogeneity observed in the pooled studies (P = 0.01; I^2 = 77%). However, there was a statistically significant subgroup difference (P = 0.005) for the intervention focus, which suggests that it may modify the effect of the pharmacist intervention, however, we cannot be certain because of the small number of studies. (Appendix 2).

3.4 | Certainty of the Evidence

The overall methodologic quality of the included studies for ADEs was moderate, and for PADEs very low. (Table 2). The results of the bias assessment for each included study are found in Appendix 3. The proportion of studies graded as “low risk” for the randomization process was 80%; for deviation from the intended interventions 67%; for missing outcome data 67%; for measurement of the outcome 67%; for the reported result 93%; and for meeting all criteria 53%. (Appendix 4). A risk of bias summary is provided (Appendix 5).

Table 2. Pharmacist intervention compared to no intervention for ADEs and PADEs

<table>
<thead>
<tr>
<th>Study Location</th>
<th>Follow Up (mo.)</th>
<th>Population Studied</th>
<th>Pharmacists</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Touchette USA</td>
<td>6</td>
<td>426</td>
<td>75</td>
<td>33</td>
<td>Mixed</td>
<td>High</td>
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<td>Yin China</td>
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<td>64</td>
<td>46</td>
<td>64</td>
<td>Renal</td>
<td>Low</td>
</tr>
</tbody>
</table>

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Focus of Intervention: CVD = cardiovascular disease; OP = outpatient; IP = inpatient; IP/OP = inpatient to outpatient; TOC = transitions in care (medication reconciliation) only; PC = pharmaceutical care (any combination of counseling, medication review, medication reconciliation, or drug-related problem identification).

Structure of Intervention: High = “tightly structured,” use of a script, protocol, or procedure manual. Low = low or no mention.

Meeting abstract

SG = study group; LOS = length of hospital stay

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PADEs, we found only fifteen randomized trials. Our results suggest, patients receiving a pharmacist care control group for six months, then the incidence of medication errors in each group is calculated, showing example is a study where patients are randomized to a pharmacist intervention group and the others to a unrandomized and most only measure process contributions to possible harm without measuring it. An The evidence from these studies is positive and robust. However, many pharmacy intervention studies are Doing “no harm” is the pharmacy profession’s primary societal purpose and reason for licensing. However, preventing medication harm is a tall order as all drugs have inherent risks for negative outcomes. Fortunately, pharmacists are not alone in the fight, but are part of a healthcare team, each member doing what they can to “first do no harm.” Still, the question holds - how well do pharmacists prevent medication harm (injury) to patients? We found in this formal meta-analysis that patients who receive a pharmacist intervention are 14% less likely to suffer an adverse event compared to those who do not.

This issue has been evaluated for over 35 years. One early study investigating the value of pharmacist interventions in preventing potential medication harm to patients was by Folli, et, al in 1987.[32] The conclusions were: the error rates for two hospitals was 1.35 and 1.77 per 100-patient days respectively, and 2) pharmacists can prevent these errors from occurring. Since this time, there have been hundreds of studies investigating whether pharmacist interventions significantly reduce medication errors, inappropriate prescribing, or medication-related problems like dosing issues, drug interactions, and contraindications.

The evidence from these studies is positive and robust. However, many pharmacy intervention studies are unrandomized and most only measure process contributions to possible harm without measuring it. An example is a study where patients are randomized to a pharmacist intervention group and the others to a control group for six months, then the incidence of medication errors in each group is calculated, showing there is a statistically significant difference in the error rate favoring pharmacist intervention. However, no mention of patient injury.

In what we believe is the first published SR/MA on assessing pharmacist interventions with ADEs and PADEs, we found only fifteen randomized trials. Our results suggest, patients receiving a pharmacist care intervention versus no such intervention, the risk of having an ADE is reduced by 14%, or about one seventh. Not all ADEs are preventable (like Type 1 adverse drug reactions), and estimates of ADE rates in hospitals vary from 27.5% to 40.3%.[3, 5, 7, 8] Using a conservative ADE preventability estimate of 28%, the data suggests pharmacist interventions may reduce preventable ADEs by 50%. Based on a 21% ADE incidence and a 14% reduction in ADEs in this study. Thirty-three (33) patients are needed to be followed across all patient locations to prevent one ADE.

Explanations

a. Deviations from the intended interventions – observed in Hanlon 1996 and Schnipper 2021. Data from outcomes was missing or not reported clearly and the outcome was not measured appropriately in Hanlon 1996, Kripalani 2012, and Phatak 2021.
b. Substantial heterogeneity was observed in pooled studies.
c. Only some studies were included in the analysis and the results of the studies were not consistent.

4 | DISCUSSION

*Primum non nocere* (first do no harm) is an expression every healthcare practitioner learns during their education and training. For pharmacists, the expression means to prevent patient harm from medication. Doing “no harm” is the pharmacy profession’s primary societal purpose and reason for licensing. However, pharmacist interventions can prevent these errors from occurring. Since this time, there have been hundreds of studies investigating whether pharmacist interventions significantly reduce medication errors, inappropriate prescribing, or medication-related problems like dosing issues, drug interactions, and contraindications.

The evidence from these studies is positive and robust. However, many pharmacy intervention studies are unrandomized and most only measure process contributions to possible harm without measuring it. An example is a study where patients are randomized to a pharmacist intervention group and the others to a control group for six months, then the incidence of medication errors in each group is calculated, showing there is a statistically significant difference in the error rate favoring pharmacist intervention. However, no mention of patient injury.

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Finding no significant effect of covariates (disease, age category, risk, follow-up, and the intervention focus and location) on preventing ADEs was a surprise as our most recent study suggested the location of the pharmacist intervention is important in improving medication adherence and quality of life.[33] We hope, these results encourage other investigators to increase the body of evidence by measuring ADEs, rather than intermediary parameters having no injury reported. This recommendation is in no means downplaying the importance of studying medication errors, as 80% of ADEs are associated with medication errors.[34]

Pharmacist interventions did not show a statistically significant association with PADEs which was not surprising because we could find only five studies to evaluate. The real surprise is locating only five PADE studies since clinical pharmacy arrived in the 1960s. Why only five, when the evidence is needed to prove the clinical and economic value of employing pharmacists to improve medication effectiveness and safety? The answer may be methodology. To assure the certainty that a pharmacist intervention prevented an ADE, there must be a panel of experts agreeing (consensus usually ≥ 69%) that injury would have occurred if not prevented. Although critical, this step adds complexity and cost for a clinical trial, but so be it – let us move ahead with better methods.

The subgroup analysis of five covariates for PADEs showed no statistical difference, including follow-up (a mean of 1.75 months for pharmacist transition management versus 5.95 months for the pharmacist care intervention). However, there was a statistically significant subgroup difference (P = 0.005) for the intervention type (TOC intervention versus a pharmacist care intervention). Although included studies only contained three PADE investigations, the results suggest that further research is necessary to help clear doubt on the merit of performing pharmacist TOC management. The controversy started with a 2012 RCT by Kripalani and colleagues,[25] a study included in our analysis. Despite receiving pharmacist intervention methods like medication education, adherence counseling or a telephone follow-up discharge, medication errors were not reduced. A series of letters to the editor followed expressing concerns and reasons these results are questionable.[35-37]

Gurwitz and colleagues published the results of a 2021 RCT (also included in our analysis) testing a pharmacist home intervention (assessment, educational material, primary care team contact, and a follow-up telephone call after 14 days) on older, recently discharged patients using high-risk medications.[22] There was no observed difference in the rate of ADEs or clinically important errors associated with a clinical pharmacist intervention. This manuscript prompted a letter to the editor titled “Adverse drug events after hospitalization: are we missing the mark?” There was a suggestion that recruiting numbers in the study were low resulting in the study being “under powered,” and that ADEs may have occurred before the first pharmacist home visit and not counted.[38] A SR/MA is the way to harmonize studies with similar study objectives and methods, but with differing results to look inside the black box. Our study suggests pharmacist TOC interventions may be working for preventing PADEs, but this needs further investigation.

Besides the evidence in this study, a pharmacy intervention improves medication adherence by 30%, reduces 30-day readmissions by 24%, reduces emergency room visits by 30%,[39] and produces a statistically significant improvement in quality of life.[33]

Study Limitations

There are some limitations to this systematic review related to the deficiencies in the included studies and not necessarily associated with the conduct of this systematic review. The two concerns with the included studies relate to publication bias at the outcome level. For example, of the 15 eligible RCTs, only 14 reported ADE and only three reported PADEs. And further, a minority of the included studies were at high-risk for bias to unclear reporting of the randomization process and allocation concealment which may impact the overall results. Another important limitation relates to heterogeneity among pooled studies.

We performed subgroup sensitivity analyses to explore heterogeneity. However, because of the few eligible studies, we could get a definitive explanation for the heterogeneity in the pooled results. Also, all the abovementioned limitations contributed to the overall certainty in the evidence being of low or very low. Nevertheless, the findings from this systematic review provides the most comprehensive evidence on the
impact of pharmacy interventions to reduce ADEs and PADEs and emphasizes on the need to improve the quality of conduct and reporting of the RCTs in the field.

Policy Implications

As discussed in the introduction, the incidence of ADEs on patient morbidity and mortality is unacceptably high, as is the cost of increased hospital stays and added medical care (often not fully reimbursed), estimated to be at least $3,244 for one ADE.[8] The cost of medical malpractice claims for ADEs also need consideration – the highest total cost of any procedure-related injury in a large study of closed insurance.[40] Another recent study suggests that ADEs are still the most frequent cause of harm in hospitals.[61]

The value in preventing ADEs and PADEs for patients is no morbidity or mortality; to prescribers, less malpractice claims; to pharmacist employers (healthcare organizations, and pharmacies) less liability and uncompensated care; and to healthcare sponsors (the payers, like Medicare, and their insurers) reduced healthcare costs. Incentives and reimbursement work well for improving other concerns of healthcare having far less potential to prevent morbidity, mortality, and save healthcare cost. Investment in pharmacist interventions to prevent medication injury and improve TOC are cost saving and produces a positive return on investment.[42, 43] Based on this value, reimbursement for pharmacist interventions in high-risk patients and high-risk medication should be considered, and care delivery organizations should require them.

5 | CONCLUSIONS

To our knowledge, this is the first systematic review and meta-analysis of RCTs seeking to understand the association of pharmacist interventions with ADEs and PADEs. The risk of having an ADE is reduced by a seventh for patients receiving a pharmacist care intervention versus no such intervention. This fraction could be higher for certain high-risk patients. The estimated number of patients needed to be followed across all patient locations to prevent one preventable ADE across all patient locations is 33. Also, a subgroup analysis of pharmacist intervention focus suggests that further research is necessary to fully understand the impact of TOC pharmacist intervention on PADEs. If validated, these findings have potential to significantly reduce drug-related morbidity and related healthcare costs.

AUTHOR CONTRIBUTIONS

Protocol development : Kelly, Bates, and Kumar

Search : Bullers and Kelly

RCT selection, data abstraction, and bias assessment : Kelly and Ho

Data analysis : Smith

Manuscript preparation : Kelly and Smith

Manuscript review : All

FUNDING INFORMATION

Unfunded

CONFLICT OF INTEREST

Disclosure: Dr. Bates reports grants and personal fees from EarlySense, personal fees from CDI Negev, equity from ValeraHealth, equity from Clew, equity from MDCClone, personal fees from and equity from AESOP, personal fees and equity from FeelBetter, personal fees and equity from Guided Clinical Solutions, and grants from IBM Watson Health, outside the submitted work. The other authors have no relevant conflict of interest or financial relationships.

ETHICS STATEMENT
The present systematic review and meta-analysis does not need ethical approval or patient consent.

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William N Kelly ID https://orchid.org/??????????????

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Figure 2. Association of pharmacist intervention with ADEs – pooled results and funnel plot.
Figure 3. Association of pharmacist with PADEs – Pooled results and funnel plot.