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Advanced Medication Reconciliation: A Systematic Review of the Impact on Medication Errors and Adverse Drug Events Associated with Transitions of Care

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Objective: The goal of this study was to conduct a systematic review on the impact of in-hospital electronic/enhanced medication reconciliation compared to basic medication reconciliation on medication errors, discrepancies, and adverse drug events (ADEs).

Methods: The study team searched for peer-reviewed English-language articles in EMBASE, OVID, and Scopus databases up to October 2019. Included were randomized controlled trials (RCTs), pre-post, or interrupted time series designs with medication errors, discrepancies, or ADEs as an outcome, and medication reconciliation applied at hospital discharge. Basic medication reconciliation was defined as using a paper-based format, electronic medication reconciliation as using an electronic format, and enhanced medication reconciliation as incorporating additional interventions to reduce medication errors.

Results: Ten studies (three RCTs, one retrospective cohort study, two interrupted time series studies, three pre-post studies, and one longitudinal study) were identified, with six and four studies comparing basic medication reconciliation to electronic and enhanced medication reconciliation, respectively. The overall risk of bias of the included studies was low (three), unclear (two), moderate (three), and serious/high (two). In general, studies demonstrated that electronic medication reconciliation reduced the odds of a medication discrepancy or ADE and may reduce the mean number of medication discrepancies. Enhanced medication reconciliation was more equivocal, with some studies showing improvement; however, risk of bias was generally significant.

Conclusion: Electronic medication reconciliation tends to reduce the risk of ADE; however, these conclusions were limited due to a lack of consistency in study settings, interventions, and outcome definitions. Future studies with more rigorous designs and standardized outcome definitions would provide clarity on this topic.

Transitions of care occur when patients move across or out of sites of care within the health system. These transitions may pose a threat to patient safety, as miscommunication or simple transcription errors can lead to unintentional changes in a patients' medication regimen.[1–8] Although some changes in a patient's medication regimen between hospital admission and discharge are deliberate, other discrepancies are unintentional and can occur due to incomplete or inaccurate information about a patient's current medications or doses.[3] These medication errors can include inappropriate continuation or discontinuation of medications after hospital discharge, errors of duplication, and incorrect dosing.[3]

Both unintentional continuation and discontinuation of medications after discharge are associated with death, emergency department visits, and unplanned hospitalizations.[9,10] It has been estimated that 19% of patients discharged from the hospital experience an adverse event within three weeks, with 66% of these being adverse drug events (ADEs) and 62% being preventable.[11] *ADE* describes harm caused to a patient as a result of a medication, which includes medication errors.[11] In one study, system errors contributed to all of the preventable adverse events, with poor communication between hospital staff and patients or primary care physicians being the most common deficit in the provision of discharge care.[11]

Medication reconciliation is one solution to improve communication during transitions of care. It involves obtaining and maintaining an accurate list of all medications taken by a patient.[12–15] Multiple methods of medication reconciliation exist, including standardized forms, collaborative programs, and pharmacy-led programs.[16–21] Recently there has been a movement away from standard paper-based medication reconciliation to electronic medication reconciliation, in which electronic tools are used to deliver and support medication reconciliation. These tools may allow health care providers to better reconcile medications and doses.[22,23] Also, medication reconciliation programs have evolved to enhanced medication reconciliation, which incorporates multiple components (for example, multidisciplinary checklists and discharge summaries in addition to basic medication reconciliation processes). Previous system-

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atic reviews have focused on describing the electronic tools and evaluating their usability, user adherence, and satisfaction,[24] or they have focused primarily on medication reconciliation at the time of admission.[25] Discharge medication reconciliation appears to be the most important intervention to reduce errors at home after a hospital admission.[8,26] Previous reviews have not specifically included enhanced medication reconciliation programs.

Our objective was to conduct a systematic review of the existing literature on the impact of electronic and enhanced medication reconciliation at hospital discharge on medication errors, discrepancies, and ADEs. We specifically sought studies that compared the efficacy of basic medication reconciliation programs to electronic or enhanced medication reconciliation programs.

METHODS

Search Strategy

This review follows PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) reporting guidelines for systematic reviews. We conducted an electronic search of the Embase and MEDLINE databases using the Ovid platform and Scopus database with the date range of 1946 (Embase, Ovid MEDLINE) or 1966 (Scopus) to October 9, 2019. We conducted the initial search up to September18, 2018, and then conducted a secondary search up to October 9, 2019, to ensure that we had identified any relevant recently published studies. We used a combination of controlled vocabulary and keywords reflecting the following concepts: "Patient transfer," "Continuity of care," "Medication errors," "Inappropriate prescribing," "Adverse drug events," and "Med rec." Details on the exact search terms and combinations are presented in Appendix 1 (available in online article). Only peer-reviewed studies in the English language were included, and no restrictions were placed on the year of publication.

Study Selection

Two independent reviewers [L.K., B.W.] performed title and abstract screening, and one reviewer [L.K.] performed full-text screening. We included studies that met the following inclusion criteria: (1) the study was conducted in the hospital setting; (2) electronic medication reconciliation or enhanced medication reconciliation was implemented at hospital discharge; (3) the study assessed ADEs or medication errors or discrepancies; and (4) the study design was a randomized controlled trial or quasi-randomized controlled trial or a controlled pre-post study or an interrupted time series design with a comparison group (basic medication reconciliation). We defined *basic medication reconciliation* as comparing a patient's medication lists (for example, home medication history taken at admission compared to a discharge summary) using a paper-based or PDF format. *Electronic medication reconciliation* processes were not limited to, but must involve, reconciling a patient's medication lists in an electronic format (for example, using the electronic medical record [EMR]). *Enhanced medication reconciliation* processes must include the components of basic medication reconciliation and another intervention designed to enhance patient safety concerning medications (for example, involving a second practitioner to further verify medication reconciliation accuracy). Studies were excluded from this review if participants were in a long term care setting or the study was conducted in an intensive care, ambulatory, or pediatric setting, as the medication reconciliation procedure in these departments may vary greatly from medication reconciliation practices in other departments. Conference proceedings, editorials, review articles, and commentaries were not included, as they do not contain all information necessary for data extraction. When there were discrepancies between the two reviewers, the final decision was made based a consensus process.

Data Extraction and Risk of Bias Assessment

Two reviewers [L.K., A.H.] performed data extraction using a standardized form. This included an assessment of the risk of bias (ROB) for all included studies using the Cochrane ROB assessment tool RoB-2 for randomized trials[27] and the Cochrane ROB tool ROBINS-1 for nonrandomized intervention studies.[28] Two independent reviewers [L.K., A.H.] performed ROB assessments. Data extracted included author, year of study, study setting and design, number of study participants, study inclusion/exclusion criteria, participant characteristics, description of the intervention, description of outcome definition, and length of the study. The outcomes of interest were the proportion of patients with medication discrepancies or ADEs, the mean number of discrepancies per patient, the proportion of medications or medication orders/discharge summaries with discrepancies, or the total number of medication errors. Study results were grouped by intervention type (electronic or enhanced medication reconciliation) and further subdivided by outcome type (such as proportion of patients with medication discrepancies or ADEs, or mean number of discrepancies per patient). Results were qualitatively compared within outcome type for each intervention type.

RESULTS

Search Results

The electronic database search yielded 1,009 (919 from the initial search and 90 from the updated search) studies from Embase, 1,074 (982 + 92) from Ovid MEDLINE, and 536 (447 + 89) from Scopus. After duplicates were removed, 1,725 (1,490 + 235) studies remained for title and abstract screening. Of those, 52 (48 + 4) studies were selected for full-text screening, and 14 met the inclusion criteria for this review (Figure 1). Reasons for study exclusion after full-text

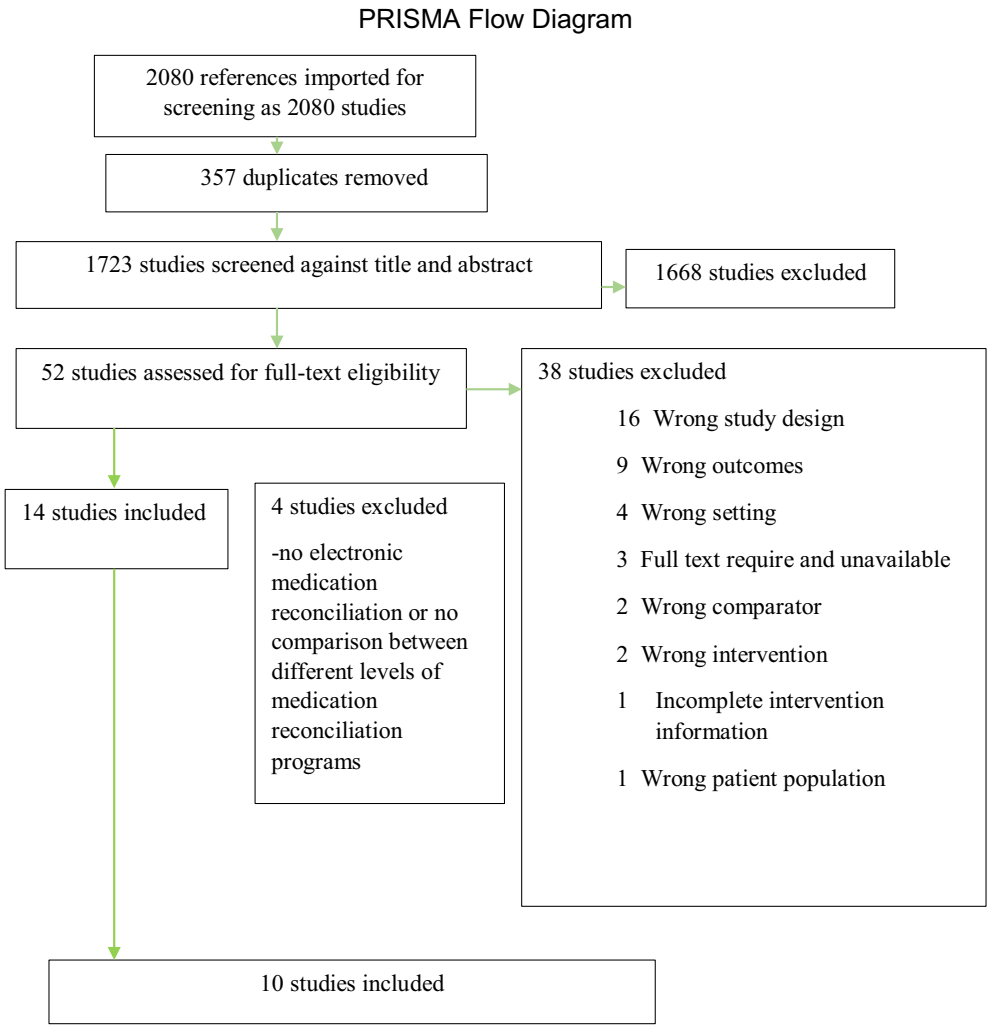

Figure 1: Shown here is the PRISMA flow diagram for the study selection.

screening are presented in Figure 1. After full-text screening, we added two additional post hoc inclusion criteria, specifically that the study compared electronic and paper-based medication reconciliation processes, or the study compared basic and enhanced medication reconciliation processes. After applying post hoc inclusion criteria, 10 studies were included in the systematic review.

Study Characteristics

Characteristics of the included studies are summarized in Appendix 2. The included studies were published between 2009 and 2018. Of the included studies, three were randomized trials[29–31] and the remainder were nonrandomized studies, with a pre-post study design being the most common. The study settings were quite heterogenous in terms of level of care and units involved; however, 6 of the 10 included studies that took place at academic hospitals.[26,29,30,32–34] The country of origin of the studies also varied, with half of the study interventions occurring in hospitals in the United States.[26,29,32–34] Some studies involved patients from single units, whereas others involved multiple units. In general, the unit of analysis in most studies was the patient. The mean/median number of medications per patients at baseline was not reported in all studies and varied between studies where it was reported, with a low of 5.7 (standard deviation 4.3)[30] and a high of 12.2 (interquartile range 11.0, 13.4).[32] It should be noted that the mean/median number of medications per patient did not appear to vary based on the hospital units involved in the study. The number of participants included in each study ranged from 85 to 3,577. With the exception of one study in which the study duration was length of hospital stay plus 90-day postdischarge follow-up,[29] all studies had a length of participation equalling the duration of a patient's hospital stay. The mean/median age of participants was not reported in all studies but varied between studies where it was reported, with the youngest mean age of 57 years[32] and an oldest mean age of 84 years.[35] The inclusion and exclusion criteria for the studies were heterogeneous, with one study not reporting any inclusion/exclusion criteria.[29] The intervention (medication reconciliation) was delivered at discharge for six of the included studies[26.30–32,34,36] and at both admission and discharge for four of the included studies.[29,33,35,37] The personnel delivering the intervention

included a physician ($n = 1$),[32] a pharmacist ($n = 1$),[29] a physician and a pharmacist team ($n = 4$),[26,35–37] a physician vs. a pharmacist in each of the intervention arms ($n = 1$),[31] a nurse and a pharmacist team ($n = 1$),[33] and unspecified hospital personnel.[34] Six of the included studies compared electronic medication reconciliation programs to another intervention (for example, paper-based medication reconciliation programs).[26,30,32,34,36,37] The remaining studies compared different medication reconciliation procedures (for example, basic medication reconciliation programs to enhanced versions).[29,31,33,35]

Summary of Study Interventions

A summary of the study interventions is presented in Table 1. Six of the included studies compared electronic medication reconciliation procedures to basic medication reconciliation.[26,30,32,34,36,37] The electronic medication reconciliation interventions typically consisted of the generation of medication lists for patients within the EMR, which was then reconciled during hospital discharge.[26,32,34,36,37] One study's electronic medication reconciliation consisted of an automated medication reconciliation app through which discharge prescriptions were generated.[30] Four of the included studies compared basic medication reconciliation to enhanced medication reconciliation.[29,31,33,35] Components of enhanced medication reconciliation varied significantly by study, but all included the components of basic medication reconciliation. A component common among three of the included studies was the collaboration between physicians and pharmacists to complete discharge medication reconciliation.[31,33,35] In addition, two of the studies with enhanced medication reconciliation had admission medication reconciliation performed by a pharmacist who checked for potential drug-related symptoms, drug-related problems, and inappropriate drug use.[29,35] Outcome definitions also varied between studies, as described in Table 2. In the included studies, a discrepancy (medication, discharge summary, or medication order) referred to a difference between two medications lists (typically before and after transitions of care).[29,31,35] Comparatively, a medication error also required an absence of a documented reason for the change in medication.[31,34–37] Two exceptions exist—one study fails to mention an outcome definition for medication error,[33] and another uses the term *medication error* but gives a definition that is more similar to a medication discrepancy.[26] An ADE is unique from a medication error or discrepancy and describes a clinically significant event.[34]

ROB Assessment

ROB was assessed separately for randomized and nonrandomized studies. Results for the three randomized studies are described in Table 3. The ROB due to random sequence generation procedures was unclear in two studies[29,30] and high in another.[31] Allocation concealment bias was low, unclear, and high.[29–31] The ROB presented in the blinding of personnel and participants was unclear in all three studies.[29–31] The ROB in the blinding of outcome assessments was low for one study[31] and unclear in the other two.[29,30] Using the ROBINS-1 tool, the overall ROB among nonrandomized studies was judged to be low in three studies,[32,34,35] moderate in three studies,[26,36,37] and serious in one study[33] (Table 4).

Summary of Study Findings

Study outcomes were grouped and organized into two tables—one for studies with electronic medication reconciliation interventions (Table 5) and one for studies with enhanced medication reconciliation interventions (Table 6). Within each outcome category, studies were organized from lowest to highest ROB, which was done to emphasize the studies with lower (better) ROB, as the results varied by study.

Electronic medication reconciliation, compared to basic medication reconciliation, was associated with a lower proportion of patients with at least one medication discrepancy or ADE in two[32,34] out of three studies.[30,32,34] Specifically, two studies of a low ROB[32,34] found the crude and adjusted odds ratios (ORs) to be statistically significant (crude OR = 0.4, $p = 0.027$; crude OR = 0.63, $p < 0.001$), and a third with unclear ROB found no statistically significant improvement.[30] It was unclear whether electronic medication reconciliation was associated with a significant reduction in the mean number of medication discrepancies or medication errors per patient. In one study there was a significant decrease observed in the intervention period compared to the preintervention period ($p < 0.01$)[37]; however, another study did not report the statistical significance of the findings.[36] Electronic medication reconciliation was found to be associated with a significant reduction in the proportion of medications with errors compared to basic medication reconciliation ($p < 0.001$).[26]

Enhanced medication reconciliation showed no significant impact on the proportion of patients with at least one medication discrepancy.[33] The impact of enhanced medication reconciliation on the mean number of medication errors/discrepancies per patient is less clear, with one study of unclear ROB finding no significant impact,[29] and another of high ROB finding a significant positive impact ($p < 0.01$).[31] The impact of enhanced medication reconciliation on the proportion of medications/medication orders/discharge summaries with discrepancies is also unclear. Two studies of low and high ROB (Bergkvist et al.[35] and Tong et al.,[31] respectively) found statistically significant reductions ($p = 0.012$; $p < 0.01$). In Tong et al., clinically relevant errors (those of moderate, high, and extremely severe magnitude) were reduced.[31] Bergkvist et al. observed a decrease from 66 total medication errors across all study patients to 25 total across all study patients, which in a comparable previous study was found to reduce negative clinical outcomes (hospital readmission associated with medication

Table 1. Description of Study Interventions

Study	Type of Intervention	Components of the Comparison	Components of the Intervention
Allison et al. (2015)[32]	Electronic medication reconciliation	Discharge: paper-based discharge medication reconciliation with discharge medications transcribed by hand from the inpatient electronic medication list	Admission/during hospital stay: Physicians input home medications electronically, allowing them to easily select which home medications are appropriate for inpatient orders. The electronic list has mandatory fill-in boxes for strength, form, dose, route, and time for every medication. The current inpatient list shows which medications were home medications and which are medications added during the inpatient stay. Discharge: At time of hospital discharge, the prescribing physician creates an electronic list of medications from the current inpatient list. Inpatient and home medications that stay on the discharge list can be easily selected, and new medications for discharge can be added as required.
Bergkvist et al. (2009)[35]	Enhanced medication reconciliation	Admission/during hospital stay: Medication reconciliation performed by a pharmacist. The patient's potential drug-related symptoms were checked. A medication review was performed to identify drug-related problems and inappropriate drug use. Based on identified problems, a systematic medication care plan was created in which all changes to the medication therapy were noted. The care plan was updated continuously and was decided on by the team. Discharge: Physician completed the discharge summary, which here included a medication report and a medication list, with no evaluation by pharmacist.	Admission/during hospital stay: Medication reconciliation performed by a pharmacist. The patient's potential drug-related symptoms were checked. A medication review was performed to identify drug-related problems and inappropriate drug use. Based on identified problems, a systematic medication care plan was created in which all changes to the medication therapy were noted. The care plan was updated continuously and was decided on by the team. Discharge: Physician completed the discharge summary, which here included a medication report and a medication list, at the day of discharge, and the pharmacist then evaluated (reconciled) the document for errors.
Cunningham et al. (2014)[33]	Enhanced medication reconciliation	Provider updated and nurse theoretically reviewed with the patient and connected with the providers for any issues they encountered. Platforms for the medication home list and inpatient list did not interface.	Admission: Nurse/pharmacist collaboration to collect and document medication history and conduct medication history verification prior to making chronic continuity therapy orders. Discharge: Pharmacist and prescriber work together to verify medications with a multidisciplinary checklist, with discharge medications issued after the discharge huddle.
Farley et al. (2014)[29]	Enhanced medication reconciliation	Control—no specific medication reconciliation process. Minimal intervention—Admission/during stay: Patients received medication counselling from a pharmacist case manager (PCM). The PCM took a detailed medication history, followed by medication reconciliation comparing the inpatient medications to the patent's home medication list. Discharge: medication reconciliation focused on comparing current inpatient medications to medications prior to hospital admission. A discharge medication teaching session was provided, and patients received a discharge medication list.	Admission/during stay: Patients received medication counselling from PCM. The PCM took a detailed medication history, followed by medication reconciliation comparing the inpatient medications to the patent's home medication list. Discharge: medication reconciliation focused on comparing current inpatient medications to medications prior to hospital admission. A discharge medication teaching session was provided, and patients received a discharge medication list. Discharge care plan prepared and faxed to community physician and pharmacy. Plan focused on medication issues and changed during hospitalization. Follow-up phone call from PCM 3–5 days postdischarge to address any medication related issues since discharge.

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Table 1. (*continued*)

Study	Type of Intervention	Components of the Comparison	Components of the Intervention
García-Molina Sáez et al. (2016)[37]	Electronic medication reconciliation	Basic medication reconciliation—Admission: Home medication history of patients obtained via structured interview by clinical pharmacist. This was compared to the treatment recorded in computerized primary care register. Prescription bottle or medical reports supplied by patients checked and recorded in form. Discharge: Medication reconciliation performed comparing the treatment prescribed to a patient at discharge with the patient's home medication history (taken at admission) accounting for treatments initiated during a patient's hospital stay.	Admission: Home medication history of patients obtained via structured interview by clinical pharmacist and entered into a computerized tool integrated into the electronic clinical history of the patient. This tool was designed to facilitate medication reconciliation by identifying every field necessary to correctly define a medication (route, dose, active ingredient, frequency). Discharge: Medication reconciliation performed comparing the treatment prescribed to a patient at discharge with the patient's home medication history (taken at admission) accounting for treatments initiated during a patient's hospital stay. Other: A training session at the beginning of the intervention period explained to physicians the concept of reconciliation errors.
Midlov et al. (2012)[36]	Electronic medication reconciliation	Phase 1—Discharge: paper-based medication reconciliation in a form containing general information, a medication report (contains information on changes to medications during hospital stay), and a list of current medications. At discharge, this form is discussed with and given to the patient and, if applicable, sent to the community health care and the patient's general practitioner within the same day.	Phase 2—Discharge: Medication list in electronic patient record is reconciled by a physician and then by a pharmacist for quality control. Other components of the form and discharge process remain the same as preintervention. Phase 3—Builds on phase 1 processes to incorporate physicians reconciling medications listed in an electronic Web-based medication dispensing system called ApoDos. A pharmacist checked the correctness of the ApoDos list and made suggestions for changes to the physician.
Murphy et al. (2009)[26]	Electronic medication reconciliation	Paper-based discharge medication reconciliation program in place but components not described.	Admission: Clinical pharmacist obtains patient's home medication list and enters into the electronic medical record. Discharge: A discharge medication reconciliation report form was created through the electronic medical record. This form captures patients' home and inpatient medications and is used to order medications at discharge. It contains all active inpatient medications at the time the report is printed After the physician completes the order form, the final discharge orders are updated on the patient's medication list within the electronic medical record by pharmacist assistants. The discharge orders are then reviewed and verified by pharmacists for accuracy. Patients' updated discharge medication lists are immediately available for review across the continuum of care.
Smith et al. (2016)[34]	Electronic medication reconciliation	Discharge: A paper-based nonmandatory discharge medication reconciliation process reconciling a patient's discharge medication list against medication histories obtained by hospital personnel.	Discharge: A mandatory electronic medical record–based discharge medication reconciliation procedure involving reconciling discharge medications against medication histories obtained at hospital admission. Discharge reports given to patients and sent to primary care physicians.

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Table 1. (*continued*)

Study	Type of Intervention	Components of the Comparison	Components of the Intervention
Tamblyn et al. (2018)[30]	Electronic medication reconciliation	Admission through discharge: Used a fillable PDF form to complete medication reconciliation.	Admission through discharge: An automated medication reconciliation application retrieves community-based medications from the provincial insurance agency and aligns it with in-hospital medications from the hospital drug information system. Discharge prescription generated using a one-click action bar where the community and hospital drugs to be continued, stopped, modified, or started are determined.
Tong et al. (2017)[31]	Enhanced medication reconciliation	Discharge: Discharge summaries prepared as usual.	Discharge: Discharge summaries prepared by physician with medication management plans completed by a pharmacist.

errors).[35] A third study of serious ROB did not report any statistical measures for their results but did consider the results clinically significant.[33]

Discussion

In our review of the included papers, we found significant heterogeneity in trial measures, quality, and interventions, making it difficult to draw conclusions about the impact of enhanced medication reconciliation in general. However, the available studies do offer some suggestion of successful vs. unsuccessful approaches and reasoning behind differences in observed outcomes. For example, both studies with electronic medication reconciliation interventions that reported no significant improvement used automated interventions.[30,36] This suggests that quality of automated procedures for electronic medication reconciliation could be improved. In addition, both studies that reported a positive impact of electronic medication reconciliation on reducing the proportion of patients with at least one medication discrepancy or ADE used gold standards as a comparison to identify medication errors,[32,34] whereas no gold standard was used in the study that showed no significant effect.[30] This difference in ascertaining the presence of medication errors may contribute to the difference in the observed outcome between studies. It should be noted that in the study by Allison et al.[32] only medication errors for intravenous antibiotics were considered; focusing on one medication class may have allowed for greater ease of reconciliation, which may have contributed to a positive impact of electronic medication reconciliation found here and not in other studies. There were no other major variables (such as patient age, mean number of medications per patient at discharge, setting) that seemed systematically different between studies that showed a positive impact vs. no impact of electronic medication reconciliation.

In trying to understand the observed differences in outcomes involving enhanced medication reconciliation interventions, it is of note that studies showing a positive impact of enhanced medication reconciliation involved only medical units[31,35] whereas studies that showed no significant impact of enhanced medication reconciliation involved medical and surgical units.[30,33] The reason for this difference is unknown, and it is unknown if this finding is merely by chance. All studies involved some form of provider-pharmacist collaboration; however, there was no deeper commonality in intervention components between studies showing a positive impact of enhanced medication reconciliation vs. those showing no impact. There were no other major variables (for example, patient age, mean number of medications per patient at discharge, setting) common to all studies showing a positive impact of enhanced medication reconciliation that were not also common among studies showing no impact.

Although the available studies are inconsistent, it appears that electronic medication reconciliation may have a positive impact on medication errors and discrepancies. This finding is stronger when considering the trials with a low ROB. The two studies of low ROB that focused on electronic medication reconciliation both showed a significant positive impact of the intervention.[32,34] In addition, of the two studies that did not report a statistically significant positive impact of electronic medication reconciliation, one study did consider the intervention to have had a clinically significant positive impact, which should not be dismissed.[30] In the second study, there was already a small number of medication discrepancies per patient preintervention as compared to other studies in our review. Perhaps this small initial number explains why a statistically significant decrease was not observed with implementation of the intervention.[36]

The studies with enhanced medication reconciliation as an intervention varied widely in the components of the intervention, the components of the basic medication reconciliation comparison group, and their outcome definitions.

Table 2. Summary of Study Outcome Definitions

Study	Outcome Definition	Gold Standard
Allison et al. (2015)[32]	**Medication discrepancies:** Were categorized by dose, frequency, and route. When a drug was present on the gold standard list and absent on the discharge list, this was considered an antibiotic omission. Conversely, when a drug was absent on the gold standard list and present on the discharge list, this was considered an antibiotic addition. If a drug was prescribed that differed from the gold standard, this was considered two medication errors: an antibiotic omission and an antibiotic addition. Antibiotic error was summarized by type (omission, dose, route, frequency, addition) as well as the total errors in aggregate.	For every patient, an inpatient infectious disease consulting physician documented recommended postdischarge oral and intravenous antibiotics. This recommendation was considered the gold standard and compared to the antibiotics in a patient's discharge summary.
Bergkvist et al. (2009)[35]	**Medication error:** The occurrence of one of the following discrepancies (identified by the pharmacist when comparing the medication list in the discharge summary with the medication list in the community health care) together with the lack of documentation to indicate that the change in the medication therapy was done deliberately: 1. A medication was missing in the medication list from the community health care. 2. A medication had been added to the medication list from the community health care. 3. The total dosage over 24 hours had been changed in the medication list from the community health care.	N/A
Cunningham et al. (2014)[33]	Not reported.	N/A
Farley et al. (2014)[29]	**Medication discrepancy:** If (a) medications that documentation indicated should be active were not on the patient's medication list (unintended omission), (b) medications were on the list without documentation (unintended addition) or (c) medications were found with different dose or frequency.	N/A
Garcia-Molina Sáez et al. (2016)[37]	**Reconciliation error:** Any discrepancy between the medication upon admission and that prescribed at discharge that could not be justified clinically.	N/A
Midlov et al. (2012)[36]	**Medication error:** Any discrepancy between medication lists before and after transfer to a community care/nursing home. If there was any indication (from comments or notes in any record or written documentation for a patient), it was not regarded as an error. Change of generic meds or withdrawal of drugs with long dosage intervals was not regarded as error. In-hospital medication list on day of discharge considered correct if no other information was documented and this was compared to community care dispensing list when first dose had been given. For ApoDos patients the ApoDos-list when packages delivered were checked.	N/A
Murphy et al. (2009)[26]	**Medication error:** Errors and omissions in physician discharge orders, errors on written prescriptions given to patients, and errors on the nursing discharge summary. Includes omission of home or inpatient medications, missing routes of administration, missing medication dosages, missing directions, missing durations of treatment, unacceptable medical abbreviations in discharge orders.	N/A
Smith et al. (2016)[34]	**Medication variances:** Any differences between the study-based preadmission medication case summary (gold standard) and discharge medications. **Medication errors:** Medication variances not considered changes required by the patient's clinical status. **Clinically important medication errors:** Errors in which there was the potential to cause death, permanent or temporary disability, prolonged hospital stay, readmission, or additional treatment or monitoring to protect the patient from harm.	A gold standard preadmission case summary was created for each patient retrospectively by research personnel examining ambulatory electronic medical record data on a patient's medications at the time of their last encounter with a primary care physician. This gold standard for preadmission medications was compared to inpatient medication orders and discharge medication orders to identify medication variances and errors.

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Table 2. (*continued*)

Study	Outcome Definition	Gold Standard
Tamblyn et al. (2018)[30]	**Potential adverse drug events:** Errors in omission of community medications and therapy duplications of two or more medications from the same therapeutic class.	N/A
Tong et al. (2017)[31]	**Medication error:** An omitted drug, an incorrect dose or dose frequency, an incorrect or unnecessary drug, or an incorrect route of administration. **Types and risks of error:** Errors were classified on an ordinal severity scale of 5 (corresponding to insignificant risk, low risk, moderate risk, high risk, and extreme risk).	N/A

Table 3. Summary of Risk of Bias (ROB) Assessment for Randomized Studies According to a Cochrane ROB Assessment Tool for Randomized Controlled Trials (RoB-2)[27]

Author	Bias in Random Sequence Generation	Bias in Allocation Concealment	Bias in Blinding of Participants and Personnel	Bias in Blinding of Outcome Assessment	Bias in Selective Outcome Reporting	Other Bias
Farley et al.[29]	Unclear	Low	Unclear	Unclear	Unclear	Low
Tamblyn et al.[30]	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Tong et al.[31]	High	High	Unclear	Low	Low	Low

Low ROB

Unclear ROB

High ROB

Because of this, it is more accurate to say that we observed inconsistent studies vs. inconsistent results.

To the best of our knowledge, no previous reviews have explored the impact of enhanced medication reconciliation. However, we identified one previous review examining the impact of electronic medication reconciliation on unintentional medication discrepancies during transitions of hospital care. In contrast to our study, which focused on discharge medication reconciliation, the systematic review by Mekonnen et al. focused on electronic medication reconciliation at admission and the impact on clinical outcomes; namely, medication discrepancies between a patient's home medications and admission orders.[25] However, admission medication reconciliation does not directly help improve communication across the transition of patients returning home from the hospital, and hence does not directly target the issue of patients being sent home on unnecessary medications or medications with errors (such as incorrect dosing). This was shown in a study by Murphy et al. that evaluated discharge medication errors—first, after an admission medication reconciliation system was implemented, and then again after a discharge medication reconciliation system was implemented.[26] They found that errors remained after admission-only medication reconciliation but were significantly reduced after the addition of discharge medication reconciliation.[26] To build on this review,

Table 4. Summary of Risk of Bias (ROB) Assessment for Nonrandomized Studies According to a Cochrane ROB Assessment Tool for Nonrandomized Studies of Interventions (ROBINS-1)[28]

Author	Bias Due to Confounding	Bias in Selection of Participants into the Study	Bias in Measurement of Interventions	Bias Due to Departures from Intended Interventions	Bias Due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Result	Overall Bias
Allison et al.[32]	Low	Low	Low	Low	Low	Low	Low	Low
Bergkvist et al.[37]	Moderate	Low	Low	Low	Low	Moderate	Low	Low
Garcia-Molina Sáez et al.[38]	Low	Low	Low	Low	Low	Serious	Low	Moderate
Cunningham et al.[33]	Low	Moderate	Low	Low	Low	Serious	Serious	Serious
Midlov et al.36	Low	Moderate	Low	Low	Low	Serious	Low	Moderate
Murphy et al.[34]	Low	Low	Low	Low	Low	Moderate	Serious	Moderate
Smith et al.[35]	Low	Low	Low	Low	Low	Low	Low	Low

Low ROB
Moderate ROB
Serious ROB
Critical ROB

Table 5. Primary Outcomes Across Studies with Electronic Medication Reconciliation Interventions Organized Low to High Risk of Bias (ROB) for Each Outcome

Author	Study design	ROB	Outcome Measure	Effect Measure
Outcome 1: Proportion of patients with minimum of one medication discrepancy or adverse drug event				
Allison et al.[32]	Pre-post retrospective cohort study	Low	Preintervention 23.0% Postintervention: 11.0%	Crude OR = 0.41 (95% CI = 0.19–0.90, $p = 0.027$) Adjusted† OR = 0.39 (95% CI = 0.18–0.87, $p = 0.021$)
Smith et al.[34]	Pre-post quasi-experimental study design	Low	Not reported	Crude OR = 0.63, (95% CI = 0.51–0.77, $p < 0.001$) Adjusted‡ OR = 0.54, (95% CI = 0.43–0.69, $p < 0.001$) Adjusted§ OR = 0.52, (95% CI = 0.41–0.67, $p < 0.001$) Adjusted‖ OR = 0.57 (95% CI = 0.44–0.74, $p < 0.001$)
Tamblyn et al.[30]	Pragmatic randomized trial	Unclear	Intervention ward: 21.0% Control ward: 44.1%	OR = 0.31 (95% CI = 0.27–0.37)
Outcome 2: Mean number of medication discrepancies/medication errors per patient				
Garcia-Molina et al.[37]	Quasi-experimental interrupted time series study	Moderate	Preintervention: 4.4 ± 3.2 During intervention: 1.8 ± 2.6 Postintervention: 3.9 ± 3.7	$p < 0.001$ between pre and intervention and intervention and post $p = 0.288$ between pre and post
Midlov et al.[36]	Interrupted time series	Moderate	Time period 1: 1.5 Time period 2: 1.1 Time period 3: 0.46	Not reported
Outcome 3: Proportion of medication or medication orders/discharge summaries with discrepancies				
Murphy et al.[26]	Controlled before/after pilot study	Moderate	1. Surgical unit: Preintervention: 90% medications with errors: Postintervention: 47% medications with errors 2. Medical unit: Preintervention: 57% medications with errors Postintervention: 33% medications with errors	1. 95% CI = 42–53%; $p < 0.001$ 2. 95% CI = 28–38%; $p < 0.001$)

Moderate and unclear ROB considered equivalent, and serious and high ROB considered equivalent for the purposes of the table.

† Adjusted for day of discharge and total number of discharge medications.

‡ Adjusted for age, sex, and insurance.

§ Adjusted for age, sex, insurance, and comorbidity score.

‖ Adjusted for age, sex, insurance, comorbidity score, and number of medications.

OR, odds ratio; CI, confidence interval.

we chose to exclude studies with admission-only medication reconciliation to evaluate interventions targeted at the issue of patients being sent home with unnecessary medications or medications with errors. Despite our change in approach, we came to the same conclusion as Mekonnen et al.; namely, that the impact of electronic medication reconciliation on minimizing the occurrence of unintentional medication discrepancies was inconsistent, with no statistically significant reduction in patients with medication discrepancies or mean number of medication discrepancies per patient.

One landmark study involving enhanced medication reconciliation is the Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS) by Schipper et al.[38] This pragmatic quality improvement study involved five US sites—three academic medical centers, two community hospitals, and one US Department of Veterans Affairs Medical Center. Medication reconciliation was implemented at all five sites using an evidence-based, 11-component medication reconciliation toolkit. Toolkit components included taking the best possible medication history (BPMH); discharge medication reconciliation and counseling; clarifying roles and responsibilities of health care personnel; risk stratification; health information technology improvements to the electronic health record; improving access to medication sources; measuring then intervening to correct discrepancies in real time; and stakeholder engagement. Not all domains were addressed by all sites, and the intervention components implemented differed by site.[38] We chose to exclude the MARQUIS study from our

Table 6. Primary Outcomes Across Studies with Enhanced Medication Reconciliation Interventions Organized Low to High Risk of Bias (ROB) for Each Outcome

Author	Study Design	ROB	Outcome Measure	Effect Measure
Outcome 1: Proportion of patients with minimum of one medication discrepancy or adverse drug event				
Cunningham et al.[33]	Controlled before/after pilot study	Serious	Baseline: 67.0%–90.0% Enhanced:16.0%–33.0%	No statistical test reported
Outcome 2: Mean number of medication discrepancies/medication errors per patient				
Farley et al.[29]	Randomized controlled trial	Unclear	At 30 days (control, minimal, enhanced): HPR—0.51, 0.49, 0.26 MPR—2.89, 2.45, 2.61 LPR—2.31, 2.14, 2.31 HPharm—0.38, 0.40, 0.45 MPharm—3.36, 3.68, 3.42, 0.655 LPharm—3.92, 4.34, 4.56 At 90 days: HPR—0.50, 0.41, 0.44 MPR—3.03, 2.56, 2.83 LPR—2.78, 2.50, 2.78 HPharm—0.41, 0.44, 0.49 MPharm—3.25, 3.44, 3.62 LPharm—4.12, 4.60, 5.04	At 30 days (p values): HPR—0.013 MPR—0.688 LPR—0.429 HPharm—0.783 MPharm—0.655 LPharm—0.134 At 90 days (p values): HPR—0.656 MPR—0.568 LPR—0.217 HPharm—0.954 MPharm—0.688 LPharm—0.030
Tong et al.[31]	Cluster randomized controlled investigation	High	Intervention: 0—$n = 341$ (85%) 1—$n = 41$ (10.2%) 2—$n = 13$ (3.2%) 3—$n = 1$ (0.2%) 4—$n = 1$ (0.2%) ≥ 5—$n = 4$ (1%) Preintervention: 1—$n = 50$ (18.9%) 2—$n = 86$ (32.5%) 3—$n = 81$ (30.6%) ≥ 5—$n = 2{,}312$ (4.5%)	$p < 0.01$ ARR (95% CI): 46.5% (40.7–52.3%). If 100 discharge summaries were reconciled, 46.5 of them would be prevented from containing a minimum of 1 error. NNT (95% CI): Need to reconcile 2.2 (1.9–2.5) discharge summaries to prevent 1 discharge summary from containing minimum 1 error.
Outcome 3: Proportion of medication or medication orders/discharge summaries with discrepancies				
Bergkvist et al.[35]	Longitudinal study with intervention and control group	Low	Intervention group: 4.8% of medications with medication errors Control group: 12% of medications with medication errors	$p = 0.012$
Cunningham et al.[33]	Controlled before/after pilot study	Serious	At baseline: 8–26% of medications With enhanced medication reconciliation: 1–6% of medications	Not reported
Tong et al.[31]	Cluster randomized controlled investigation	High	Preintervention: 61.5% of discharge summaries Postintervention (pharmacist): 15.0% of discharge summaries	$p < 0.01$

HPR, high-level physician record; MPR, mid-level physician record; LPR, low-level physician record; HPharm, high-level pharmacist record; MPharm, mid-level pharmacist record; LPharm; low-level pharmacist record; ARR, attributable risk ratio; CI, confidence interval; NNT, number needed to treat.

review due to this inconsistency. Results of studies included in our review would likely be difficult to compare due to differences between interventions across studies, and we did not want to include a study within which interventions varied. The study authors concluded that implementation of a multifaceted medication reconciliation program was associated with a reduction in total medication discrepancies, but not in potentially harmful medication discrepancies. As this study did not show a clinically meaningful impact of a multifaceted medication reconciliation program (that is, a lack of reduction in potentially harmful medication discrepancies), we do not believe the results alter the conclusions drawn in this review concerning enhanced medication reconciliation.

Limitations

Our study is not without its limitations. We did not have access to unpublished research and restricted our search to studies published in the English language, which may have introduced publication bias. In addition, there was a lack of consistency across the included studies for the terms *medication error / medication discrepancy* and *ADE* as well as how the outcome was measured. Consequently, what qualifies as a medication error or discrepancy may differ between studies and may reduce the comparability of the outcomes of different studies. This is one of the reasons we chose not to perform a meta-analysis. The interventions evaluated also displayed heterogeneity, in particular among studies evaluating enhanced medication reconciliation, which made comparing the effects of studies challenging. Variability in setting (for example, different health care systems, single-unit vs. multiunit interventions, outpatient programs involved in some studies) posed additional limitations to accurate comparison of study results. There were also some limitations in terms of study design: Only three studies were randomized controlled trials, with the remaining predominantly controlled before-after studies. However, very few controlled before-after studies adjusted for postintervention covariates, which could explain the lack of changes in pre-post measures such as medication errors. Furthermore, the majority of studies lacked information on whether blinding of participants/assessors was present, the randomization protocol (as applicable), or allocation concealment (as applicable), which contributed to a large number of studies being of unclear, moderate, or serious ROB. In addition, medication reconciliation was mandatory in only one study intervention, and the majority of studies did not report on the completeness of medication reconciliation delivery.[34] Hence, a lack of significant observed effect in some studies may be due to a failure to consistently deliver medication reconciliation to patients. As enhanced medication reconciliation programs contain multiple components, it is not possible to decipher the impact that each intervention component had alone, which is a limitation inherent to the nature of these interventions.

CONCLUSION

Electronic medication reconciliation may have a positive impact on medication errors and discrepancies, but there is a lack of agreement across studies. Because of this, and due to some inconsistencies in the interventions and outcome definitions between studies, we were unable to come to a definitive conclusion. The lack of comparability of studies is more pronounced in studies with enhanced medication reconciliation, making a clear conclusion on the effect of enhanced medication reconciliation difficult. Future studies should focus on reducing the ROB; evaluating consistently implemented interventions; ensuring that there is a uniform definition for medication discrepancies, medication errors, and ADEs; and improving the comparability of the intervention and comparison group components. Development of a universal definition for medication discrepancies, medication errors, and ADEs would allow for increased comparability in this field of research. The creation of a gold standard for these outcome definitions may be useful, as they offer a standardized approach to appraising outcomes and, within this review, were present in only two studies.

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SUPPLEMENTARY MATERIALS

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