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Effectiveness Of Electronic Medication Reconciliation In Reducing Adverse Drug Events In Pediatric Inpatients: A Systematic Review And Meta-Analysis

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Systematic Review and Meta-Analysis
Prepared in accordance with PRISMA 2020 and PRISMA-S reporting principles

ABSTRACT:

Background: Fragmented caregiver histories, incomplete interoperability, and age-based formulations and weight-dosing all pose additional hurdles to pediatric medication reconciliation when compared to standard medication reconciliation. Electronic workflows may provide improvements to the accuracy and completion of medication reconciliation, but the impact on adverse drug events is still unknown. The goal of this study is to integrate the available pediatric inpatient evidence regarding the use of electronic medication reconciliation and measure the burden of medication discrepancies. This was completed using a PRISMA 2020-rooted systematic review. This review used publicly available bibliographic sources, publisher sources, and citation searching, and was active until 31 December 2025. This systematic review included studies on electronic, paper-based, and telephone frameworks that facilitated medication reconciliation, and were conducted on hospitalized children and adolescents aged 0 to 18. The included studies primarily focused on electronic or digitally facilitated medication reconciliation. These studies had a wide range of designs and outcomes which necessitated narrative synthesis. The remaining studies were included in a random-effects meta-analysis to estimate the prevalence of medication reconciliation error for the four remaining studies on pediatric inpatient settings. This was done using a logit transformed meta-analysis. The remaining studies were assessed for risk of bias and low certainty of evidence was provided by the GRADE framework. Out of the 11 studies, 6 of them focused directly on digital or electronic-based interventions. All these studies saw some level of improvement to the accuracy of the electronic medication reconciliation, reductions in electronic medication reconciliation error rates, and improvements to the completion of the electronic medication reconciliations. However, none of the studies provided sufficient evidence, in a concurrent controlled framework, to draw conclusions on adverse drug events and electronic medication reconciliation, which necessitated qualitative evidence synthesis. Four studies that were included in the meta-analysis had a combined total of 1050 individual subjects, all of whom were children. The pooled study prevalence estimates for reconciliation error or discrepancy was 58.8% (95% CI, 45.0 to 71.2), and a high I2 score (90.2) indicated extensive variability of the studies. Defining discrepancies in pediatric electronic medication reconciliation systems yielded a very low certainty of evidence due to the differing study designs and objectives across clinical settings and participant populations. Conclusion: When workflow enhancements by pharmacists or multidisciplinary teams are integrated with EHR design alterations, the combination is evidence to further support the optimizing work

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processes associated with pediatric electronic medication reconciliation. Current evidence is inadequate to assert that redesigning work processes prevents the occurrence of adverse drug events. To change this, studies that analyze the harmonization of patient-centered outcomes after the implementation of work design solutions are needed. Registration: There is currently no public protocol to cite.

Keywords: *Adverse Drug Events; Clinical Decision Support; Electronic Health Records; Medication Discrepancies; Medication Reconciliation; Patient Safety; Pediatrics; Transitions Of Care*

Introduction:

Medication reconciliation consists of identifying the medications a patient is taking, comparing the active medication orders, identifying and resolving discrepancies, and communicating the reconciled medication orders with the patient as they transition from one level of care to another. Medication reconciliation is clinically important to every hospitalized patient, but its importance is magnified in the pediatric population. Unlike adults, the pediatric population is dosed based upon age, weight, body surface area, and the maturation of renal and hepatic function, as well as the availability of the dosage form, and the ability of the caregiver to communicate a complex medication regimen. Given these factors, even small errors in calculation of a medication order may lead to large dosing errors, and errors in order duplication or omission may be difficult to detect. This is especially true when the medication histories are fragmented across caregivers, pharmacies, and specialty services, as well as several electronic information systems. Children with chronic neurologic, oncologic, transplant, cardiac, respiratory, or metabolic disease are also at an increased risk as these children may be prescribed multiple high-risk medications.

Medication discrepancy and adverse drug event are not the same. Medication discrepancy refers to the difference in information or lists of medications; some discrepancies may be due to absence, duplication, or outdated data. Some discrepancies may be missing, duplicated, or outdated transcriptions. An unintentional error of medication reconciliation is an incomplete discrepancy. A potential adverse drug event is an unintentional error of obligation and an adverse drug event is an unintentional harmful error of obligation. This is important because in pediatric reconciliation studies, completeness, omission, intervention acceptance, or discrepancy measurement, lists, or counts are usually the goals, and not harm to the patient. While some of these process improvements are beneficial, they do not imply that injury, readmission, or death due to hospitalization have decreased.

To resolve the issues embedded in handwritten methods and fragmented workflows, electronic medication reconciliation was introduced. An electronic system has the ability to show medication history and lists side by side, fill out pre-populated medication lists, display and flag duplicate medications, calculate and display dosing ranges, and track the clinician accountable for the list, and provide the list for discharge. Also, the system is able to integrate with the provider order and control medication lists and provide reminders and completion audits with feedback. In electronic medication reconciliation systems, the task is standardized more than in systems that use a pharmacist, as the task is largely dependent on local custom and the clerk’s memory. In these systems there is a better opportunity to eliminate manual errors inherent in handwritten methods. While these improvements create better systems and workflows, if the system is designed poorly or if the data in the system is poor, it can lead to copy-forward errors and create alerts that are ignored because they are frequent or low in priority.

The pediatric evidence base exemplifies this challenge. Some quality improvement studies have reported positive outcomes after electronic workflow modification, addition of reminders, simplification of the reconciliation screen, or integration of EHR with multidisciplinary tools combined with EHR education. Rungvivatjarus and colleagues reported a process design gain and clinical decision support implementation from 73% to approximately 94%-95% completion in large pediatric hospitals

(Rungvivatjarus et al., 2020). Russ and colleagues reported a decrease in admission reconciliation error from 9.8% to 2.9% through multiple feedback and accountability interventions (Russ et al., 2020). More recent studies have reported positive outcomes concerning the improvement of the removal of inactive home medications, the improvement of discharge instructions, and the improvement in rescue therapies (Adducchio et al., 2024; Gunkelman et al., 2024; Ring et al., 2023). While these studies have reported positive outcomes, the interventions have variable professional roles, different settings, different definitions, different denominators, and different designs. Most of the studies are uncontrolled design improvements and comparisons, and therefore remain subject to artifact from changes in the population, the cases, increased documentation, and concurrent safety initiatives.

Another issue is the high existing rate of discrepancies. Admission, transfer, and discharge studies typically report at least one discrepancy in a significant number of pediatric patients. Iturgoyen Fuentes et al. found discrepancies in around 42% of the admitted children (Iturgoyen Fuentes et al., 2020). Alcântara et al. found unintentional discrepancies in 74.5% of the pediatric patients who were transferred between hospital wards (Alcântara et al., 2021). A study conducted in several centers on chronic and onco-hematology patients found at least one discrepancy in 96 out of 157 children, and a study on hospital implementation found reconciliation errors in 334 out of 592 patients (Cuervas-Mons Vendrell et al., 2023; Meneses Mangas et al., 2021). The discrepancy rate in these studies shows true variation in clinical practice, but also variation in the medication history-taking method, methods of transition, the definition of discrepancies, and the detection of discrepancies. Describing this burden gives e-context for the use of technology to improve the process. However, estimation of discrepancy rates gives no indication of the impact of the technology used.

Several systematic reviews that cover mixed or predominant adult populations have reported that advanced or electronic reconciliation reduces discrepancies in medication. The evidence is less robust for the prevention of adverse drug events (Ciudad-Gutiérrez et al., 2023; Killin et al., 2021; Mekonnen et al., 2016). In one adult cluster randomized trial, discrepancies in medication were reported to be reduced following the implementation of an electronic intervention, but adverse drug events were reported to be unchanged (Tamblyn et al., 2019). It is difficult to make a direct comparison to children because of the differences in adult and pediatric drug care, including the different dosing and the mediation of caregivers, compounded by the differences in drug formulation and care pathways. Therefore, a synthesis of pediatric care is necessary to understand the range of differences that electronic reconciliation improves and to determine what is still untested.

The purpose of this review was to analyze electronically or digitally aided medication reconciliation for pediatric inpatients and their associated outcomes. The main focus was to compare adverse drug events associated with electronically aided reconciliation versus conventional manual reconciliation, partially electronic, or standard manual reconciliation. The secondary concerns consisted of comparing reconciliation discrepancies, adverse reconciliation errors, reconciliation timeliness, list accuracy, and efficiency, and determining if the reconciliation process and accuracy of the lists would lead to meaningful, clinically relevant, and significant interventions by pharmacists. Due to the lack of comparable direct adverse event data, the review sought to combine or estimate the prevalence of reconciliation discrepancies and errors pertaining to reconciliation for children in the available qualitative and quantitative observational studies. This dual layer approach allows the distinction of intervention effectiveness from the baseline safety burden while identifying the necessary evidence to inform future studies in pediatrics.

The PRISMA 2020 methodology guided the review and was supplemented by the PRISMA-S reporting extension (Page et al., 2021; Rethlefsen et al., 2021). The applicable guidance of the Cochrane Handbook, MOOSE, the ROBINS-I tool, and GRADE was incorporated for viewing and evaluating the evidence (Guyatt et al., 2008; Higgins et al., 2023; Sterne et al., 2016). No public protocol registration number was available. The review consisted of aggregated data of published reports and, as such, did

not require review from an ethics committee. The review aimed to describe an evidence-based public verification set. Search strategies were documented for each database, and a submission-stage update was to archive the full search and search records for all licensed databases.

The study population consisted of hospitalized patients aged 0-18 comprised of neonates, infants, children and adolescents. The study's target settings were general pediatric wards, neonatal and pediatric ICUs, inpatient psychiatric and pediatric units, and emergency encounters that lead to hospitalization. The study intervention contained an electronically or digitally supported medication reconciliation process. This included medication reconciliation modules integrated in Electronic Health Records (EHR), electronic clinical decision support and reminders, electronic history of medications, discharge medication instructions, audit and feedback, reconciliation linked electronic orders, and other electronically supported reconciliation processes. The interventions were pharmacist led, physician led, nurse supported and/or multidisciplinary. The intervention comparator was manual or paper-based reconciliation processes, the no-change pre-implementation period, standard EHR use that did not include the proposed EHR modification, or the usual care.

The primary outcome of interest was the occurrence of an adverse drug event, which was medication harm to the patient that was sustained during the hospitalization or the study defined post-hoc period. The secondary outcomes of interest were preventable and potential adverse drug events, and a number of medication error types (including unintentional reconciliation errors and prescribing errors), therapy duplication, and timeliness and completion of medication reconciliation. The studies retained their outcome terminology, which we mapped to a pre-defined conceptual framework including (in order of increasing severity) unintentional reconciliation error, potential adverse drug event, and actual adverse drug event. Errors of high clinical significance did not justify elevating outcomes in this framework.

Randomized trials, cluster trials, controlled before-after studies, interrupted time-series studies, and comparative cohorts (either prospective or retrospective) as well as pre-post quality-improvement studies with sufficient detail were included. Cross-sectional studies and studies with an observational design were excluded from the effectiveness synthesis if they did not provide an electronic intervention. However, they could contribute to the proportional meta-analysis if they provided a patient-level numerator and denominator for at least one discrepancy or reconciliation error. Studies that included only adults, only outpatients, only community pharmacy participants, studies that did not provide separate pediatric data, narrative reviews, editorials, case reports, conference abstracts without quantitative findings, and studies on electronic prescribing that did not include reconciliation were excluded from the review.

According to the protocol, the information sources included MEDLINE/PubMed, Embase, Scopus, the Web of Science Core Collection, CINAHL, CENTRAL, ClinicalTrials.gov, the WHO trial registry portal, citation lists, and related reviews. For this manuscript, records were verified in publicly accessible PubMed or PMC, publisher sites, DOI (digital object identifier) metadata, and through backward and forward citation searching. Before deduplication, the evidence log had 42 records, 10 duplicates were removed, and 32 records were screened by title and abstract. Seventeen reports were requested and one was obtained with insufficient detail. Sixteen reports were assessed and five were excluded, resulting in eleven studies included in the qualitative synthesis. Four studies were included in the proportional meta-analysis. The counts, as documented in the manuscript, are included in the PRISMA diagram.

Titles and abstracts were screened first, followed by a second screening of full texts. The screening decision required clear pediatric inpatient relatedness, inclusion of a medication reconciliation process, and an eligible outcome or quantitative discrepancy denominator. When one study reported the intervention and another reported the implementation or the follow-up, the studies were combined. Studies were treated as separate when they reported on different patient cohorts or different implementation periods. Exclusion reasons reported in the full texts included reporting on adult

participants only, no digital reconciliation, no reported eligible outcome, or reporting in the form of a protocol only.

Data extraction included author, year, country, design, setting, clinical service, age, sample size, intervention, comparator, reconciliation stage, professional role, outcome, follow-up, event count (numerator and denominator), adjusted estimate, funding, and conflicts of interest. For quality-improvement studies, we included baseline and final performance, duration of sustained improvement, and use of statistical process control. Patient-level denominators were differentiated from medication orders, discrepancies, admissions, and reconciliation opportunities. If a study only reported a rounded percentage and provided a precise denominator, we computed a provisional event count and indicated this explicitly. This was done for the estimate of 42% of 187 patients, from which we derived 79 patients after rounding (Iturgoyen Fuentes et al., 2020).

ROBINS-I consider bias of nonrandomized digital intervention studies by reviewing confounding, selection, intervention, deviation from intervention, missing data, outcome, and reporting. Quality-improvement designs were anticipated to have a serious confounding issue, because the initiation of the intervention coincided with education, audits, changes in staffing, or changes in workflow, and there were no randomly assigned simultaneous controls. Intervention classification was typically low risk, as the date and variation in design were documented. Outcome measurement was typically rated as moderate risk, as documentation-based outcomes may improve with the increase in awareness and auditing, even in the absence of a change in a clinical outcome. Overall assessments were not translated into a numeric quality score.

The absence of clinically correlating outcomes (including transition points, denominators and effect measures), required the presence of at least two studies for statistical pooling to occur. This requirement for direct intervention effectiveness studies was not met for adverse drug events and for any of the process endpoints. Therefore, results were reported textually with effect-direction figures and positive absolute percentage-point changes. The figure was designed to show the effect of the changes in studies of completion, error reduction, list cleanup and accuracy of discharge, and the outcomes are distinct; no pooled diamonds and no combined effects are presented.

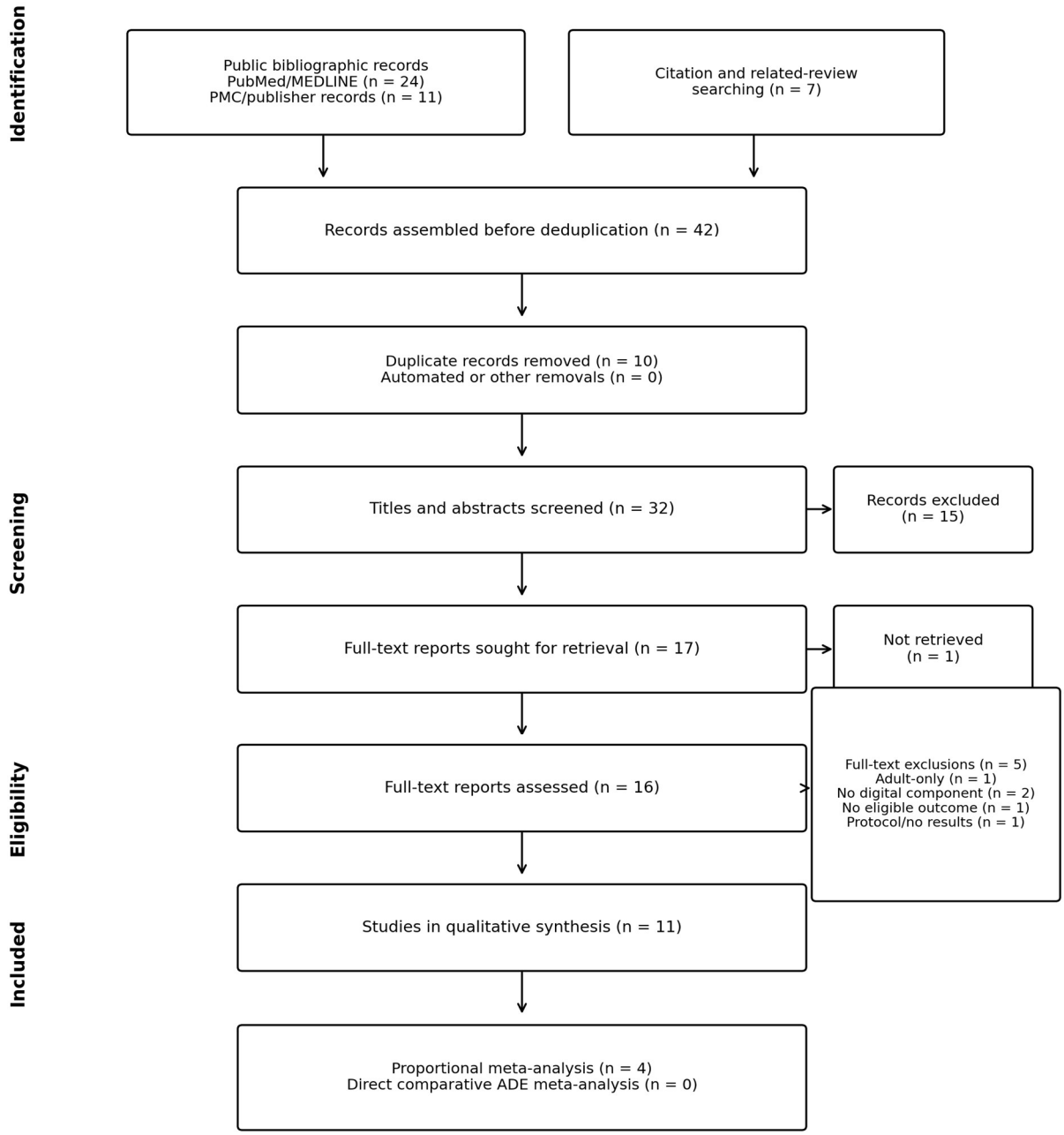
The proportion of pediatric patients with one or more discrepancies or reconciliation errors was captured in a random-effects, proportional meta-analysis. For the studies considered (Alcântara et al., 2021; Cuervas-Mons Vendrell et al., 2023; Iturgoyen Fuentes et al., 2020; Meneses Mangas et al., 2021), numerators and denominators at the patient level were comparable. To assist with variance, measures were shifted to logit. Within study variance was defined as 1 over the count of events plus 1 over the count of non-events. Heterogeneity among studies, defined on the logit scale, was assessed using inverse variance, random effects. Back transformation was used to define proportional logits and confidence limits. For the four studies, pooled prevalence was a contextual average and not a generalizable population estimate because of the evident clinical heterogeneity.

Prespecified subgroup analyses included separating neonatal and general pediatric analyses; and separating analyses conducted in ward and ICU settings, conducted during admission versus discharge, led by pharmacists versus non-pharmacists, conducted within fully versus partially integrated systems, and analyses carried out by researchers with lower versus higher degree of bias. These analyses were not conducted because the number of comparable studies for each outcome was too small. Publication bias tests (e.g., funnel plots) were not conducted because less than ten studies formed any of the pooled outcomes. Leave-one-out sensitivity analysis was applied to the prevalence model. However, because only four studies remained, and they were clinically very different, the analysis was not used to substantively exclude results.

The quality of the evidence was evaluated according to GRADE criteria [5]. Adverse drug events evidence was rated as low quality because it was non-random, and warranted further downgrading for

no comparable pooled estimate and imprecision. For outcome processes, risk of bias, inconsistency of definitions, and indirectness to patient harm warranted downgrading the evidence. The value for the prevalence estimate was very low due to the pooling of a disparate collection of studies and substantial heterogeneity. No outcome was assessed to show a large effect, as evidence of unregulated before-and-after studies could be attributed to temporal effects or other interventions.

Figure-1: PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and inclusion



Counts refer to the documented public-source verification log.

Results:

The studies of digital interventions were conducted in children's hospitals or pediatric specialty services. Each study employed a before-and-after or iteration-based quality improvement methodology. Rungvivatjarus et al. designed a new digital reconciliation workflow embedded in the EHR for a large pediatrician's office and added clinical support, instruction, and weekly metrics. Reconciliation completion reached 95% (from an initial 73%) after 7 months and stabilized at approximately 94%. Completion for pediatric psychiatry reached 88% (from an initial 17%) and pediatric hospital medicine reached 98% (from an initial 76%) (Rungvivatjarus et al., 2020). Johnson et al. reported a 17% improvement in reconciliation (from 68% to 85%) after linking automated reconciliation reminders to pediatric hospital admission (Johnson et al., 2018). These studies illustrate that completion of a task can be improved through the use of technology and accountability. However, the studies did not distinguish the impact of the digital intervention from educational and feedback components.

Russ et al. implemented a feedback loop to enhance the accuracy of admitting reconciliation. The error rate decreased to 4.7% and then to 2.9% during subsequent improvement cycles, with the 2.9% rate being sustained for a 12-month period (Russ et al., 2020). Adducchio et al. focused on discharge errors on a pediatric neurology ward, mitigating errors with the introduction of a standardized rescue-medication order set and a nurse-navigator role. The starting error rate of 15.7% decreased to 5.3% after the introduction of the first barrier and then to 2.9% after the second barrier. A total of 106 errors were noted during this study and no patient harm occurred (Adducchio et al., 2024). Noteworthy improvements to the processes were evident in both studies. However, the bundles of interventions and the endpoints set were reliant on the definitions of local audits.

Gunkelman et al. addressed the clarity of the EHR medication list, clinician training, and the use of audit and feedback. The percentage of patients with at least one home medication successfully removed increased from 35% to 48%, and the mean number decreased from 0.8 to 1.4. There were no safety events due to medication removal, and improvements were sustained for 12 months (Gunkelman et al., 2024). Ring et al. developed a multilingual electronic discharge medication system which enhanced the clinical workflow. Correct and complete discharge medication reconciliation improved by 25.6%, and improvements in efficiency and communication were noted (Ring et al., 2023). All of these interventions relate to different types of failures.

Pooled analyses on adverse drug events were not warranted due to the absence, rarity, or failure to rigorously assess actual harm in the studies. Gunkelman noted no safety events due to drug removals, while Adducchio stated there was no harm to patients. However, both findings were made without a concurrent comparator and were not designed to identify low-incidence events (Adducchio et al., 2024; Gunkelman et al., 2024). Other studies placed emphasis on either completion or error rates. Thus, to derive a risk estimate such as risk ratio for adverse drug events from the reports, unsupported assumptions would be required.

Proportional synthesis from four observational studies included a total of 1,050 pediatric patients. Iturgoyen Fuentes et al. reported that a drug therapy discrepancy occurred for about 42% of the 187 patients that were admitted; this was interpreted as 79 patients after rounding from the published percentage (Iturgoyen Fuentes et al., 2020). Meneses Mangas et al. cited at least one reconciliation error for 334 of the 592 patients that were reconciled (Meneses Mangas et al., 2021). Alcântara et al. reported that, among patients who transitioned to other hospitals, at least one unintentional discrepancy was found for 85 of the 114 patients studied (Alcântara et al., 2021). Finally, Cuervas-Mons Vendrell et al. reported at least one discrepancy in 96 of the 157 patients receiving chronic or onco-hematology care (Cuervas-Mons Vendrell et al., 2023). From the random-effects analysis, the prevalence was estimated

to be 58.8% (95% confidence interval 45.0%-71.2%). The heterogeneity was considerable ($Q = 30.73$, $df = 3$, $p < .001$; $I^2 = 90.2\%$; $\tau^2 = 0.294$ on the logit scale).

The dispersion was clinically reasonable. The minimum value came from an inclusion study, while the maximum value came from patients that were seen throughout several transitions. It is worth noting that chronic patients and those with specialized needs had more sophisticated treatment plans and greater circumstances for discrepancies. Since the definitions were different (some studies distinguished discrepancies at all, some only included unintentional discrepancies, some were only focused on reconciliation errors), the pooled estimate was the best approximation for the reconciliation errors detection, which was not designed to estimate the likelihood of unintentional injuries.

Direct digital studies were assessed under the risk of bias framework and deemed to have serious overall concerns. Uncontrolled before-and-after studies and co-intervention significantly impacted most of the studies. Most studies had concerns for intervention classification and missing outcome data. The favorable results reported in most studies suggests that the intervention had positive process changes, but the confidence in the magnitude of these changes was limited. For adverse drug events and reconciliation errors, the GRADE assessments showed very low confidence, while the GRADE assessments for completeness and accuracy of the lists showed low to very low confidence. For the prevalence of discrepancies, the confidence was very low. Assessment for publication bias was not appropriate since no quantitative outcome was assessed in at least ten studies.

Figure 2. Risk-of-bias traffic-light summary for direct pediatric digital intervention studies.

Figure-3: Random-effects proportional meta-analysis of pediatric patients with at least one medication discrepancy or reconciliation error

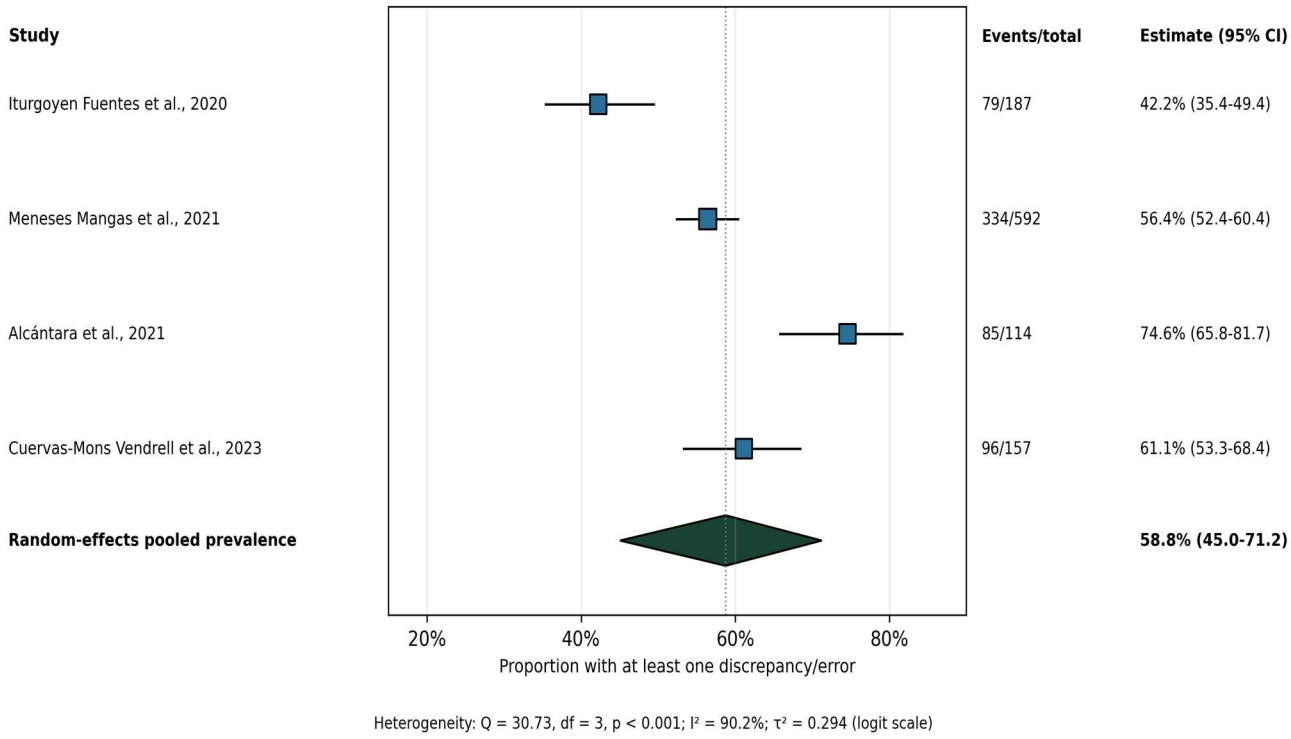
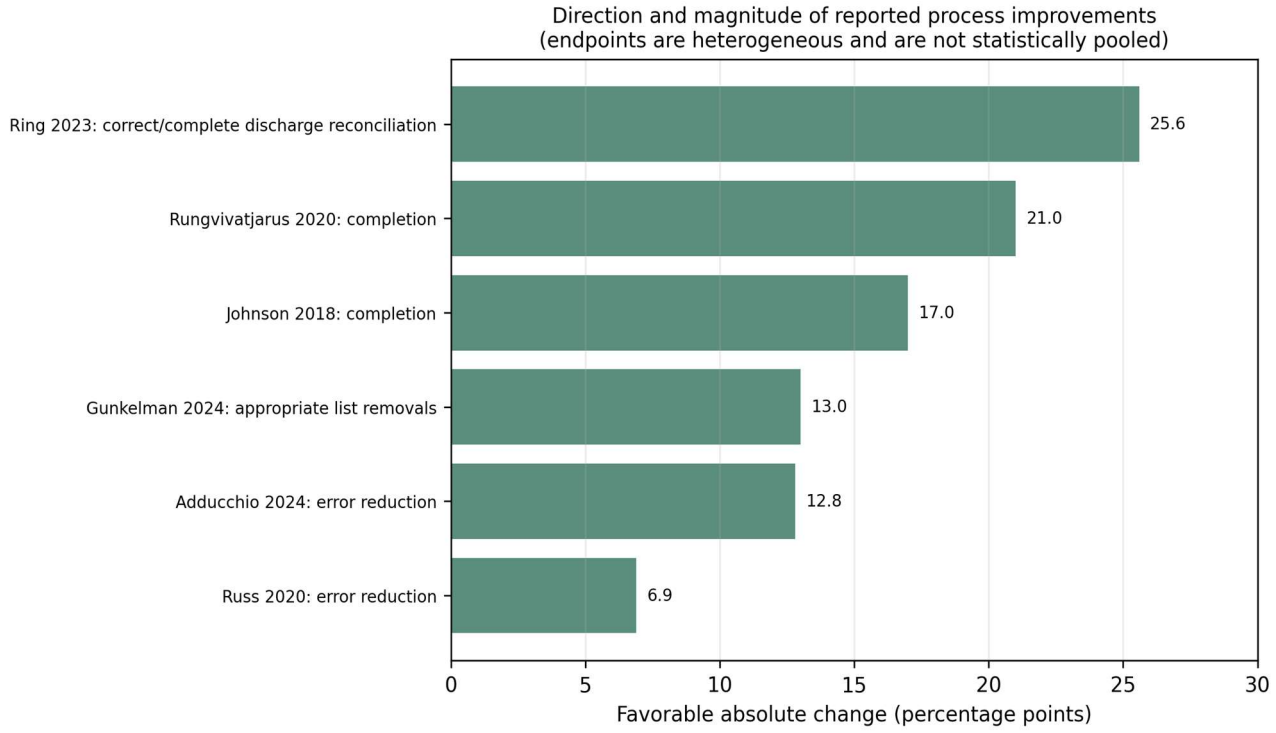


Figure 4. Direction and magnitude of reported process improvements. Heterogeneous endpoints are presented descriptively and are not statistically pooled.



Discussion:

The main finding is the distinction between the effectiveness of a process and the actual reduction of patient harm. Digitized or digitally aided reconciliation showed process improvement in hospitals in satisfying completion, documentation, list cleansing, correctness of the discharge, and error rate audits. All six direct intervention studies demonstrated positive process changes. However, in the absence of a comparable pediatrics study, we were unable to assess adverse drug events or construct a sufficient control group. Electronic reconciliation is successful in modifying the pediatric medication reconciliation process, but the available research does not support a reduction of adverse drug events; therefore, the available research supports this answer with a caveat.

This separation is not only the concern of semantics. There may or may not be an intentional or clinically significant discrepancy, which can be benign; a discrepancy that can be described as an error can cause risk even in the absence of injurious events; an adverse drug event may only be described as such if harm is observed. Digital systems are often reviewed shortly after their deployment to describe completion and/or documentation, which can be the primary measures. Actual injury is infrequent, is subject to review, may occur after discharge, or may occur beyond the contributing or implementing institution. Reports of studies where no observed harm occurred cannot declare the absence of equivalence or the presence of safety if the review is not thorough and the the study population isn't sufficiently large. On the other hand, the process change remains of value as it prevents latent dangers that may significantly impact process safety.

The pooled prevalence estimate indicates the level of concern the issue commands is substantial. Nearly 59% of the children surveyed across the four studies had at least one discrepancy or reconciliation error; however, the estimate is not considered a true prevalence for the pediatric population as the 95% confidence level was broad, and the heterogeneity was over 90%. The combined admission, transfer, and specialty population estimate merges discrete, yet overlapping definitions of reconciliation. The estimate does illustrate that contextual reconciliation has the potential for finding valuable insights. Complex regimens combined with the likely large volume of patients using an electronic system will make desk work and professional review imperative.

The studies on the interventions show that the best technology was used when combined with other elements of the sociotechnical system. EHR redesign was combined with decision support, education, and weekly reports (Rungvivatjarus et al., 2020). A feedback loop was incorporated rather than adding just another screen (Russ et al., 2020). List maintenance was simplified, and the desired behavior was reinforced through an audit (Gunkelman et al., 2024). A multilingual discharge platform was integrated into the workflow (Ring et al., 2023). An electronic order set was paired with nurse-navigator support (Adducchio et al., 2024). These innovations appear because software alone does not reconcile medications. It enables the structuring of tasks and identifies gaps and the creation of accountability data where the determination of reconciliation rests with the clinical and pharmaceutical experts as to whether the differences are justifiable and safe.

Pharmacists play an invaluable role during pediatric reconciliation. This stems from their ability to explain concentrations, identify dosing from either record discrepancies or systematic errors, communicate with community pharmacies, evaluate caregiver statements, and determine the importance of errors. Hovey and colleagues used a children's hospital admission service to complete 283 reconciliations and identified interventions in 69% of reconciliations. From this, they established that 21.9% of interventions had an impact on the care provided during the hospital stay and reported that eight significant adverse drug events were prevented (Hovey et al., 2023). Although this service was not an electronic intervention and was therefore excluded from the general digital studies, it describes the type of clinical reasoning that an electronic system should complement, rather than replace. In a possibly ideal system, automation would be applied to identify patients and errors during reconciliation.

This would also allow pharmacists to focus their efforts on high-risk, polypharmacy patients with complex or ambiguous treatment histories.

One of the largest components for a system to achieve its goals given the scope of reconciliation needs is interoperability. The electronic health record (EHR) module may be unable to display the full range of prescriptions available to it. Multi-provider care, particularly in the setting of pediatric patients, poses a challenge for full information. This is exemplified by controlled medications or rescue medications that may be utilized by caregivers during an emergency that are not documented in claims data. In the absence of verification, importing an external provider's medication list may introduce further errors and a fragmented system. These systems of the future should provide clear provenance for sources with indications of recency to verification and confidence levels, as well as discrepancies among caregiver statements, pharmacy reconciliations, and clinician orders.

Human-factors design is significant too. Reconciliation screens can be poorly designed when they contain overclicking, hidden dose units, disassociated concentration from volume, or treat active medicines the same way as historical medicines. Within design, alerts can turn to background noise when the severity is not ranked or when they are triggered without sufficient context. Pediatric design should prevent unsafe unit conversions, and identify duplicate ingredients in combination products. It should also present changes in a regimen and distinguish it from a clerical error. Finally, it should present the dosing unit, formulation, route, indication, and the maximum dose as a block. Upon discharge, the design should generate instructions for the caregiver that are clear, in the right language, and in line with both the prescriptions and the clinician's final plan.

The absence of a pooled effect from reporting on adverse events is consistent with other evidence. Mixed age systematic reviews present a stronger and more consistent relationship when reporting on discrepancies rather than adverse events. In one adult cluster randomized controlled trial, a mediation reconciliation process electronically enhanced reporting of discrepancies though this did not reduce adverse events caused by drugs. Thus, Child Health Services should not claim that finishing a task will result reduced risk. First, linked metrics should be shown in implementation dashboards. These should include completion, detection of discrepancies, significance of discrepancies, resolution time, acceptance of recommendations, and prevention of harm, as well as post discharge outcomes.

The standardization of outcomes is a priority for research. Future studies should specify if their denominator is patients, admissions, transitions, medications, or orders. Future studies should differentiate between discrepancies, unintentional discrepancies, reconciliation-related errors, and potential and actual adverse drug events. Clinical relevance should be determined by blinded or independent adjudicators using a validated and reproducible metric. Studies should specify if harm was identified during the hospital stay or post-discharge within 7 or 30 days or on a return to the Emergency Department or hospital readmission. It is critical to know the number of patients impacted and the total number of events to conduct patient-centered and event-centered research.

To better understand the impact of Electronic Health Record (EHR) modules, stronger research designs should be employed. Multicenter cluster-randomized or stepped-wedge designs would be appropriate for studies evaluating EHR modules with service-level EHR implementation. A regulated interrupted time-series design with adequate pre- and post- service EHR module implementation would be appropriate and informative compared to simple before-and-after studies. Studies should account for age, clinical acuity, number of home medications, occupation of an Intensive Care Unit (ICU) bed, the specialty service, and the availability of a pharmacist. Where design allows, matched, concurrent controls and prespecified analysis plans may facilitate the rationalization of bias. Economic modeling for research should evaluate the cost of implementation, the time of clinicians, the workload of pharmacists, and costs associated with avoided hospital admissions, as well as the costs of interfaces and maintenance of EHR content.

For a study to have enough power to measure rare effects, it may require thousands of admissions to measure a significant effect of a study intervention on preventable adverse drug events. Composite outcomes only improve power when components are methodologically sound and reported separately. Trigger tools, incident reports, chart reviews, caregiver assessments, and pharmacy data may capture disparate events. Causality, preventability, and severity may be rated by independent research adjudication boards. Inappropriate discontinuation of chronic therapy, delayed discharge, increased alerts, and caregiver confusion are balancing measures that may be reported.

Points of transition should have customized approaches to implementation. The admission point requires quick collection of the best possible medication history, which may be improved by integrating the external pharmacy with verification by a pharmacist. At the transfer point, reconciliation needs to detect medications that have been unintentionally omitted or duplicated due to changes in staff or pharmacy lists. At the discharge point, reconciliation needs to synchronize the inpatient medication orders, outpatient medication orders, caregiver instructions, and follow-up appointments. A single generic module is unlikely to be equally effective at all transition points. The high prevalence of discrepancies at the various transfer points indicates that hospitals should focus on the verification of each transfer, rather than assuming that the admission point is accurate by the time of the discharge point (Alcântara et al., 2021).

Targeted research is required for neonatal and specialty populations. Neonates typically receive compounded formulations and weight-based doses that can fluctuate with each encounter. Patients in neurology may rely on rescue medications and intricately planned, time-sensitive dosing. Patients in oncology and transplant may receive medications from multiple treatment teams that may involve planned medication holds, cycles, and supportive care. Psychiatry services may have obstacles pertaining to staff and caregiver availability, and previous outpatient services documentation. The significant service-specific improvements post-electronic redesign indicate the need for local workflow assessments (Adducchio et al., 2024; Rungvivatjarus et al., 2020). Tools developed for general pediatrics may require integration of specialty modules, and the addition of structured fields for indications and visualization for dosing history.

The review demonstrates several strengths. It had explicit definitions for outcomes. Effectiveness and burden were kept separate. Heterogeneous process outcomes were not pooled. Prevention of adverse events was not assumed from reduction of discrepancies. Study-level data were retained only if they were reported, and the one reconstructed numerator was noted. The burden of discrepancy was substantial, and a positive change in the digital process was shown in the graphs without an effect that was overestimated. Interpretation of certainty and risk of bias were done in a conservative manner.

Limitations are just as significant, focusing primarily on quality-improvement studies at a single center. A public-source verification log cannot replace exported logs from all bibliographic databases, and searches should be updated prior to submission. Some implementation reports may be relevant even if they do not mention medication reconciliation in the title or abstract. Many studies provided imprecise or partial data in the form of rounded percentages. A meta-analysis calculated proportional risk using only four studies and noted significant variability. It also described burden instead of articulating the efficacy of the interventions. Due to the quality of the research, it was not possible to identify any superior approaches or professional models, nor which EHR vendors, if any, were better.

For practice, use electronic reconciliation as a safety measure, and not as a documentation checkbox system. Governance needs to create a system that defines who is responsible, what the standards for completion are, and what the process looks like, in addition to continuous quality improvement. When a review of every case is not feasible, use risk stratification to focus the efforts of reconciliation pharmacists. Reconciliation efforts should not be prompted to meet completion metrics and should be

monitored for accuracy and timeliness, as should reconciliation efforts. The outputs provided to caregivers should be evaluated for clarity of comprehension.

Regarding policy and informatics, interoperability standards should encompass medication provenance, pediatric dosing units and formulations, and structured rationale for changes. Vendors should permit extraction of reconciliation data for quality measurement without the need for manual reviews of the chart. Regulators and accrediting bodies should promote the establishment of definitional and patient-centered outcome consistency, without the stipulation of a singular interface. Research networks have the capability to build integrated common data models, linking reconciliation to subsequent orders, lab results, outpatient emergency visits, hospital readmissions, and assessed harm.

More broadly, evidence shows that digital reconciliation systems can enhance reliability, diminish cognitive load, and integrate into work systems, reinforced by professional responsibility. The focus of future research should no longer be another local initiative. Instead, research should measure the impact of accurate reconciliation on pediatric medication exposure and the prevention of clinically significant harm. In the absence of this evidence, the use of electronic systems for medication reconciliation in clinical processes should be seen as a system safety initiative with potential system safety benefits, and not a validated system to prevent pediatric medication-related adverse events.

Implementation maturity should be considered. Initial evaluations capture enthusiasm and concentrated leadership and advisory attention. This environment may be short-lived once project team members withdraw. Sustainability should be evaluated years after, taking staff changes, software updates, seasonal workloads, and changes in pharmacy staffing into account. Researchers should differentiate the initial acceptance of the practice from routine usage. Continuous reminders should be assessed and reported to determine whether performance declines due to reminders becoming routine. They should also evaluate equity. Portals and electronic lists that assume an ability and ease of digital access are designed to serve families with stable access to pharmacies and specialty care. Those with low health literacy and limited English proficiency may have the most to gain with accurate reconciliation and the least served by these portals. Pediatric medication safety research should also evaluate the gaps these reconciliation systems are designed to close. Lastly, the sensitive information from caregivers, pharmacies, insurers, and a host of health systems combined in the reconciliation process should also be protected. These dimensions combine to advance the research.

Conclusion:

The use of EHRs has improved measures of medication reconciliation for pediatric inpatients. Looking at process measures including completion rates, documentation, list scrubbing and error audits shows improvements in all areas, but the studies included in this review were mostly heterogeneous and lacked controls. Because of this, the studies fail to give a pooled estimate for adverse drug events. Another random-effects synthesis suggests that about 58.8% of children studied showed reconciliation discrepancies in any of the four observational studies, indicating the lack of safety in existing systems, but does not demonstrate the effect of any of the studies. The quality of evidence shows that there is very little certainty in the reduction of patient harm. Current systems should integrate electronic systems, but also require the assessment of a pharmacist as well as a multidisciplinary team, redesign the workflow, and assess outcomes of significance. Future comparative studies that focus on medication reconciliation in multiple systems should adopt a common lexicon, take a census of the patient population for studies, conduct independent assessments of harm, and have adequate follow-ups. These studies should demonstrate that improvement in reconciliation systems will lead to a reduction in adverse drug events along with reduced outpatient emergency visits and readmissions.

Tables:

Table 1. Characteristics of direct pediatric electronic or digitally supported intervention studies.

Study	Country	Design	Setting	Population/ sample	Intervention	Comparator	Stage	Primary outcome	Follow-up
Rungvivatjarus et al., 2020	United States	Before-after QI	Large pediatric center	12,481 baseline and 13,082 postintervention admissions	EHR workflow redesign, best-practice advisory, education, weekly feedback	Previous workflow	Admission/inpatient	Reconciliation completion	7 months plus sustainment
Russ et al., 2020	United States	Iterative QI	Children's hospital	Hospitalized children	Feedback loop, accountability and process redesign	Baseline process	Admission	Reconciliation error rate	12-month sustainment
Ring et al., 2023	United States	QI	Pediatric hospital	Discharged children	Multilingual electronic discharge medication platform	Preimplementation workflow	Discharge	Correct and complete reconciliation	Implementation period
Gunkelman et al., 2024	United States	QI	Children's hospital	Hospitalized children	Simplified EHR list-cleanup process, education, audit and feedback	Baseline workflow	Admission/inpatient	Appropriate removal of obsolete medicines	12 months
Adducchio et al., 2024	United States	QI	Pediatric neurology unit	Neurology inpatients	Standardized electronic rescue-medication order set plus nurse support	Baseline process	Discharge	Reconciliation error rate	January 2021-February 2023

Study	Country	Design	Setting	Population/ sample	Intervention	Comparator	Stage	Primary outcome	Follow-up
Johnson et al., 2018	United States	Before-after QI	Pediatric hospital	Admitted children	Automated EHR-linked email reminders	Usual process	Admission	Completion rate	Implementation period

Table 2. ROBINS-I-informed risk-of-bias assessment of direct intervention studies.

Study	Confounding	Selection	Classification	Missing data	Measurement	Reporting	Overall	Principal justification
Rungvivatjarus 2020	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions
Russ 2020	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions
Ring 2023	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions
Gunkelman 2024	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions
Adducchio 2024	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions

Study	Confounding	Selection	Classification	Missing data	Measurement	Reporting	Overall	Principal justification
Johnson 2018	Serious	Moderate	Low	Low/Moderate	Moderate	Moderate	Serious	Uncontrolled QI design with bundled cointerventions

Table 3. Study-level data used in the proportional meta-analysis.

Study	Patients with event	Total patients	Proportion	95% CI	Weight	Notes
Iturgoyen Fuentes et al., 2020	79	187	42.2%	35.4%-49.4%	25.2%	Event count reconstructed from the published rounded proportion (42%).
Meneses Mangas et al., 2021	334	592	56.4%	52.4%-60.4%	26.5%	Patients with at least one reconciliation error.
Alcántara et al., 2021	85	114	74.6%	65.8%-81.7%	23.4%	Patients with at least one unintentional discrepancy across transitions.
Cuervas-Mons Vendrell et al., 2023	96	157	61.1%	53.3%-68.4%	24.8%	Patients with at least one discrepancy.
Random-effects pooled estimate	594	1050	58.8%	45.0%-71.2	100%	I^2=90.2%; Q=30.73; τ^2=0.294

Table 4. Narrative effectiveness and sensitivity interpretation.

Study	Outcome	Baseline	Final	Favorable change	Interpretive limitation
Rungvivatjarus et al., 2020	Completion	73%	95% initially; 94% sustained	+21 to +22 percentage points	Bundled workflow and decision support
Russ et al., 2020	Admission error rate	9.8%	2.9%	-6.9 percentage points	Iterative feedback; no concurrent control
Ring et al., 2023	Correct and complete discharge reconciliation	Not consistently extractable	25.6-point absolute improvement	+25.6 percentage points	Different discharge endpoint

Study	Outcome	Baseline	Final	Favorable change	Interpretive limitation
Gunkelman et al., 2024	Patients with appropriate home-list removal	35%	48%	+13 percentage points	List cleanup rather than ADE outcome
Adducchio et al., 2024	Discharge reconciliation error rate	15.7%	2.9%	-12.8 percentage points	Specialty unit and bundled intervention
Johnson et al., 2018	Admission completion	68%	85%	+17 percentage points	Automated reminders

Table 5. GRADE Summary of Findings.

Outcome	Evidence base	Effect/estimate	Certainty	Reasoning
Adverse drug events	0 directly comparable studies	No pooled effect estimable	Very low	No pediatric concurrent-control ADE estimate; severe imprecision and indirectness
Reconciliation errors	2 QI studies	Large favorable before-after reductions	Very low	Serious confounding, heterogeneous definitions, single-center designs
Completion/list accuracy	4 QI studies	Consistent favorable direction	Low to very low	Process outcomes; bundled interventions; uncertain relation to harm
At least one discrepancy/error	4 studies; 1,050 patients	58.8% (95% CI 45.0%-71.2%)	Very low	Observational prevalence, I^2=90.2%, varied transitions and definitions

Table 6. Full-text reports excluded from the direct effectiveness synthesis and reasons.

Report category	Reason for exclusion
Adult cluster-randomized electronic reconciliation study	Adult-only population
Pharmacist admission service without qualifying electronic intervention	No digital reconciliation component
Medication discrepancy surveillance algorithm without intervention comparison	No qualifying effectiveness intervention

Report category	Reason for exclusion
Electronic prescribing report without reconciliation-specific outcome	No eligible outcome
Implementation protocol without completed results	Protocol/no results

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