Implementation of a Medication Reconciliation Toolkit to Improve Patient Safety (MARQUIS2)

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Structured Abstract:

Purpose: Determine the effects of mentored implementation of a refined medication reconciliation best practices toolkit on medication discrepancies across multiple hospitals.

Scope: Unintentional medication discrepancies during care transitions are common - on average, more than one per patient - and potentially harmful to patients. The first Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS1) demonstrated that implementation of a medication reconciliation best practices toolkit decreased total unintentional medication discrepancies in five hospitals, but results varied by site. MARQUIS2 was designed to take the lessons learned from MARQUIS1 and apply them to a larger group of hospitals. It was conducted on medical and surgical wards at 18 hospitals in the US and Canada.

Methods: A pragmatic clinical trial, with three implementation waves each lasting 18 months, was conducted from 2016 through 2018. The intervention was a refined version of a medication reconciliation best practices toolkit, offering 17 intervention components. One of eight mentors coached each site via monthly calls and one to two site visits. Each site's Quality Improvement (QI) team assessed local practices, identified improvement opportunities, and implemented one or more toolkit components. A random sample of up to 22 patients per month per site was selected for outcome assessment. The primary outcome was unintentional medication discrepancies in admission or discharge orders, measured by comparing orders to a gold-standard medication history taken by trained study pharmacists.

Results: During the intervention, sites saw a steady decline in their medication discrepancy rate from approximately 2.85 discrepancies/patient to 0.98 discrepancy/patient. In interrupted time-series (ITS) analysis, the intervention was associated with a 5% relative decrease in discrepancies per month over baseline temporal trends (adjusted incidence rate ratio 0.95, 95% CI 0.93-0.98, $p<0.001$). The results demonstrated that a multicenter medication reconciliation QI initiative using mentored implementation of a refined best practices toolkit was associated with a significant reduction in unintentional medication discrepancies over time. Future efforts should focus on ensuring that as many patients as possible receive effective interventions to minimize medication discrepancies.

Key words: medication reconciliation, patient safety, hospitals, care transitions

Purpose
The goals of this study were 1) to implement the refined MARQUIS evidence-based medication reconciliation toolkit at 18 diverse hospitals, using a mentored quality improvement implementation model; 2) to rigorously evaluate the effect of the MARQUIS program on unintentional medication discrepancies; and 3) to inform future spread of medication reconciliation interventions by performing an evaluation of program implementation using the Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework.

Scope:
Transitions of care (e.g., into and out of the hospital) are vulnerable times for patients due to several factors, including discontinuity of care, multiple changes to patients' medication regimens, inadequate patient education, the rushed nature of the discharge process, and lack of follow-up. Among the hazards to patients after care transitions are medication discrepancies, defined as unexplained differences among documented regimens across different sites of care.[1] Highly prevalent, up to 67% of inpatients have at least one unexplained discrepancy in their prescription medication history at the time of hospital admission,[2] and some studies have found that general medical inpatients experience on average more than one discrepancy in either their admission or discharge medication orders with potential for patient harm.[3]

Medication reconciliation is "a process of identifying the most accurate list of all medications a patient is taking… and using this list to provide correct medications for patients anywhere within the health system."[4] Inpatient medication reconciliation involves several steps: 1) developing an accurate list of each patient's medications; 2) validating each medication, dose, and frequency at the time of writing orders; 3) identifying and correcting discrepancies; 4) documenting intentional changes to the medication regimen; and 5) communicating the new list (e.g., at discharge) to the patient, caregiver, and next provider(s) of care.[5] Implementing medication reconciliation has proven more challenging than expected for many organizations, and there are reports of *pro-forma* compliance with regulatory requirements around med rec (e.g., checking a box that medications have been reconciled) without actual improvements in patient safety. Furthermore, though several studies have demonstrated the benefits of medication reconciliation interventions of several types,[6-8] until recently, these best practices were not widely known, and a broad implementation gap remains.

In 2011, in order to address the above issues, the project team conducted MARQUIS1 at five US hospitals.[9] From this work, the project team developed a toolkit of best practices in medication reconciliation[10] and mentored its implementation. Overall, the intervention was associated with an 8% relative reduction in medication discrepancies per month over baseline temporal trends.[11] However, improvement was not consistent. One site did not implement any interventions. Of the other four sites, three had improvements in total discrepancy rates. As part of the study, the team iteratively refined the toolkit and conducted qualitative and mixed-methods analyses to determine barriers and facilitators of implementation.

Based on these results, the team received funding to conduct a second study (MARQUIS2), taking the lessons learned from MARQUIS1 and applying it to a much larger and more diverse group of hospitals and health systems.[12] The aims of MARQUIS2 were to implement the refined MARQUIS evidence-based medication reconciliation toolkit at 18 diverse hospitals, using a mentored quality improvement implementation model; rigorously evaluate the effect of the MARQUIS program on unintentional medication discrepancies; and inform future spread of medication reconciliation interventions by performing an evaluation of program implementation using the RE-AIM framework.

From hospitals and hospital systems, 18 sites were selected via a formal application and review process to implement the revised toolkit. Sites were chosen, from 72 applicants, based on several criteria, including institutional support, a local site leader with QI experience and dedicated project time, an interdisciplinary QI team, institutional experience with successful patient safety projects, support and resources to collect data on discrepancies, and intention to implement one or more toolkit components. Sites were also chosen for heterogeneity in size, academic affiliation, region, and urban location. Sites that had already implemented two or more interventions from the MARQUIS1 toolkit were excluded. Sites varied in size from 88 to 1,541 beds; included seven sites from the northeastern US, six from the west, four from the south, and one from Canada; included nine urban hospitals, eight suburban hospitals, and one rural hospital; and involved eight university medical centers, six community teaching hospitals, two community non-teaching hospitals, one safety-net hospital, and one Veterans Affairs hospital (**Table 1**). Sites were divided into three waves of six sites each, with staggered implementation start times based on their planned implementation timelines. The first sites started mentored implementation in April 2016, and the last sites ended mentored implementation in April 2018. The direct participants in the study were the QI teams that implemented the intervention and the clinical personnel involved in the medication reconciliation process at each site, including attending physicians, residents, advanced practice providers, nurses, pharmacists, and pharmacy technicians. Each site chose which non-intensive care hospital units would be evaluated (typically all or most medical and surgical units). The patients who were the recipient of these interventions were adult patients admitted to these medical and surgical inpatient units.

Table 2 describes how the characteristics of participating sites compares with the 72 sites that applied, all hospitals contacted and asked to apply, and all US hospitals. This is essentially the reach of the intervention: the representativeness of the hospitals - and, by extension, their patients - that received the intervention. Compared with all hospitals, the 18 that participated were more often large, in the northeast, university teaching hospitals, not for profit, and urban.

Methods:

Trial design
This was a multisite, pragmatic clinical trial using interrupted time-series methodology to quantify the effects of implementation on outcomes over and above baseline temporal trends. The study was approved by the Partners Health Institutional Review Board (IRB); participating sites either deferred to the Partners IRB or waived IRB as a QI project at the local level.

Interventions
The MARQUIS2 toolkit consisted of 17 interventions grouped into eight domains: taking the best possible medication history (BPMH); discharge medication reconciliation and counseling; clarifying roles and responsibilities; risk stratification; health information technology improvements to the electronic health record (EHR); improving access to medication sources; “measure-vention” (i.e., measuring then intervening to correct discrepancies in real time); and stakeholder engagement.[13] All sites were provided an updated implementation manual, instructional videos, presentations, and return-on-investment (ROI) calculators (i.e., from investing in medication reconciliation personnel). Several changes were made to the toolkit in response to lessons learned from MARQUIS1, including the addition of simulated cases to train and certify competency in BPMH taking; an increased emphasis on pharmacy technicians as history takers and taking the BPMH as early in the hospitalization as possible; additional refinement of our ROI calculations and development of talking points when advocating for more resources; a focus on relatively simple changes to vendor EHRs’ medication reconciliation modules; and refinement of patient/caregiver discharge education materials with input from our Patient Family Advisory Council (PFAC).

In addition, the project team made several improvements to the implementation approach; again, these were made based on the lessons learned from MARQUIS1.[12] These included the addition of four regional in-person workshops for sites to receive hands-on training in teaching others to take a BPMH, do discharge counseling, and discuss how to overcome barriers to implementation; conducting site visits earlier, within the first 6 months of implementation, to establish mentor-mentee rapport and gain institutional support; establishment of a PFAC and their engagement in all aspects of the study; and the addition of peer-to-peer webinars from which sites could learn, and be motivated by, each other. See **Table 3** for a detailed description of these changes.

One of eight hospitalists trained in physician-mentored QI coached each site's QI team leaders via monthly calls and one to two site visits over the 18-month intervention period. Mentors were hospitalists with experience in QI and medication safety and underwent an all-day orientation to the project and "Mentor University" training[14] at the Society of Hospital Medicine's national office. In addition to monthly calls with their assigned sites, mentors engaged in "mentor council" calls with each other, the principal investigator, and senior mentors - senior faculty who were mentors for MARQUIS1 - to discuss challenges and share best practices. Throughout the 18-month implementation period, each site's QI team met internally; assessed local policies and practices; identified improvement opportunities; and implemented, refined, and spread one or more toolkit components to as many of the designated study units as possible.

Outcomes

The pre-specified primary outcome was the total number of medication discrepancies in admission orders and discharge orders. This was determined in the same manner to how it was measured in the MARQUIS1 study, measured in other previous studies conducted by our investigative team, and now measured by the Leapfrog Group.[3 9 12 15] Briefly, a study pharmacist at each site took a "gold-standard" medication history on a random sample of patients - goal of 22 per month - using all available data sources, typically the day after admission, and this history was then compared with the admission and discharge orders. If there were differences, the pharmacist reviewed the medical record for a clinical explanation; if necessary, the pharmacist also talked with the medical team for a possible explanation, allowing sites to distinguish unintentional from intentional discrepancies. Discrepancies were recorded and categorized with respect to timing (admission or discharge), type (omission, additional medication, change in dose, route, frequency, formulation, or other), and reason (history error or reconciliation error).[3] Study pharmacists could not be blinded to the intervention given the pragmatic design of the study, but they did collect the "gold-standard" medication history before evaluating any discrepancies in medication orders. Unlike in MARQUIS1, given the focus on scale and implementation, the project team did not perform physician adjudication to assess potential for harm for each discrepancy. Past studies have already shown the relationship between all discrepancies and those with potential for harm.[3 16]

Sample size

The Cochrane group and other experts typically recommend 20-30 observations per data point for an interrupted time-series analysis, with at least three data points at pre- and post-intervention times.[17] The project team recommended that each site collect data on approximately 22 patients per month (i.e., one patient per weekday) and collect baseline data for at least 3 months before implementing any interventions. This approach minimized data collection burden while still allowing for rigorous data collection and an adequate sample size to evaluate changes over time.

Because of the study design, the team did not know how many sites would adopt a particular intervention, nor at what time they would implement that particular intervention (i.e., how many

months of post-intervention data would be available for analysis). However, the target sample size was 8,100 patients across 18 sites, with one third of the data anticipated to be from the pre-intervention period. This would yield, on average, 150 patients per site pre-intervention and 300 patients per site post-intervention. Even a very conservative power calculation based on evaluating an intervention at a single site suggested that we would have adequate data to detect fairly small changes in outcome with 90% power. For example, based on MARQUIS1 data suggesting that the number of medication discrepancies would average 3.3 per patient and follow a Poisson distribution,[11] the project would have 90% power if an intervention at a single site reduced the number of discrepancies by 18%, from 3.3 per patient to 2.7 per patient (with a 5% type-1 error). If the same intervention was implemented at two sites, the detectable difference would be reduced to a 12% decline, from 3.3 discrepancies per patient to 2.9 per patient.

Randomization of Patient Sample

The project statistician used the random number generator in Excel (Microsoft, Redmond, WA) to create the random sample of patients for outcome assessment. Each date in the study period was associated with a random string of numbers from 1 to 30, different for each site. The QI team at each site would produce a list of patients admitted that day, then choose which patients to evaluate in the order of the string of numbers until the target number of patients had been seen. For example, if on a given day the string of numbers was 6, 13, 5, 1, then the first patient to evaluate would be 6th patient admitted that day, followed by the 13th patient, etc.

Statistical methods

Primary Analysis: Effect of the Intervention on Discrepancy Rates

The project used ITS analysis to determine the effects of the intervention over time, adjusting for baseline temporal trends. We modeled the number of discrepancies per patient using multivariable Poisson regression adjusted for patient covariates, with total number of medications as a model offset, and clustered by site. This approach measures both sudden improvement with implementation of the intervention as a whole (change in y-intercept) and change in the baseline temporal trend (change in slope). Covariates were captured manually by each study pharmacist and included patient age, service (medical, surgical, other), whether medication information had to be provided by a caregiver (a previously identified risk factor for discrepancies[3]), and patient understanding of their medications (high, medium, or low), as determined by study pharmacists using previously established methods and also previously identified as a risk factor for discrepancies.[3 11]

To better understand the shape of the discrepancy curve over time, the team created statistical process control charts[18] and conducted a restricted cubic spline analysis using standard methods.

Ancillary analyses: Determination of Mechanisms of Action

To better understand how the intervention improved discrepancy rates over time, the team performed two secondary, post-hoc analyses. Specifically, the team wanted to distinguish between the effects of system-level interventions, such as hiring or training personnel to take a BPMH, clarifying roles and responsibilities among clinical personnel, or improving health information technology, from patient-level interventions, such as receiving a BPMH in the emergency department or receiving discharge medication reconciliation from dedicated and trained personnel. To do this, the team first measured the average cumulative number of system-level interventions implemented by each site over time (the intervention “dose”). The team then analyzed discrepancy rates in the first versus last 6 months of the implementation period among patients who did not receive any patient-level interventions as a measure of the independent effects of system-level interventions (i.e., under conditions of low versus

high implementation). Second, the team measured the proportion of patients who received at least one patient-level intervention over time (intervention "fidelity"). Then, the team analyzed relative improvements in discrepancy rates between those who did and did not receive any patient-level interventions in the first, middle, and last 6 months of the study as a measure of the effects of patient-level interventions under conditions of low, medium, and high implementation of system-level interventions.

Unless otherwise stated, two-sided p values < 0.05 were used to determine significance, and all analyses were conducted using SAS v9.4 (SAS Institute, Cary, NC).

Results

Participant Flow and Baseline Data
One site did not collect enough data on discrepancies to be included in the analyses. During the pre-implementation period, the remaining 17 sites randomly sampled 1,229 patients for outcome assessment. During the post-implementation period, sites sampled 3,719 patients (total sample size=4,948). Patient characteristics are shown in **Table 4**. Patients in the post-implementation period were slightly older, were more often on medicine services, and had less understanding of their medications.

Principal Findings: Effect of the Intervention on Discrepancy Rates
During the period of data collection, sites saw a steady decline in their medication discrepancy rate from approximately three discrepancies per patient to one discrepancy per patient (**Figure 1a**). In the restricted cubic spline analysis (**Figure 1b**), the only significant terms were linear terms, demonstrating a slightly steeper decline in discrepancy rates after the first 6 months of the study. There were no statistically significant quadratic or cubic terms.

In ITS analysis, sites saw a 5% relative decrease in discrepancies per month over baseline temporal trends (i.e., change in slope; adjusted incidence rate ratio 0.95, 95% CI 0.93-0.97, p<0.001). There was no significant change in the y intercept (i.e., no sudden improvement at the beginning of implementation; adjusted IRR 0.97, 95% CI 0.90-1.04, p=0.38).

Ancillary Analyses and Secondary Outcomes

<u>System-Level Interventions</u>
Over the course of the implementation period, the mean number of system-level interventions cumulatively implemented by sites increased from approximately two per site to eight per site (**Figure 2a**). The most commonly implemented system-level interventions were training existing staff and reallocating staff to take BPMHs, clarifying roles and responsibilities, and identifying high-risk patients, but all 17 components were implemented by at least one site, and eight sites hired new staff (usually pharmacy technicians) to take BPMHs (**Table 5**). Among patients who did not receive any patient-level interventions, discrepancy rates were 2.40 per patient (95% CI 1.91-3.00) during the first 6 months of the study (when adoption of system-level interventions was low) compared with 2.25 (95% CI 1.78-2.83) during the last 6 months (when adoption of system-level interventions was high), a nonsignificant difference (adjusted rate ratio 0.94, 95% CI 0.87-1.01, p=0.07).

<u>Patient-Level Interventions</u>
Patient-level interventions included the following: BPMH in Emergency Department (ED); BPMH outside ED; admission medication reconciliation by trained personnel; discharge medication

reconciliation by trained personnel; patient counseling at discharge by trained personnel; and other intensive intervention in high-risk patients. During the implementation period, the mean proportion of patients who received at least one patient-level intervention increased from approximately 20% to approximately 60%, at which point it plateaued (**Figure 2b**). Patients who received any patient-level intervention had significantly fewer discrepancies than those who did not receive any (**Table 6**). Moreover, this effect grew larger over time, such that, by the last 6 months of the intervention, those patients who received patient-level interventions had approximately one third the number of discrepancies of those who did not (adjusted rate ratio 0.34, 95% CI 0.31-0.38, p<0.001).

Discussion and Significance

Mentored implementation of a refined evidence-based toolkit of medication reconciliation best practices was associated with a large, statistically significant, and steady decline in medication discrepancy rates across 17 diverse North American hospitals. By the end of the study period, discrepancy rates per patient dropped to approximately one third their rate at the beginning of the study. Implementation of both system-level and patient-level interventions (i.e., “dose” and “fidelity”) increased over time. System-level interventions by themselves, without patient-level interventions, did not have a significant effect on discrepancy rates. In contrast, patient-level interventions, such as receipt of a BPMH by a trained professional or admission or discharge medication reconciliation performed by trained personnel, had a large effect. Moreover, this effect grew over time, suggesting a possible synergistic effect of patient- and system-level interventions. In other words, for example, once a site hires and properly trains staff to take a BPMH, improves their HIT, clarifies roles and responsibilities, and improves their access to preadmission medication sources, when that staff takes a BPMH, the benefits to patients are even larger.

One possible reason for the success of this study was its ability to build on the previous work from MARQUIS1, both in terms of refining the intervention and the approach to implementation. This suggests the benefits of conducting mixed-methods program evaluation, applying implementation science methods, and learning from those results. Another possible reason for the results was careful site selection and choosing sites close to the time of implementation that were ready and willing to implement interventions and collect study data. The fact that six of the sites hired new personnel, usually pharmacy technicians, to take BPMHs is a testament to both this site selection and the refinement of our toolkit to effectively make the case to hospital leadership of the return on investment of hiring these personnel (i.e., in reducing adverse drug events and inpatient length of stay).

Several studies have been conducted on the benefits of hospital-based medication reconciliation interventions. A recent systematic review of 19 studies focused on pharmacist-led interventions found a significant 66% reduction in patients with medication discrepancies,[6] driven mostly by one large before-after study of 8,959 patients in an integrated health care system[19]; only one other study had a sample size of over a thousand patients.[20] A systematic review of electronic medication reconciliation tools[7] identified 13 studies and demonstrated a significant decrease in the number of medications with unintended discrepancies. To our knowledge, our study is unique in the number and variety of sites involved, the scope of the toolkit and its ability to be adapted to each site’s particular circumstances, and the mentored implementation approach - all of which increase its generalizability and its ability to be widely implemented.

Limitations

The results of the study should be viewed in light of its limitations. Unlike in previous studies, we did not adjudicate unintentional discrepancies for potential for harm. This allowed us to scale up the study to many sites. As noted above, based on previous studies[3 16], the project team knows that improvements in total discrepancies track with improvements in the potentially harmful discrepancies.

Second, this was not a randomized, controlled trial. However, the ITS methodology adjusted for temporal trends, taking into account each site's baseline performance. Third, not every site contributed equal amounts of data, but the ability to collect data on large numbers of patients did not correlate with implementation success, thus making it unlikely that this biased results. Fourth, results to date do not explain any site-level differences or which intervention components were associated with the biggest improvements; these analyses are ongoing. In MARQUIS1, the most effective components were clarifying roles and responsibilities among clinical staff and hiring and training personnel in discharge medication reconciliation and patient counseling,[21] but these need to be confirmed in this larger cohort of hospitals. Last, in terms of generalizability, sites were selected and therefore may not be representative of hospitals in general. However, the sites were very diverse, using a variety of criteria. Moreover, based on the team's experiences to date, only sites committed to improvement in a specific clinical area are most likely to succeed in that domain; it would be a poor use of resources, now and in the future, to foist a mentored QI project on sites unwilling to do the hard work required for it to succeed.

Implications and Conclusions

Next steps include helping MARQUIS2 sites sustain their gains and developing a MARQUIS Collaborative to spread this intervention to as many interested sites as possible. The American Society of Health-System Pharmacists and the Pharmacy Technician Certification Board are currently working on developing curricula to train and then certify pharmacy technicians in how to take a BPMH, thus increasing the workforce able to do this important task. As noted above, Leapfrog is measuring medication discrepancies among the hundreds of hospitals it works with, providing much-needed data to measure the quality of medication reconciliation and drive further improvement at individual sites. There is also an ongoing need to work with EHR vendors on their medication reconciliation modules[22] and to demonstrate the effects of med rec interventions on healthcare utilization outcomes, which often drive resource allocation decisions.

In conclusion, mentored implementation of a medication reconciliation best practices toolkit resulted in a significant reduction in unintentional medication discrepancies in admission and discharge orders across multiple hospitals. Future work should focus on sustainability and spread of these interventions.

Table 1. Characteristics of Participating Sites

Site	# Beds	Region	Location (Urban, Suburban, Rural)	Teaching Status	Profit Status	EHR
A	534	Northeast	Urban	University Medical Center	Non-profit	Epic
B	88/160	Northeast	Rural	Community Teaching	Non-profit	Meditech
C	266	Northeast	Suburban	Community Hospital with Some Teaching Opportunities	Non-profit	Epic
D	255	West	Urban	Community Teaching	Non-profit	Cerner
E	563	West	Suburban	University Medical Center	Non-profit	Epic
F	638	West	Urban	University Medical Center	Non-profit	Epic
G	453	South	Suburban	Community Teaching	Non-profit	Cerner Soarian
H	836*	Ontario, Canada	Suburban/77% Large Urban, 11% Small Pop. Center, and 12% Rural	Community Teaching/multi-site community hospital, partnership with McMaster Medical school and accept learners	$500M Budget	None
I	576	West	Urban	University Medical Center	Non-profit	Epic
J	365	Northeast	Suburban	Community Teaching	Non-profit	Cerner/Allscripts
K	627	West	Urban	University Medical Center	Non-profit	Epic
L	1,541	Northeast	Urban	University Medical Center	Non-profit	Epic
M	525	West	Urban	County – Publicly funded safety net hospital	Non-profit	Epic
N	232	Northeast	Suburban	Community Non-teaching	Non-profit	Meditech
O	763	South	Urban	Community Teaching	Non-profit	Cerner - Intermed RxHX
P	850/996	South	Suburban	University Medical Center	Non-profit	Epic
Q	744	South	Urban	University Medical Center	Non-profit	Allscripts
R	112**	Northeast	Suburban	Department of Veterans Affairs	Non-profit	Computerized Patient Record System (CPRS)

*456 Acute Beds, 150 Mental Health Beds, 115 Long-Term Care Beds, 177 Complex Care Beds

**65 Sub-Acute Beds, 32 Long-Term Care Beds, 15 Hospice and Palliative Care Beds

Table 2. Reach: Hospital Characteristics of Participating and Non-Participating Sites

	Participating Hospitals (N=18)	Applicants (N=72)	All Contacted Hospitals (N=988) May Remove	All US Hospitals (N=6,239)
Size Small (<99 beds) Medium (100-399) Large (400+)	Small (1) 5.6% Medium (5) 41.7% Large (12) 66.7%	Small (3) 4.2% Medium (23) 31.9% Large (46) 63.9%	Small (263) 26.6% Medium (494) 50% Large (231) 23.4%	Small (3,432) 55.1% Medium (2,288) 36.7% Large (519) 8.3%
Hospital Region Northeast Midwest South West	Northeast (7) 38.9% Midwest (1) 5.6% South (4) 22.2% West (5) 27.8% Puerto Rico/Other (1) 5.6%	Northeast (21) 29.2% Midwest (15) 20.8% South (21) 29.2% West (11) 15.3% Puerto Rico/Other (4) 5.6%	Northeast (215) 21.8% Midwest (261) 26.4% South (330) 33.4% West (174) 17.6% Puerto Rico/Other (8) .8%	Northeast (804) 12.9% Midwest (1,756) 28.1% South (2,507) 40.2% West (1,107) 17.7% Puerto Rico/Other (65) 1.0%
Teaching Status University Teaching Community Teaching Non-Teaching	University Teaching (8) 44.4% Community Teaching (7) 38.9% Non-Teaching (2) 11.1% VA (1) 5.6%	University Teaching (26) 36.1% Community Teaching (31) 43.1% Non-Teaching (15) 20.8%	University Teaching (157) 15.8% Community Teaching (320) 32.4% Non-Teaching (511) 51.7%	University Teaching (302) 4.8% Community Teaching (1,344) 21.5% Non-Teaching (4,593) 73.6%
Profit Status For Profit Not for Profit Public	Not for Profit (13) 72.2% Public (5) 27.8%	For Profit (7) 9.7% Not for Profit (44) 61% Public (17) 23.6% Unknown (4) 5.6%	For Profit (100) 10.1% Not for Profit (663) 67.1% Public (221) 22.4% Unknown (4) .4%	For Profit (1,644) 26.4% Not for Profit (3,104) 49.8% Public (1,491) 23.9%
Location Urban Suburban Rural	Urban (18) 100%	Urban (53) Suburban (4) Rural (3)	Urban (673) Suburban (171) Rural (135)	Urban (3,455) 55.4% Suburban (1,102) 17.7% Rural (1,682) 27.0%

Table 3. Differences between MARQUIS1 and MARQUIS2

Domain	Specific Aspect	MARQUIS1	MARQUIS2
Site Selection	How and when sites were recruited	Informal process, sites identified prior to submission of grant application	Widespread search, formal application process, most sites identified at beginning of study period
Toolkit	Best possible medication history (BPMH)	Didactic materials only, including slide presentations and videos	Didactic materials plus simulation materials with standardized cases and role-playing to enhance learning and verify competency
	Role of staff taking BPMH	Agnostic to type of personnel	Increased emphasis on the value of pharmacy technicians as "medication reconciliation assistants" trained to take accurate medication histories
	Return on investment	Rudimentary calculations	More precise calculations based on MARQUIS1 data
	Patient counseling tools	Didactic materials, including slide presentations and videos	Enhanced didactic materials plus scripts and worksheets developed with Patient and Family Advisory Council (PFAC) input
Implementation approach	Site team training	Webinars	Webinars + four regional workshops
	Site visits, number and timing	Two site visits: first visit in months 5-10, second in months 16-19	One site visit within first 6 months
	Patient-family engagement	No formalized program	Established and engaged PFAC in monthly discussions
	Intersite sharing	No formalized sharing	Three peer-to-peer webinars featuring sites' stories of successes and challenges
	Health information technology (HIT)	Discovered significant challenges exist with the design, implementation, and use of HIT during medication reconciliation processes that, together with health systems issues, impacted medication safety	Provided guidance on how best to work with existing HIT—e.g., allowing pharmacists to make changes to medication lists, documenting the quality of the medication history taken and its sources, and customizing discharge instructions to make medication changes clear to patients and providers
Analyses	Intervention assessment	Scoring system of interventions; categorization of site-level intervention components based on meeting minutes analyzed retrospectively; no data on receipt of interventions at the patient level	Prospective collection of site-level interventions based on monthly site surveys; prospective collection of patient-level interventions as part of data collection on discrepancies
	Outcome assessment	Total medication discrepancies with potential for harm, involving adjudication; total medication discrepancies	Total medication discrepancies per medication per patient, as adopted by the Leapfrog Group[23]
	Program evaluation	Surveys, direct observation, interviews, focus groups of contextual factors, intervention fidelity	Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework

Table 4. Patient Characteristics: Pre- vs. Post-implementation

Characteristic	Pre-implementation[1] N=1,229	Post-implementation N=3,718	P value
Age in years, mean (SD)	60.3 (17.6)	62 (18.3)	P=0.002
Service, n (%) **Medicine** **Surgery** **Other**	 890 (72%) 262 (21%) 77 (6%)	 2,988 (80%) 495 (13%) 235 (6%)	P<0.001
Medication information provided by caregiver, n (%)	227 (18%)	600 (16%)	P=0.059
Patient understanding of medications,[2] n (%) **High** **Medium** **Low**	 468 (45%) 362 (35%) 217 (21%)	 1,166 (37%) 1,362 (43%) 612 (19%)	P=0.02

1. Includes the 3-month “wash-in period”

2. Based on study pharmacist assessment. High indicates understanding of medication indications, dose, strength, and frequency of most medications. Moderate indicates inconsistent or incomplete understanding of indications, dose, strength, and frequency of medications, or otherwise not high or low. Low indicates at most can identify medications by name or indication but not both, has little understanding of dose. This analysis excluded patients on no home medications in order to run a chi square test for trend.

Table 5. Adoption and Implementation of System-Level Interventions by Site

	Best Possible Medication History-Taking				Discharge Medication Reconciliation and Counseling			Roles and Responsibilities		Risk Stratification		HIT	Improve Access to Medication Sources		Measure-vention	Stakeholder Engagement		
Site	Train Existing Staff	Reallocate Staff	Hire New Staff	Communicate when additional work needed	Train Existing Staff	Reallocate Staff	Hire New Staff	Clarify and Assign Roles	Provide Audit and Feedback on Role	Identify High-Risk Patients	Implement Intensive Intervention If High Risk	Improve Med Rec HIT	Community Medication Sources	Patient-Owned Med Lists	Identify and Correct Defects in Real-Time	Social Marketing	Community Engagement	Total No. By Site
A	■	■			■			■	■	■								6
B	■	■		■					■	■			■					6
C	■								■			■	■	■	■	■		7
D	■	■	■	■				■	■	■	■	■		■	■			11
E	■	■		■	■			■	■	■	■							8
F	■	■	■	■	■	■		■	■	■	■	■		■			■	13
G	■		■	■		■		■	■	■				■				8
H	■	■	■	■	■	■	■	■	■	■		■	■	■	■	■	■	16
I	■	■		■				■		■		■	■					7
J	■	■	■	■	■	■		■	■	■	■	■	■		■			13
K	■	■	■	■	■	■		■	■	■	■	■	■					12
L	■	■	■		■	■		■	■	■	■	■	■		■			12
M	■	■		■	■	■		■	■	■		■	■					10
N	■	■	■					■	■			■	■	■			■	9
O	■									■								2
P	■	■		■	■	■		■	■	■	■	■	■					11
Q	■	■			■			■		■	■	■				■		8
R	■	■		■	■			■		■	■	■	■		■			10
Total Sites	18	15	8	12	11	8	1	15	14	16	9	13	11	6	6	3	3	

Table 6. Effects of Receipt of Patient-Level Interventions Over Time

Study Period	Number of Discrepancies per Patient (95% CI)		Adjusted Rate Ratio (95% CI)*	p
	No patient-level interventions	At least one patient-level Intervention		
Months 1-6	2.34 (1.67-3.28)	1.36 (0.96-1.92)	0.58 (0.53-0.64)	<0.001
Months 7-12	2.36 (1.95-2.84)	1.25 (1.03-1.51)	0.53 (0.49-0.57)	<0.001
Months 13-18	2.69 (2.17-3.34)	0.93 (0.74-1.16)	0.34 (0.31-0.38)	<0.001

*Adjusted for patient age, service (medical vs. surgical), patient understanding of medications, need for caregiver as a source of medication information. Number of medications used as a model offset in all models. Clustered by site in all models.

Figure 1a. Statistical process control chart demonstrating special cause variation in total unintentional medication discrepancies per patient over time

Figure 1b. Restricted cubic spline analysis demonstrating the shape of the discrepancy curve over time

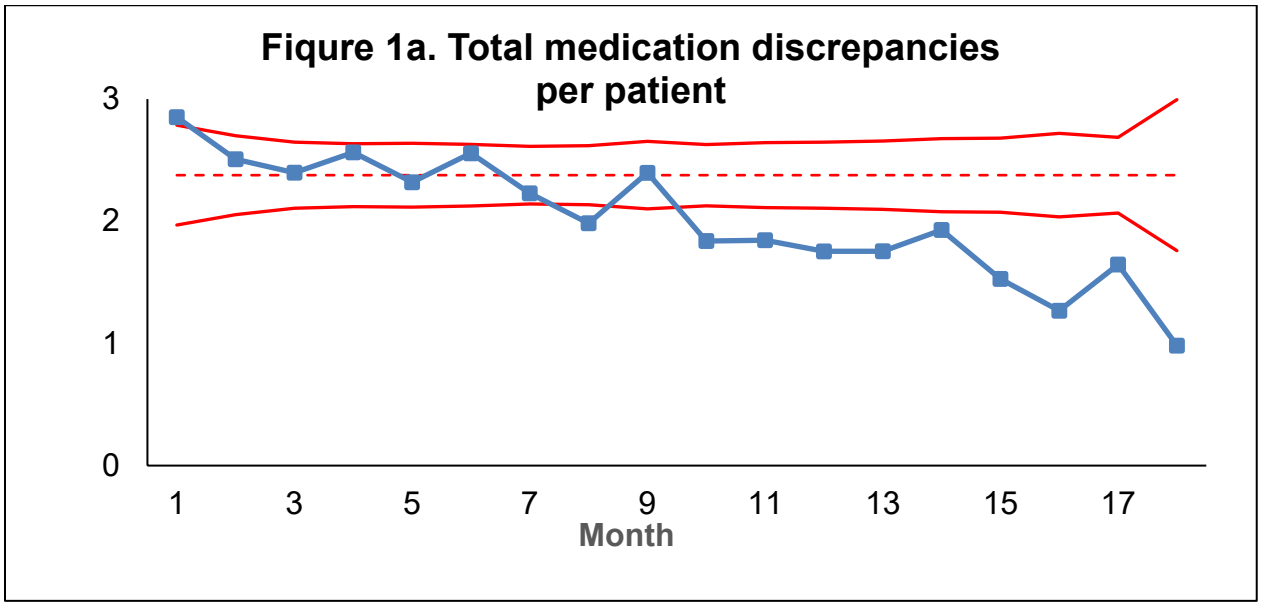
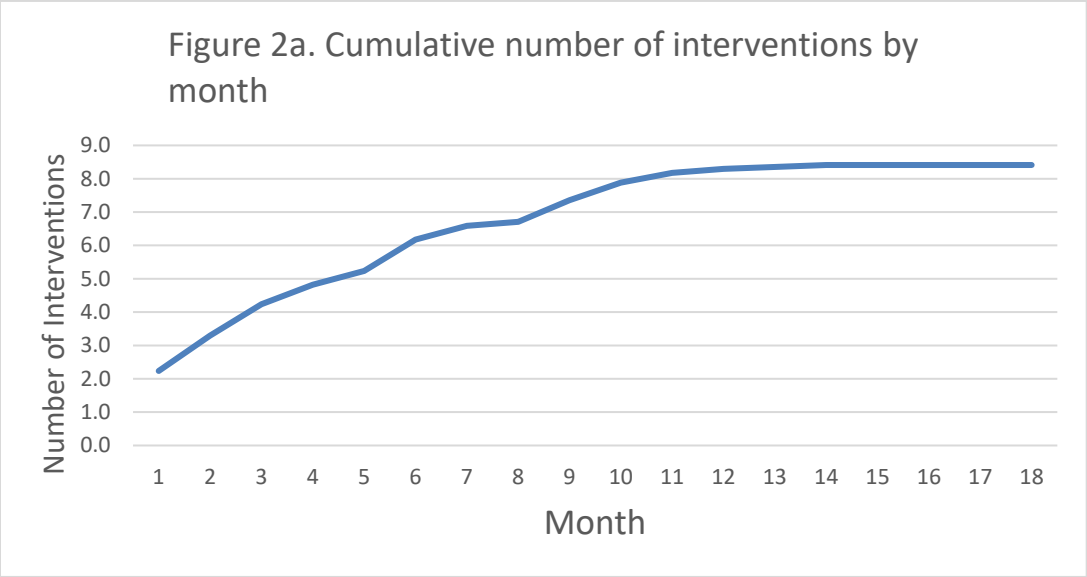
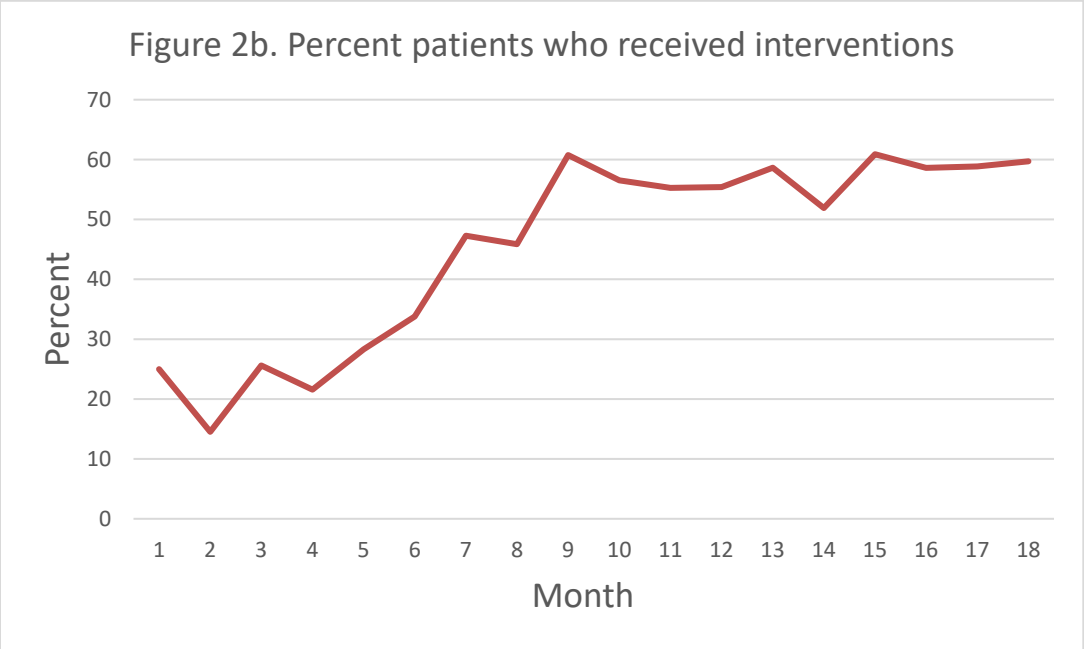


Figure 2a. Cumulative number of system-level interventions per site by month

Figure 2b. Percent patients who received patient-level interventions per month





List of Publications and Products

Manuscripts:

1. Mixon AS, Smith GR, Mallouk M, Reyes Nieva H, Kripalani S, Rennke S, Chu E, Sridharan A, Dalal A, Mueller S, Williams M, Wetterneck T, Stein JM, Stolldorf D, Howell E, Orav EJ, Labonville S, Levin B, Yoon C, Gresham M, Goldstein J, Platt S, Nyenpan C, Schnipper JL, MARQUIS2 Site Leaders. Design of MARQUIS2: study protocol for a mentored implementation study of an evidence-based toolkit to improve patient safety through medication reconciliation. BMC Health Serv Res 2019.

2. Stollford D, Ridner S, Vogus T, Rournie C, Schnipper JL, Dietrich M, Schlundt D, Kripalani S, Implementation strategies in the context of medication reconciliation: a qualitative study. Implementation Science Communications, 2021

3. Chu E, El-Kareh R, Biondo A, Chang J, Hartman S, Huynh T, Medders K, Nguyen A, Yam N, Succari L, Koenig K, Schnipper JL. Development and implementation of a medication reconciliation risk stratification tool integrated within a vendor EHR: a case series of three academic medical centers. Healthcare, 2022

4. Stollford D, Kripalani S, Schnipper JL, et al. Organizational context of hospitals that participated in a multi-site medication reconciliation quality improvement project (MARQUIS2): a cross-sectional observational study. BMJ Open, 2019

5. Schnipper JL, Reyes Nieva H, Mallouk M, Mixon A, Rennke S, Chu ES, Mueller SK, Smith GR, Williams MV, Wetterneck TB, Stein J, Dalal AK, Labonville S, Sridharan A, Stolldorf DP, Orav EJ, Levin B, Gresham M, Yoon C, Goldstein J, Platt S, Nyenpan C, Howell E, Kripalani S, MARQUIS2 Site Leaders, for the MARQUIS2 Study Group. Effects of a refined evidence-based toolkit on medication reconciliation quality and safety at multiple hospitals: results of the MARQUIS2 pragmatic clinical trial. BMJ Qual Saf, 2022

Lay Publications:

1. Schnipper JL, Levine C. The important thing to do before leaving the hospital. Next Avenue. October 22, 2019. https://www.nextavenue.org/before-leaving-hospital/

2. Levine C. Ask our experts. AARP October Bulletin, 2019.

Abstracts:

1. El-Kareh R, Huynh T, Chang J, Schnipper J, Nguyen A, Medders K, Yam N, Hartman S, Shipman C, Biondo A, Chu E. Development and implementation of an electronic health record based medication reconciliation risk stratification tool to optimally deploy limited pharmacy resources. Society of Hospital Medicine Annual Meeting, Orlando, FL, 2018.

2. Baughman A, Murphy N, Driscoll L, Norstrom J, Nelson S, Roehm J, Lange K, Shen W, Hanson A, Ruopp M, Jindal S, Tavares C, Chim S, Sandstrum S, Cain G, Schnipper J, Mixon A. Improving medication reconciliation in a Veterans Affairs skilled nursing facility as part of MARQUIS2. Society of General Internal Medicine Annual Meeting, Denver, CO, 2018.

Abstracts (continued):

3. Chu E, Stolldorf D, Mixon A, Sridharan A, Mueller S, Smith GR, Dalal A, Schnipper J. Development of a sustainment program for the MARQUIS2 Collaborative. Society of General Internal Medicine Annual Meeting, Denver, CO, 2018.

4. Schnipper JL, Reyes Nieva H, Mallouk M, Mixon A, Rennke S, Chu ES, Mueller SK, Smith GR, Williams MV, Wetterneck TB, Stein J, Dalal AK, Labonville S, Sridharan A, Orav EJ, Levin B, Yoon C, Gresham M, Goldstein J, Kripalani S. Effects of a refined evidence-based toolkit on medication reconciliation quality and safety at multiple hospitals: results of the MARQUIS2 study. Society of General Internal Medicine Annual Meeting, Washington, DC, 2019.

5. Schnipper JL, Reyes Nieva H, Mallouk M, Mixon A, Rennke S, Chu ES, Mueller SK, Smith GR, Williams MV, Wetterneck TB, Stein J, Dalal AK, Labonville S, Sridharan A, Orav EJ, Levin B, Yoon C, Gresham M, Goldstein J, Kripalani S. Effects of a refined evidence-based toolkit on medication reconciliation quality and safety at multiple hospitals: results of the MARQUIS2 study. Plenary Presentation, Society of Hospital Medicine Annual Meeting, National Harbor, MD, 2019.

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