Enhancing Medication CPOE Quality & Safety by Indications Based Prescribing

Final Report

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Structured Abstract

Purpose: Medication computerized prescriber order entry (CPOE) currently lacks an essential safety feature — the indication for the prescription. This project was developed to further the goal of incorporating indications into prescribing.

Scope: This project developed the rationale, approach, and addressed limitations through consensus with stakeholders around the need for indications based CPOE. Leveraging lessons from the requirements and consensus-building phase, we designed a prototype that incorporates drug indication into the prescription and ordering workflow. We also assessed patient and pharmacist preferences regarding the addition of indications on medication lists and bottles.

Methods: We convened six stakeholder panels to achieve consensus on the rationale, needs, requirements, and implications of incorporating medication indication into CPOE. Using a user-centered design process and incorporating the recommendations from the panels, we designed and built a working prototype of an indications-based CPOE system. We evaluated this prototype against two widely deployed commercial CPOE systems to test the hypothesis that this new system will demonstrate significant improvements in ordering speed, error rate, and user experience and satisfaction of the prescribers. We interviewed patients and pharmacists for their feedback on sample medication lists and bottles with indications.

Results: It is imperative to design CPOE systems to efficiently and effectively incorporate indications into prescriber workflows and optimize ways this can best be accomplished. Our novel CPOE system outperformed 2 leading commercial systems for all scenarios in terms of participants' efficiency, effectiveness and satisfaction.

Key Words: CPOE, drug safety, medication errors, user-centered design, patient safety, prescription drug indications

Purpose

Based on our team's previous work in two large computerized prescriber order entry (CPOE) medication safety projects, one funded by the FDA (CPOEMS- Computerized Prescribing Order Entry Medication Safety)[1,2] and the other by the National Patient Safety Foundation (MedMarx CPOE Medical Error Report Analysis)[3], it is clear that *indications-based prescribing* has the potential to prevent many medication errors and patient harm, as well as provide benefits to improve prescribing appropriateness and safety overall. However, current CPOE systems do not effectively support adding indications to prescriptions.

Our AHRQ funded project, Enhancing Medication CPOE Quality & Safety by Indications Based Prescribing, aimed to correct this deficiency by developing the rationale, approach, and addressing limitations around the need for indications enabled CPOE. We brought together safety and health information technology (HIT) experts, pharmacists, electronic health records (EHR) and knowledge vendors, and a diverse collection of stakeholders to advance the state of the art related to indications-based prescribing. Based on lessons from the requirements and consensus-building phase with stakeholders, we designed a prototype that incorporates drug indication into the prescription and ordering workflow, and tested it against two leading commercial CPOE systems.

Scope

While inclusion of drug indication on prescriptions has been long advocated by pharmacists and patients, as well as various regulatory and safety organizations (including State pharmacy boards, the Joint Commission, Institute for Safe Medical Practices (ISMP), American Society for Health Systems Pharmacists (ASHP), United States Pharmacopeia (USP)), drug indication is a prescription component that is currently missing in the order-entry screen/fields and workflow of most electronic medication ordering.[4] This is more than simply a missing piece of information. The "prescription indication" is needed to guide safe medication prescription choices, communicate with others on the team (particularly pharmacists and patients), and afford safety checks and provide safety nets to protect from harm when errors do occur. Because drug safety is the culmination of activities and interactions of multiple professional disciplines, the patient, and the HIT infrastructure, documenting and communicating drug indications is essential.

The idea of encouraging or even mandating indication on prescriptions is not new, and has been the subject of various discussions, recommendations and even State (TX, OR) legislation for more than a decade, without gaining requisite traction. Except for isolated successful examples,[5] various professional and practical barriers have inhibited progress. However, multiple developments have now converged to make this an auspicious time for promoting indications-based prescribing. These include: a) growing numbers and complexity of pharmacotherapy agents and regimens, along with cost concerns/considerations in drug selection,[6] b) maturing of CPOE to the point where many fundamental design and acceptability issues related to electronic ordering in general have been solved, along with a critical mass of users/practices now using electronic prescribing,[7] c) emerging and growing concerns and research on CPOE safety, pointing to the need to improve interface design for safety, efficiency, and usability [8], d) growing wariness on the part of developers and users related to "after-the-fact" CDS alerts, alerts not specific to an individual patient, "alert fatigue", along with recognizing that "help constructing the order" type of CDS (which indications-based prescribing provides) is much better conceived and received,[9] e) development and consensus around USP's Chapter 17 standard for placing indication on medication labels,[10] while at the same time ubiquitous secure electronic transmission of scripts to pharmacies bypassing potential privacy concerns risked by writing and carrying the indication on a paper script, f) ready-made content from electronic knowledge vendors, and others with newly available drug-indication tables that are interoperable with many EMRs.[11]

Despite these prior national and international efforts, little progress had been made to incorporate indications into the prescribing process as a standard way of prescribing in the U.S. and elsewhere. In response to a 2014 call by the Agency for Healthcare Research and Quality (AHRQ) for improved health information technology (HIT) safety[12], our team based at Brigham and Women's Hospital (BWH) proposed this project to try to advance the state of the art in indication prescribing.[13]

AHRQ was seeking proposals to develop research ideas and implementation projects that would help advance HIT on four broad fronts[12]:

1. User-centered design, human factors principles applied to HIT safety
2. Design, implement usable safe HIT for all users, including patients
3. Use HIT socio-technical systems to improve safety
4. Policy to impact decisions on the safe use of clinical HIT

Our proposal targeted the four AHRQ HIT safety improvement areas, with six key areas where we envisioned indications could impact safer and more effective medication use (Figure 1).

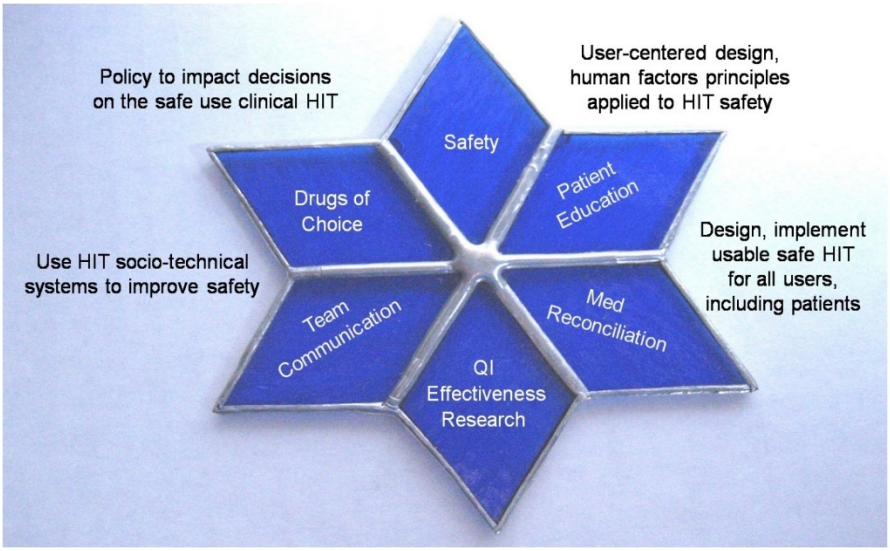

Figure 1: Scope and Impact of Indications Based prescribing

This project had the following aims:

Specific Aim 1: Convene six high-level stakeholder expert panels to achieve consensus and buy-in on the rationale, multi-user needs, operational and interoperability requirements, interface design principles, limitations and barriers, and policy implications of incorporating medication indication into CPOE with publication of a Sounding Board and a White Paper summarizing this consensus.

Specific Aim 2: Using a rigorous user-centered design process and incorporating the recommendations from Aim 1, design and build a working prototype of an indications-enabled CPOE system.

Specific Aim 3: Formally test and compare this indications-based prototype to two widely deployed CPOE systems using 8 pre-defined use-case clinical scenarios, to test the hypothesis that this new system will demonstrate significant improvements in ordering speed, error rate, user experience and satisfaction of the prescribers, as well as enhanced usefulness and safety of the prescriptions generated for pharmacists and patients.

In addition, several supplemental, unfunded projects were conducted with collaborators to better understand the use of indications in prescriptions, and the potential benefits of indications-based prescribing. We have described these projects in Appendix A.

Methods

Aim 1 - Stakeholder Panels

We successfully brought together more than 300 individuals from more than 75 organizations to define requirements, broadly discuss implications in-depth, and create model features of an innovative and transformative CPOE system that would incorporate medication indications into the prescription (see list in Appendix C). To better delineate and discuss these areas we hosted six international 90 minute webinars covering the landscape of issues related to indications based prescribing. The topics covered

by each webinar are listed below, and recordings and powerpoint slides from all six webinars are available online at https://www.ahrq.gov/chain/research-tools/featured-certs/improving-hit-prescribing-safety.html.

- Webinar 1: Delineating and defining the construct of indications-based prescribing.
- Webinar 2: Role of indications in strengthening patient safety and preventing medication errors.
- Webinar 3: Drug indications and the role of pharmacists and pharmacies.
- Webinar 4: Benefits of drug indications in patient education, information, and activation.
- Webinar 5: Drugs of Choice: How Indications based prescribing can facilitate selection of most appropriate medications.
- Webinar 6: Health IT technical and CPOE design issues for indications-based prescribing.

These exciting, and broadly attended sessions were key for identifying areas of consensus, complexity, and differences of opinion across the many stakeholder groups.[13,14]

Aim 2 - Prototype Design

The team took the lessons and key insights learned from the stakeholder panel webinar phase, and worked to design a working prototype that centered around indications-based prescribing. This entailed more than a full year of user research which included expert input, contextual inquiry sessions, participatory design sessions, usability roundtables, and formative usability testing.

Aim 3 - Usability Testing -Head-to-Head comparison with 2 leading commercial vendors

In this final phase, we conducted summative usability testing on our final prototype comparing performance of our prototype to two existing leading, commercial vendor EHRs. Eligible participants included outpatient internal medicine physicians, residents, physician assistants and nurse practitioners who currently use the EHR to order medications. We recruited clinician participants from the University of Illinois - Chicago and Partners HealthCare in Boston.

We designed eight clinical scenarios. These were created by our clinical team and the drug of choice selections were developed by the clinical pharmacists on our team in collaboration with practicing clinicians and academic faculty with expertise in therapeutics. The scenarios included a combination of problems seen by primary care providers that are common in practice such as poorly controlled hypertension, migraine prophylaxis, gout flare and newly diagnosed diabetes. In addition, 2 scenarios -- gonorrhea and Helicobacter pylori infection-- required multi-medication combinations with specific dosing schedule and treatment duration. Each scenario was designed to consider various challenges that providers often encounter at the time of medication ordering such as patient specific factors that affect treatment choice (e.g., renal impairment, medication allergies). We also included two scenarios designed to test common look-alike-sound-alike (LASA) medication errors. For example, to attempt to provoke a common LASA error-mixing hydroxyzine and hydralazine, one test scenario asked the provider to renew what the patient erroneously recalled and communicated to his provider as hydralazine “for itching”. A similar approach was used to test the LASA pair risperidone and ropinirole.

Test Procedures

Each of the one-on-one test sessions lasted approximately 45-60 minutes. We deployed Morae software on a laptop with a wireless mouse to record keystrokes, mouse-clicks as well as audio and visual of the

session. An observer/note-taker attended each session along with the moderator. Each participant completed four scenarios with the prototype system and four scenarios with their usual commercial EHR. We randomly alternated which system and which four scenarios they did first to avoid ordering bias. Participants were provided with a two-minute demonstration introduction to the prototype system before using it to complete the tasks.

Usability Metrics/Analysis

We recorded the medications ordered with each task and calculated an error rate based on the appropriateness of the drug ordered as determined by an independent review by two pharmacists. In the prototype, the indication was automatically captured in the system, whereas in the commercial systems, the user could either add an indication using free text in the patient sig or check pre-specified fields that the vendors included. We marked whether participants sought outside reference resources for additional information during each scenario.

The Single Ease Question (SEQ) was administered at the completion of each scenario drug order. Participants were asked to respond to the question, "Overall, how difficult or easy was this task to complete" on a scale from one to seven (7=very difficult). Average SEQ rating was calculated across participants for each scenario.

Participants completed an overall System Usability Scale (SUS) at the end of the test session. The total SUS was averaged across all participants. The debriefing interview included questions regarding the participants' likes and dislikes, suggestions for enhancement, feedback on the prototype and patient safety, and preference. We performed a content analysis on the comments from the interviews and identified major feedback categories.

Patient/Pharmacist Interviews

As the final part of aim 3, we interviewed both patients and pharmacists for feedback on ways indications could help them if they were included on their medication lists or medication bottle labels. We recruited patients to provide feedback at the Phyllis Jen Center for Primary Care at Brigham and Women's Hospital and recruited pharmacists who were faculty at MCPHS University. As planned, a total of eight eligible patients and eight eligible pharmacists were recruited and interviewed.

For this study, two separate medication lists were created based on the existing medication list generated by our home institution, but with an added section for indications in different formats. The interview also involved the creation of dummy medication bottles. Three medications were chosen: Allopurinol (prevention of gout), Paroxetine (depression), and Hydroxyzine (itching) to represent three distinct types of medications: daily medications (gout), sensitive issues (depression), and PRN (itching). Five separate labels were generated for each medication, based off a commonly used prescription label, representing different ways the directions could be phrased (such as 'Take 1 pill three times daily as needed for itching' or 'Take 1 pill three times daily as needed. Reason: Itching'). Information on the bottles and medication lists was checked by two pharmacists to insure their validity and accuracy.

These interviews were coded using formal qualitative analysis. This was done by having two coders listen and code each interview separately. Then they reconciled the codes between them to create a coding scheme. Once the coding was complete, they were analyzed for themes.

Results

The prototype was designed with the option to start a drug order by searching an indication or selecting a problem from the patient's existing problem list. Providers continued to have the option of searching for a drug but were required to select an indication before proceeding, and at that point were presented with a list of drug alternatives for the indication chosen (Figure 2). Other requirements that our design addressed included a way to support multi-drug combinations and multiple indications. One major benefit of this workflow is that it allowed us to design a system that could present a list of "drugs of choice" best practices options to the provider based on the selected clinical indication, practice guidelines, FDA prescribing information, and other patient-specific factors. The list of medication options for any given indication was presented as Suggested Choice (in green), Alternative (in yellow), or Not Recommended (in red) based on the indication, clinical practice guidelines, and patient-specific factors (allergies, renal status). Additionally, the prototype presented default dosing, frequency, and other order details based on the indication chosen.

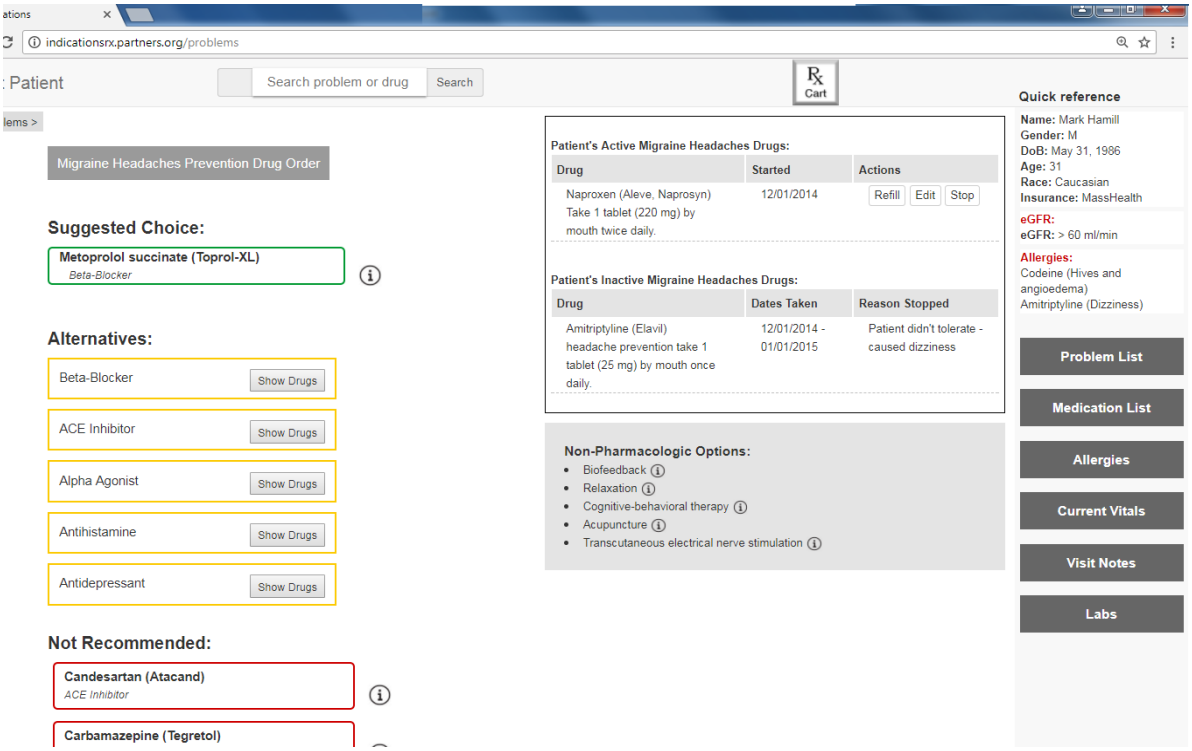

Figure 2: Indications prototype screenshot of recommended medications based on indication of migraine prevention

In the head-to-head comparison between our prototype and two leading, commercial vendors, 17 attending physicians, 13 resident physicians and 2 physician assistants completed a usability test. 32 participants used the prototype system, while 20 used one vendor and 12 used the other vendor. Most participants had more than two years of experience with their current EHR vendor system and 82% reported having an intermediate or higher level of skill with technology.

Across all 32 participants, the average time on task to complete a medication order using the prototype was 1.78 minutes (SD=1.17). Participants using vendor 1 took an average of 3.37 minutes (SD=1.90) and those using vendor 2 took an average of 2.93 minutes (SD=1.52). When comparing the participants who

used both the prototype and vendor 1, ordering with the prototype was significantly faster for four of the scenarios. For the participants who used vendor 2, the prototype was significantly faster for two scenarios (Figure 3). When we pooled the data across all the scenarios, the average time for the prototype was significantly faster than either of the vendor systems (Figure 3).

The average number of clicks to complete a scenario in the prototype was 19.0, significantly less than vendor 1 (46.5) and vendor 2 (38.2) (P<0.01). The number of clicks for those participants using both the prototype and vendor 1 was significantly less for all scenarios but itching (p<01). Compared to vendor 2 the number of clicks was significantly less in six of the eight scenarios (Figure 3).

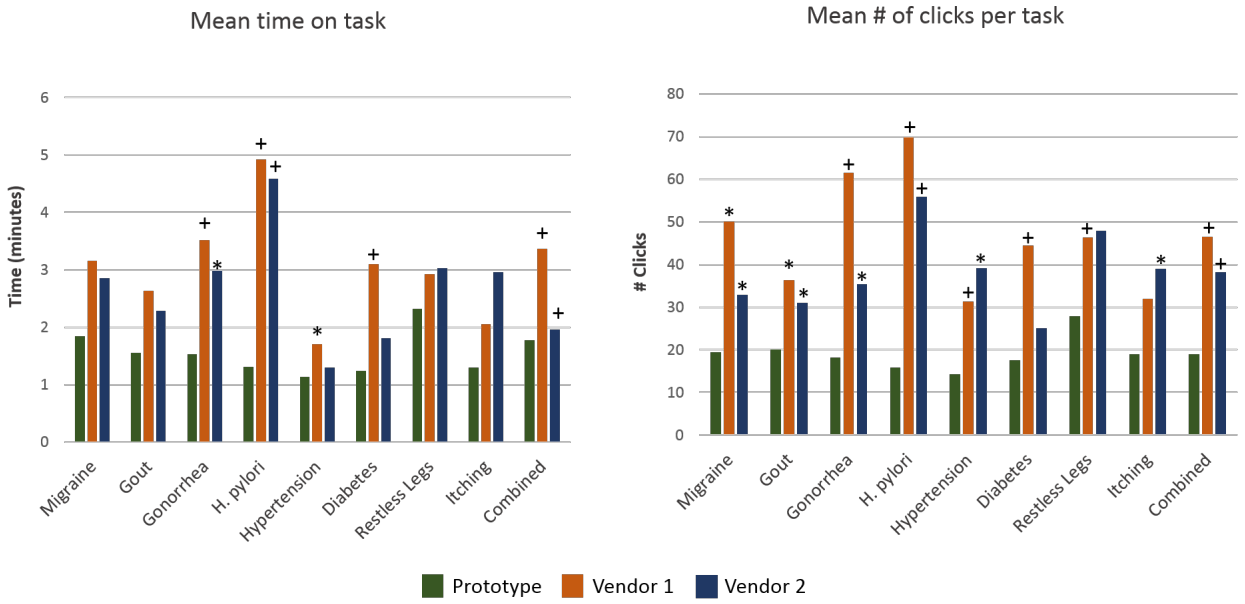

Figure 3: Results of the usability testing on the prototype (n=32), vendor 1 (n=20) and vendor 2 (n=12) are shown for time-on-task and # of clicks. Though the prototype measure shown is that for all participants, for statistical tests the participants that used vendor 1 were compared to their performance on the prototype as also done with vendor 2. P<0.05 shown as "*", P<0.01 shown as "+".

Across all 32 participants, 5% of orders made in the prototype were classified as inappropriate for the patient and indication. 39% of orders made in vendor 1 and 15% by vendor 2 were classified as inappropriate for the patient and indication. <1% of orders had an LASA error in the prototype, 2.5% in vendor 1 and 2% in vendor 2. Some of the reasons that an order was considered inappropriate included an incorrect route, frequency, duration or dose or the treatment was missing ceftriaxone as part of the therapy for gonorrhea or the PPI as part of the therapy for h. pylori.

The prototype included the indication on the order for the patient and pharmacist 100% of the time except for Gonorrhea when it was purposely removed for sensitivity purposes. Orders made in vendor 1 and vendor 2 included the indication 61% and 62% of the time, respectively, on electronic prescriptions and 83% of the time if the prescription was printed.

Overall for the eight scenarios, 28.8% of participants accessed an outside reference source for additional information during the ordering task when using the prototype and 58.8% of participants accessed an outside reference when using vendor 1 ($p = 0.0001$). Moreover, there is also a statistically significant difference ($p < 0.05$) between the participants who sought an outside reference source using the

prototype (31.3%) and vendor 2 (56.3%) (Figure 4).

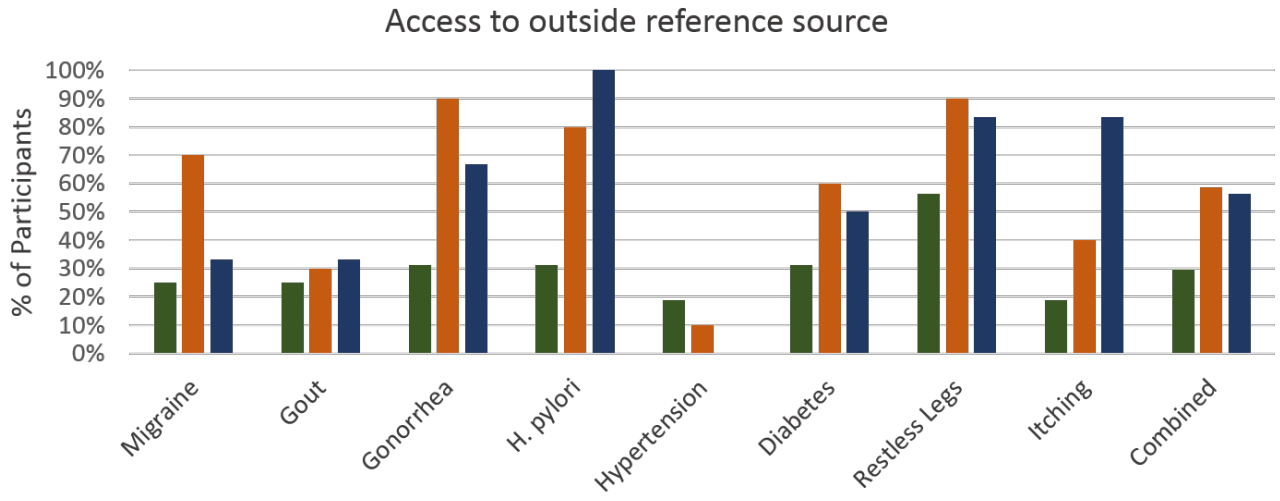

Figure 4: Access to outside reference source

The average response to the SEQ was a 1.73 (1=Very Easy) across all scenarios on the prototype, while the average rating for vendor 1 was 3.7 and vendor 2 was 2.75. For the participants who used the prototype and vendor 1, there was a significant difference in SEQ rating for all but one scenario, itching. For the participants who used the prototype and vendor 2, the prototype was more highly rated although the only scenario that reached a statistically significant difference in SEQ rating was the *H. pylori* case ($p<0.001$) (Table 1).

Table 1: Single Ease Question (SEQ) (1=Very Easy; 7=Very Difficult)

	Site 1 (n=20)		Site 2 (n=12)	
	Prototype Average	Vendor 1 Average	Prototype Average	Vendor 2 Average
Migraine	1.80	3.90[b]	2.00	2.50
Gout	1.90	3.50[a]	1.50	2.83
Gonorrhea	1.30	4.10[b]	2.00	2.83
H. pylori	1.80	4.60[b]	1.33	3.83[b]
Hypertension	1.10	2.50[b]	1.67	2.17
Diabetes Mellitus	1.50	3.90[b]	1.50	2.17
Restless legs	1.70	3.50[b]	2.67	2.67
Itching	2.00	3.60	2.33	3.00
Combined	1.64	3.7[b]	1.86	2.75[b]

[a] Significant at $p< 0.05$
[b] Significant at $p<0.01$

The average SUS score across all 32 participants in the study was 89.69 which can be classified as excellent in comparison to a wide range of other applications.[15]

System Usability Scale

Post Survey Results (System Usability Scale) (1= Strongly Disagree, 5= Strongly Agree)	Mean Rating
I think that I would like to use this system frequently.	4.72
I found the system unnecessarily complex.	1.38
I thought the system was easy to use.	4.84
I think that I would need the support of a technical person to be able to use this system.	1.47
I found the various functions in this system were well integrated	4.59
I thought there was too much inconsistency in this system	1.38
I imagine that most people would learn to use this system very quickly	4.66
I found the system very cumbersome to use.	1.19
I felt very confident using the system.	4.34
I needed to learn a lot of things before I could get going with this system.	1.63

Patient/Pharmacist Interviews

The patient/pharmacist interviews are still undergoing final data analysis. However, preliminary results show an overall preference for inclusion of the indication. Patients expressed frustration with the lack of knowledge around the reason they are taking their medications. However, many patients also had concerns around privacy issues if the indications were to be included on certain, sensitive medications such as for mental health issues or STDs. Pharmacists almost universally supported the inclusion of indications. They cited reasons such as improving the ease of counseling patients, insuring no medication errors were made, and improving patient adherence with their medications. Final data analysis will be complete by mid-July and a manuscript is already underway with the goal of submission by the end of July.

Overall Study Limitations

Although our webinar was attended by a broad range of individuals and organizations, webinar participation and input came primarily from a sample of individuals and organizations with an interest in and/or support of indications-based prescribing.

The prototype was developed as a stand-alone demonstration project performed in a simulated test environment. Although it was a functional working model for our test scenarios, we did not and could not compare performance in complexities of an actual clinical setting. We also acknowledge that for this type of system/design to be successful, maintaining other clinical data that informs the decision support is required, such as the problem list. Our hope is that this type of workflow would support a better integration of the problem list and ordering system. Further, our system included a feature to permit adding the problem related to the indication to the problem list with a single click.

The prototype was built around only eight scenarios. While we carefully chose scenarios that would test typical and frequently arising primary care prescribing issues, we recognize that additional usability issues may arise when we increase the scope and complexity of the indications and medications. This would require more research and development to overcome and requires a process for reaching consensus on drugs of choice; such a trusted accepted process/organization does not currently exist. Also, the fidelity of the fully functioning vendor EHRs and our prototype CPOE system was not a direct comparison although we attempted to ensure that all clinical data available in the record and the point of access was the same regardless of the system. While our pharmacists independently reviewing the safety and appropriateness of the orders were blinded to which system was used to generate them, the participants and observers obviously were not. While this could have introduced bias in favor of the test system, our tasks requiring clinicians to enter indications on each of these scenarios and order the appropriate medications were standardized across the systems. Participants had limited training on our system and varying lengths of training (usually several years or more) on the other systems, which should have advantaged their speed and comfort with their familiar ordering systems.

A final limitation is that there is a current lack of definitive evidence showing indications-based prescribing is safer or results in higher quality prescriptions. Most evidence in favor comes from expert opinions and demonstration projects such as ours, which showed strong evidence for improved satisfaction and efficiency with an indications-based prescribing system.

Discussion

Although there are numerous compelling reasons to incorporate indications into computerized prescribing, there are also many challenges and complexities that are currently impeding implementation. Addressing these is likely to be pivotal for adoption. The most common concerns, summarized below, were initially outlined in our first stakeholder webinar, and continued to emerge in various ways over the subsequent discussions with both participants and stakeholders.[16]

- Concerns about extra prescriber time/effort
    - Functionality must reduce, rather than increase, the prescribing workflow burden
- Competing options for alternative ways to capture/infer indications
- Privacy concerns and patient specificity
    - Sensitive patient diagnosis (e.g. HIV/mental health medications)
    - Patient option to “opt out” or suppress indication from appearing on prescription label
    - Maintain patient autonomy/confidentiality
    - Complexities in creating “smart” drug recommendations based on indications
    - Need to incorporate patient-specific factors (e.g. allergies, contraindicated coexisting conditions and previously failed medications, lab values)
    - Incorporation of complex insurance and formulary requirements
- Complexities in defining and creating indications
    - Sorting out how to differentiate an indication from a diagnosis or symptom
    - Empirical treatment when no definite diagnosis exists
    - Which standardized terminologies to use (symptom, health problem, ICD-10, SNOMED-CT)

    - Standardizing and maintaining indications knowledge databases
    - Drugs being given for multiple indications
- Complexities in transmitting indication information
    - Interoperability between EHRs and pharmacy systems
    - Limited real estate for placing indication on prescription label
- Limited evidence
    - No randomized trials; only limited data that selected use of indications has been beneficial
- Clinical autonomy concerns
    - Need to transform indications from hindrance to help
    - "Big Brother" vs. just-in-time help and streamlined prescription ordering
- Legal and billing issues (e.g., off-label FDA use)
    - Potential for inhibiting legitimate off-label use, reimbursement
- Overcoming policy & market fragmentation (EHR/knowledge vendor/PBM/payer indications)

Taking these challenges into account, we designed an innovative CPOE prototype that changed the way prescribers order drugs by offering the option of starting with the indication and permitting the computer to suggest drug choices. This novel CPOE system outperformed 2 leading commercial systems for all scenarios in terms of participants' efficiency, effectiveness and satisfaction. Participants could complete tasks in less time using less clicks with the prototype than with both vendor systems. In addition, orders generated with the prototype system resulted in higher quality orders that included fewer inappropriate medication orders than those placed in the vendor systems.
The prototype offers several interface design features in alignment with human factors and usability principles that help explain our positive findings. To better align with clinician's thought process, the prototype was organized with a focus on problem-based workflow. In addition, providing a list of drugs of choice that proactively considered patient specific factors upstream (i.e. they were not alerts generated downstream after an order was placed) off-loaded the cognitive burden on the clinician and has major implications for decreasing alert fatigue. The clinician could expend their working memory on making the decision regarding an appropriate medication choice rather than having to recall medication names or searching/remembering details of a patient's history. While clinicians used to the current way of ordering might be expected to prefer their traditional way of ordering drugs and thus might resist a shift in their electronic ordering workflow, in our study with minimal training on the prototype, they quickly learned, adopted and overwhelmingly preferred this new workflow.

One noteworthy finding was the frequency with which participants accessed outside reference materials with their usual ordering systems, and how dramatically this decreased with the prototype system. Each of the suggested drug choices included information (the prescriber could view by hovering over the choice) explaining the rationale for that recommendation. Only in rarer instances where they questioned whether they could "trust" the offered recommendations did they choose to check other reference sources. The "info button" function in our system to go directly to outside reference sources further discussing treatment for that indication, was not fully functional in our prototype, but if fully developed this could have further saved time for the participants.

The primary driver of our redesigned ordering system was the need to more effectively capture the indication for the patient's prescription. By recording the indication, the reason for the medication could

be communicated to the pharmacist, as well as automatically placed on the patient's medication bottle to help patient and caregiver's understanding of the medication and, thereby, potentially improve medication safety by preventing medication mix-ups and even aiding adherence. By default, participants using our prototype included the indication on the prescription for each of the scenarios, except the gonorrhea case where it was automatically not included. Our interviews with both patients and pharmacists also support this idea of inclusion of indications for a variety of reasons, from improved counseling to patient adherence.

Our interviews with the 32 clinicians following the prototype usability tests confirmed several features and concerns we had collected in earlier design phases of this project. [14,16] These issues and suggestions centered around the integration with the rest of the EHR and the quality and trustworthiness of back-end knowledge required for the drug/regiment choice recommendations. Adding indications and medications will also highlight challenges in dealing with potentially difficult medications or situations where the diagnosis is uncertain. Differentiating an "indication" from a "diagnosis" (at times required for billing purposes) is a related issue that requires further conceptual and design consideration. In addition to defining and maintaining the indication drug database, there are other technical and policy issues surrounding the generation of drug recommendations based on patient factors, as well as transmitting the indication information to pharmacist systems and mapping indications to patient friendly terms to place on patient medication labels and accompanying leaflets.

Conclusion

We have completed a highly successful project that has advanced the state of the art related to incorporating indications into medication prescriptions.

- We have brought the need for indications to front stage from the periphery. Decades of urging inclusion of indications into the prescription had, to a large extent, been sidelined in the face of other issues related to electronic medication ordering. We have involved a broad range of national stakeholders, and achieved buy-in and consensus around a series of rationales and practice design issues. We have also created, and widely disseminated, an inventory of benefits and challenges of indications-based prescribing.
- We have successfully designed, demonstrated, and tested an innovate prescribing prototype, incorporating broad stakeholder input, field testing, and interactive features and workflow redesign that can generate indications-based prescriptions for 8 common clinical scenarios for which it was programmed.
- We have compared our prototype with the 2 leading, commercial vendor CPOE systems with favorable results in terms of speed, safety, and user satisfaction.

While there are numerous barriers and complexities to successful implementation, the groundwork has been laid and the time is right to advance indications-based prescribing. Electronic prescribing is now in routine nearly universal use, both inside hospitals and in ambulatory prescribing, and most prescriptions are now being transmitted electronically.[17] Surescripts, using consensus-based standards developed by NCPDP, has incorporated indications as one of the standard fields that is transmitted with each prescription from the CPOE-prescribing clinician and software to the pharmacist and pharmacy IT

systems.[13] A number of knowledge vendors, who supply content to EHRs, have developed tables that list indications (including both labeled and unlabeled) for each drug, which could serve as the basis for templates to link each drug with its indication.

Thus, the infrastructure for indications-based prescribing is in place. However, requiring the extra step of adding the indication is not likely to be welcomed unless CPOE is redesigned to make it easier and less time consuming. Simply requiring prescribers to add the indication risks succumbing to the type of alert fatigue, prescriber push-back, and poor prescriber adherence (or even putting in false information to bypass alert/requirements) to which much of current CDS (clinical decision support alerts and requirements) has fallen prey. Thus, we need to design a smarter system.

Our team has worked to design a prototype that enables clinicians to start with the indication. What is needed next is multi-stakeholder leadership to make it happen. It will require vendors and prescribers to take action to develop and incorporate indications into the prescribing workflow. We believe that our CPOE prototype and results will serve as a starting point of a future of indications-based prescribing. We envision that it can be incorporated in one of several ways including as a standalone interfaced module, revision/tweaking of current CPOE systems interface and work flows, or a through a more thorough redesign of current commercial systems to more closely emulate our open source prototype design.

To this end, we have begun talking with vendors and organizations about next steps needed to further the goal of indications-based prescribing. We are planning to continue these efforts after the project ends and to look for new possibilities for studies and collaborations.

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Appendix A: Supplemental Collaborative Projects

The following are summaries of supplemental, unfunded projects related to our indications-based prescribing project that were conducted with collaborators:

Using indications to distinguish between LASA drugs

In collaboration with partners at First Databank our team at BWH studied whether drug indications knowledgebase content could be used to distinguish between look-alike-sound-alike (LASA) drugs. We extracted drug indications disease concepts from the MedKnowledge Indications module from First Databank Inc. and associated them with drugs on the Institute for Safe Medication practices (ISMP) list of commonly confused drug names. High-level indications we compared for each commonly confused drug pair and each pair was categorized as having a complete overlap, partial overlap or no overlap in high-level indications. This study showed that nearly 60% of the ISMP confused drug pairs included in the dataset had no overlap in indications, and another 21% of the drug pairs had just a partial overlap in indications. Associating indications with these drugs may help to differentiate these pairs and eliminate confusion between them. Adding indications to LASA pairs during prescription ordering is a newer, potentially less labor-intensive way to prevent name confusion electronically and make computerized medication ordering safer.[18]

Free-text prescription analysis

To better understand the current state of indications-based prescribing we collaborated with a large Midwest academic medical center to analyze a large database of free-text sigs affording a unique look at clinician prescribing behaviors related to inclusion of indications. We extracted the anonymous, unstructured free-text sigs from all prescriptions generated by their CPOE system during a 5-year period from 2011 to 2015. The data were analyzed using NLP to determine the rates at which prescribers included indications, stratified by provider specialty, drug class, and specific medication. The data was also analyzed for as needed (PRN) vs non-PRN instructions and look-alike sound-alike (LASA) drugs. Results showed that, overall, the percentage of providers who added indications is low, and of the 7.41% of all prescriptions that did include an indication, the majority were for PRN indications – reflecting a trend of adding indications only for short- term medications instead of those for chronic use.

Pharmacy Observation

We performed a study to understand how providing indications on prescriptions could be of benefit in the pharmacy setting. This was done by having pharmacy student interns observe and document prescriptions filled at different pharmacy locations (academic teaching hospital and an independent pharmacy). Preliminary results suggest that there are many instances and many medications for which knowing the indications would help pharmacists provide the safest and most accurate patient care possible. There were many instances of medications that had two or more different indications where knowing the true indication could help the pharmacist verify the dosing and accuracy of the prescribing. In addition, the data shows that indications are rarely included and that it is often not possible for the pharmacist to “guess” the correct indications based off context clues.

Appendix B: List of Publications, Presentations, and Outside Meetings

Below is a list of the publications, presentations and other products that have come from this study. We have also included placeholders for manuscripts/presentations which are still in development. In addition, we have included a list of outside groups we have had discussions with around developing and furthering the goal of indication-based prescribing.

Full Citations (Manuscripts and Presentations):

	Citation	Status
1.	Schiff GD, Seoane-Vazquez E, Wright A. Incorporating Indications into Medication Ordering – Time to Enter the Age of Reason. N Engl J Med 2016 July; 375:306-309. PMID: 27464201	Published
2.	Schiff GD. Incorporating Medication Indication into CPOE Ordering: Views of Physicians and Pharmacists. Society of General Internal Medicine, 2016 Annual Meeting; May 11-14; Hollywood, FL. Journal of General Internal Medicine; 2016.	Presented
3.	Kron KW. Incorporating the Indication into CPOE: Transforming Primary Care Medication Workflow. Society of General Internal Medicine, 2017 Annual Meeting; Apr 19-22; Washington, DC. Journal of General Internal Medicine; 2017.	Presented
4.	Forsythe K. "Why am I Taking this Medication Doctor?": Failure to include Indications in Outpatient Drug Orders and Instructions. Society of General Internal Medicine, 2018 Annual Meeting; 2018 Apr 11-14; Denver, CO. Journal of General Internal Medicine; 2018.	Presented
5.	Newbury I. A Better Way to Prescribe: Comparing an Indications-Based Medication-ordering Prototype to Leading Commercial CPOE Systems. Society of General Internal Medicine, 2018 Annual Meeting; 2018 Apr 11-14; Denver, CO. Journal of General Internal Medicine; 2018.	Presented
6.	Kron K, Myers S, Volk L, et al. Incorporating medication indications into the prescribing process. Am J Health Syst Pharm 2018 Jun; 75(11):774-783. PMID: 29674327	Published
7.	User Centered Design Process – Prototype creation (Aim 2)	Manuscript in progress
8.	Prototype Usability Trial Results (Aim 3)	Manuscript undergoing final review before submission
9.	Patient/Pharmacist Interviews (Aim 3)	Final analysis underway
10.	Seoane-Vazquez E, Rodiguez-Monguio R, Algahtani S, et al. Exploring the potential for using drug indications to prevent look-alike and sound-alike drug errors. Expert Opin Drug Saf. 2017 Oct;16(10):1103-1109.	Published
11.	Cheng CM, Salazar A, Amato MG, et al. Using drug knowledgebase information to distinguish between look-alike-sound-alike drugs. J Am Med Inform Assoc 2018 Jul; 25(7):872-884. PMID: 29800453	Published
12.	Northwestern Data Paper	Manuscript undergoing final review before submission
13.	Pharmacy Observation Study	Final analysis underway

Presentations: Title/topic	Date	Presenters(s)
Presentation at BWH Interpreter Service: "Indications-Based CPOE "Translating" Good Idea into Practice"	02/18/15	Schiff
Poster presented at DGIM Research Day: "Indications-Based Prescribing: Enhancing Medication CPOE Safety & Quality"	06/10/15	Nathan
Presentation at DGIM: "AHRQ-BWH Indications-based Prescribing Project"	03/18/16	Schiff
Presentation at the International Medical Interpreters Association: "Translating Drug Indications into Action: Improving Communication and Drug Use. The Brigham and Women's-AHRQ Indications-based Prescribing Project"	04/29/16	Schiff

Presentations: Title/topic	Date	Presenters(s)
Presentation at CUR-IT Meeting: "AHRQ-BWH Indications-based Prescribing Project: Designing the System"	05/03/16	Schiff
Poster presented at DGIM Research Day: "Incorporating Medication Indication into CPOE Ordering: Views of Physicians and Pharmacists"	05/06/16	Nathan
Presentation at AMIA iHealth 2016 Clinical Informatics Conference: "Incorporating Medication Indication into CPOE: What Do We Need to Build?"	05/06/16	Schiff
Poster presented at SGIM National: "Incorporating Medication Indication into CPOE Ordering: Views of Physicians and Pharmacists"	05/11/16	Kron
Presentation at ASHP Informatics Institute: "Passive Decision Support: Supporting Decision Support"	06/14/16	Patel, Schiff, Chan
Presentation at Atrius Grand Rounds: "Building a Better CPOE: Incorporating Indications into Prescribing"	08/04/16	Schiff
Presentation at APHA: "Incorporating Medication Indication into CPOE: What Do We Need to build?"	10/29/26	Schiff
Late breaking presentation at AMIA: "The Future of CPOE: Reengineering the Prescriber Workflow Incorporating Indications"	11/15/16	Schiff
Presentation at ASHP Midyear 2016: "Incorporating Medication Indications into the Prescribing Process AHRQ-BWH Indications-based Prescribing Project"	12/04/16	Schiff, Amato, Nathan
Presentation at MA Coalition for Prevention of Medical Errors: "AHRQ-BWH Indications-based Prescribing Project"	12/19/16	Schiff
Presentation at UMass Worcester Grand Rounds: "AHRQ-BWH Indications-based Prescribing Project"	01/19/17	Schiff
Poster presented at SGIM National: "Incorporating the Indication into CPOE: Transforming Primary Care Medication Workflow"	04/19/17	Kron
Poster presented at AMIA iHealth 2017: "Improving Medication Safety by Knowing Why Drugs are Prescribed: Informatics Solutions"	05/04/17	Nathan
Presentation at DGIM Research Day: "Prototyping the Future of CPOE: Starting with Indications"	05/19/17	Kron, Myers
Poster presented Discover Brigham: "Indications-based Prescribing"	09/09/17	Newbury
Poster presented at Discover Brigham: "Incorporating the Indication into CPOE: Transforming Primary Care Medication Workflow"	09/09/17	Forsythe
Presentation at HIMSS18: "Why Am I Taking This Drug? Incorporating Indications in CPOE"	03/08/18	Schiff, Neri
Poster presented at HFES: "A Paradigm Shift: Design and Testing Of An Innovative Computerized Provider Order Entry System"	03/26/18	Neri
Presentation at SGIM: "A Better Way to Prescribe: Comparing an Indications-Based Medication-ordering Prototype to Leading Commercial CPOE Systems"	04/11/18	Newbury
Presentation at SGIM: ""Why am I taking this medication doctor?": Failure to include indications in outpatient drug orders and instructions"	04/11/18	Forsythe
Presentation at MA Coalition for Prevention of Medical Errors: "A Safer Way to Prescribe Medications: A MA-Based Project to Incorporate Indications into Electronic Prescriptions"	05/04/18	Schiff, Garabedian
Presentation at AMIA: "New Approaches for Improving CPOE Safety: Indications-based Prescribing and CancelRx"	05/10/18	Wright, Garabedian, Cheng, Pitts
Presentation at IHI/NPSF Patient Safety Congress: "Improving Medication Safety by Incorporating Indications into Prescribing, Communicating, and Educating about Drugs"	05/25/18	Schiff, Garabedian
Upcoming presentation at APHA Annual Meeting and Expo: ""Why am I taking this medication doctor?: Failure to include indications in outpatient drug orders and instructions"	11/11/18	Schiff
Other: Title/topic	**Date**	**Speaker(s)/ Author(s)**
AJHP Voices Podcast "Incorporating Medication Indications into the Prescribing Process" http://www.ajhpvoices.org/	May 2018	Schiff, Amato, Bates
Indications website with links to panels "Indications-Based Prescribing Research Project (AHRQ-BWH)" https://sites.google.com/site/indicationsrx/	N/A	N/A

Outside Meetings: Group	Date	Contact Person
Surescripts	10/24/16	Ajit Dhavle
Northwestern University	9/12/16	Neeha Misra
American Society of Health-System Pharmacists (ASHP)	2/22/16	Shekhar Mehta
AHRQ	12/1/15	Arelene Bierman
American Medical Association (AMA)	11/6/15	Chris Sinsky
First Databank (FDB)	10/23/15	Christine Cheng
University of Maryland	10/9/15	Catherine Plaisant
UMass Memorial	10/9/15	Steve Erba.
Brigham & Women's Hospital (BWH)	9/9/15	Jerry Avorn
Surescripts	9/9/15	Joe DeLisle
U.S Department of Veterans Affairs (VA)	9/4/15	Bernie Good
Cambridge Health Alliance	8/4/15	Ziva Mann
Kaiser Northwest	7/13/15	Sunshine Sommers
American Medical Association (AMA)	7/8/15	Matthew Wynia
Centers for Medicare and Medicaid (CMA)	6/29/15	Madelyn Kruh
American Medical Association (AMA)	3/18/15	Chris Sinsky
American Medical Association (AMA)	3/6/15	Omar Hasan
Epic	11/14/17	Josh Holzenbour
Cerner	12/20/17	David McCallie
RxRevu	01/24/18	Kyle Kiser and Foster Goss
Epic	02/07/18	Josh Holzenbour
Dell Medical School	03/21/18	Rick Peters and Justin Rousseau
Surescripts	05/03/18	Aaron Studt
Park Nicolette Health Services	03/02/16	Molly Eckstrand
UT Southwestern	05/22/18	Ling Chu
University of Maryland, UPMC University of Pittsburg, Baycrest	04/03/18	Barbara Zarowitz, Steve Handler, Andrea Molser, Nicole Brandt
eBroselow	02/13/18	John Gobron
United States Pharmacopeia (USP)	01/23/18	Donna Bohannon
American Medical Association (AMA) – Digital Health Team	06/12/18	Chris Sinsky
Health2047	06/14/18	Lucia Soares

Appendix C: List of organizations from which members participated on stakeholder calls

Participation of these individuals should not be construed as providing official endorsements from their organizations.

AbbVie
National Council on Patient Information and Education (NCPIE)
Academy of Managed Care Pharmacy
National Osteoporosis Foundation
Accreditation Council for Graduate Medical Education
National Patient Safety Foundation
Agency for Healthcare Research and Quality (AHRQ)
National Council for Prescription Drug Programs (NCPDP)
Agilex
New York State Board of Pharmacy
Albany Medical Center
NextGen Healthcare
American Academy of Family Physicians
Northeastern University
American Association of Colleges of Pharmacy
Northwestern University
American Board of Internal Medicine
Ohio Pharmacists Association
American Cancer Society
Ohio Public Employees Retirement System
American College of Physicians
Oklahoma Health Care Authority
American Heart Association
Omnicare, Inc.
American Medical Association (AMA)
OPERS Healthcare
American Pharmacists Association (APhA)
Optum
American Society of Health Systems Pharmacists
OptumInsight, Inc.
Anthem Blue Cross Blue Shield
Oregon Health and Science University
Ashleigh Fisher Consulting
Osterhaus Pharmacy
Athenahealth
Partners Healthcare
Baptist Healthcare System
Patient Safety America
Baton Rouge General Hospital
Patients for Patient Safety Canada
Becton Dickinson and Company
Patients Like Me
Betsy Lehman Center for Patient Safety and Medical Error Reduction
PDX Inc
Boesen & Snow LLC
Pharmaceutical Research and Manufacturers of America
Boston Children's Hospital
Pharmacy HIT Collaborative
Brigham and Women's Hospital
Phil Burgess Consulting
Catamaran
Point-of-Care Partners
Centers for Medicare & Medicaid Services (CMS)
Project Patient Care
Cerner
Purdue Pharma L.P.
CMI Project
Quantros, Inc.
Colcamex Resources
RAND Corporation
Cone Health
Rite Aid
Consumer Reports
S and R Consulting Associates
CVS Caremark
Salem Memorial District Hospital
CVS Health
San Francisco State University
Department of Health and Human Services Office of the National Coordinator for Health IT
Sanofi
District of Columbia Board of Pharmacy
South Carolina Pharmacy Association
DrFirst
Spectrum Health
Duke University
St. David's Round Rock Medical Center
Elsevier Clinical Solutions
Stratis Health
Emedeon
SUNY Buffalo
Enhance Value
Surescripts
Epic
Target
Epilepsy Foundation of America
The Dartmouth Institute for Health Policy and Clinical Practice
Fairview Pharmacy Services
The Joint Commission
First Data Bank (FDB)
The Lynx Group
First DataBank
The Medical Letter
Food and Drug Administration (FDA)
The PSO Advisory
Genelex
The University of Alcala de Henares
Government of Western Australia Department of Health
The University of Illinois at Chicago
Granada Health, Inc
Truven Health Analytics
Harvard Medical School
Tufts Medical Center
Harvard Primary Care Center
UCL School of Pharmacy, London
Healthcare Compliance Packaging Council
UIC College of Pharmacy
Healthy Motivation
UNC School of Pharmacy
Hearst Magazine
Uniformed Services University of the Health Sciences (USUHS)
Indian Health Service
United States Pharmacopeia (USP)
Indiana University
Universite Catholique de Louvain
Institute for Healthcare Improvement
Université Laval
Institute for Safe Medication Practices (ISMP)
University of Alabama at Birmingham
International Medical Interpreters Association
University of Arizona College of Pharmacy
International Pharmaceutical Federation
University of British Columbia (UBC)
Kaiser Northwest
University of California Los Angeles (UCLA)
Kaiser Permanente Center for Health Research
University of Colorado
King Fahad Medical City
University of Connecticut
Kroger
University of Edinburgh
Lee Memorial Health System
University of Illinois - Chicago
Massachusetts College of Pharmacy and Health Sciences University (MCPHSU)
University of Maryland
Massachusetts General Hospital
University of Massachusetts Memorial Medical Center
Massachusetts Pharmacy Association
University of Minnesota
Mayo Clinic Rochester
University of Pennsylvania
McKesson
University of Sydney
Memorial Pediatrics
University of Washington
Merck & Co., Inc.
US Public Health Service
Midwestern University
Vanderbilt University
Molina Healthcare
Veterans Affairs
Molina Medicaid Solutions
Veterans' Association
Montefiore Medical Center
Walgreens
National Academy on an Aging Society
Weil Cornell Medical College
National Alliance of State Pharmacy Associations
Wisconsin Department of Health Services
National Association of Boards of Pharmacy (NABP)
Wolters Kluwer
National Association of Chain Drug Stores
Yale University
National Association of Managed Care Physicians
York University, Toronto
National Community Pharmacists Association
Zynx Health