



Enhanced Medication Histories



Final Report

Enhanced Medication Histories

Prepared for:

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. HHS A2902006000131

Author:

Linas Simonaitis, M.D.
Indiana University School of Medicine
Regenstrief Institute, Inc.

Corresponding Authors:

Changyu Shen
Biostatistician, Indiana University School of Medicine
Joe Kesterson
Regenstrief Institute, Inc.

**AHRQ Publication No. 11-0077-EF
October 2011**

This document is in the public domain and may be used and reprinted with permission except those copyrighted materials that are clearly noted in the document. Further reproduction of those copyrighted materials is prohibited without the specific permission of copyright holders.

Suggested Citation:

Simonaitis L. Enhanced Medication Histories—Final Report. (Prepared by Indiana University and Regenstrief Institute under Contract No. HHS A2902006000131.) AHRQ Publication No. 11-0077-EF. Rockville, MD: Agency for Healthcare Research and Quality. October 2011.

None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

This project was funded by the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The opinions expressed in this document are those of the authors and do not reflect the official position of AHRQ or the U.S. Department of Health and Human Services.

Preface

This project was funded as an Accelerating Change and Transformation in Organizations and Networks (ACTION) task order contract. ACTION is a 5-year implementation model of field-based research that fosters public–private collaboration in rapid-cycle, applied studies. ACTION promotes innovation in health care delivery by accelerating the development, implementation, diffusion, and uptake of demand-driven and evidence-based products, tools, strategies, and findings. ACTION also develops and diffuses scientific evidence about what does and does not work to improve health care delivery systems. It provides an impressive cadre of delivery-affiliated researchers and sites with a means of testing the application and uptake of research knowledge. With a goal of turning research into practice, ACTION links many of the Nation's largest health care systems with its top health services researchers. For more information about this initiative, go to <http://www.ahrq.gov/research/action.htm>.

This project was one of seven task order contracts awarded under the *Improving Quality through Health IT: Testing the Feasibility and Assessing the Impact of Using Existing Health IT Infrastructure for Better Care Delivery* request for task order (RFTO). The goal of this RFTO was to fund projects that used implemented health IT system functionality to improve care delivery. Of particular interest were projects that demonstrated how health IT can be used to improve decision support, automate quality measurement, improve high-risk transitions across care settings, reduce error or harm, and support system and workflow design, new care models, team-based care, or patient-centered care.

Acknowledgments

The Enhanced Medication History project was constructed at Indiana University and Regenstrief Institute with the generous support of AHRQ (Contract HHS 2902006000131). The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services.

We are very grateful to HealthNet, Inc. of Indianapolis for allowing two of its community health centers to participate in this project. We thank Katie Allen, Andy Frantz, Shahid Khokhar, Larry Lemmon, and Andrew Martin for their hard work developing, implementing, and evaluating this system.

Contents

Introduction	1
Problem Statement	1
Research Hypothesis	3
Indiana Network for Patient Care.....	3
Development and Implementation	6
Trigger: Arrival of the Patient.....	6
EMH Process Controls Generation of a Medication History	7
Obtaining the Continuity of Care Document	8
Laboratory Results	9
Medication Hub Obtains Pharmacy Data From Three Sources	10
Medication Hub Translates, Aggregates, and Filters Pharmacy Records	11
Decision Support Service	12
Formatting and Printing a Readable Document	12
Implementation in the Clinic.....	14
Study Design	14
Patient Demographics.....	15
Patient Visits.....	15
Medications	17
Decision Support Reminders.....	19
Decision Support Reminders: Specifications	20
Decision Support Reminders: Overall Counts	22
Category 1 of Decision Support Reminders: Laboratory Monitoring Recommended for Chronic Medication Use	25
Category 2 of Decision Support Reminders: Laboratory Testing for Patients with Diabetes	28
Category 3 of Decision Support Reminders: Abnormal Laboratory Warnings	32
Category 4 of Decision Support Reminders: Drugs to Avoid in the Elderly	34
Category 5 of Decision Support Reminders: Drug-Drug Interactions	36
Chart Review: Comparison with the Paper Charts already in the Clinic	37
Performance Metrics	38
Physician Survey	40
Discussion	42
Lessons Learned.....	43
References	48

Tables

Table 1. Patient demographics.....	15
Table 2. Total number of clinic visits over the course of the 46 week study.	15
Table 3. Distribution of Patients with respect to Number of Visits over the 46 week study time period.	16
Table 4. Time intervals separating the first visit from the last visit	17
Table 5. Top ten most frequently occurring medications, as a percentage of all dispensing events.....	18

Table 6. Annual lab monitoring reminder rates, restricted to ACE-Inhibitors/Angiotensin Receptor Blockers	26
Table 7. Annual lab monitoring reminder rates, restricted to Digoxin.....	26
Table 8. Annual lab monitoring reminder rates, restricted to Diuretics	26
Table 9. Annual lab monitoring reminder rates, restricted to Anticonvulsants.....	26
Table 10. Combined rate of annual lab monitoring for all four above medication groups (ACE-I/ARB, Digoxin, Diuretic, Anticonvulsant).....	26
Table 11. Combined rate of annual lab monitoring for all medication groups (ACE-I/ARB, Digoxin, Diuretic, Anticonvulsant, Statin, Levothyroxine).....	27
Table 12. Parameter estimates from the Generalized Estimating Equations analysis.....	27
Table 13. Reminder rates for Poor Control of HgbA1C (>9.0%).....	30
Table 14. Reminder rates for No HgbA1C testing within 12 months	30
Table 15. Reminder rates for Poor Control of LDL (>=100)	30
Table 16. Reminder rates for No LDL testing within 12 months.....	30
Table 17. Parameter estimates from the Generalized Estimating Equations analysis.....	31
Table 18. Abnormal laboratory warning reminders across all 4449 patients, across all 10498 visits, in sorted order of decreasing frequency	33
Table 19. Parameter estimates from the Generalized Estimating Equations analysis.....	33
Table 20. Reminder rates for elderly patients taking at least one drug from the list of “Drugs to Avoid in the Elderly”	34
Table 21. Reminder rates for elderly patients taking at least two drugs from the list of “Drugs to Avoid in the Elderly”	34
Table 22. Top ten most frequent drugs to avoid in the elderly	35
Table 23. Parameter estimates from the Generalized Estimating Equations analysis.....	35
Table 24. Drug-Drug Interactions (across all patients, all visits)	36
Table 25. Results of written survey, based on 7 (of 9) physician responses.	40

Figures

Figure 1. De-identified sample “Enhanced Medication History”	5
Figure 2. How the EMH software is activated by the arrival of a patient for a clinic visit	6
Figure 3. Overview illustration of the steps taken by EMHP software to generate and print an Enhanced Medication History.....	8
Figure 4. CCD Generator Service queries the INPC Data Repository for laboratory test data, and calls the Medication Hub for medication dispensing records.	9
Figure 5. Distribution of Patients with respect to Number of Visits over the 46 week study time period.	17
Figure 6. Categories of medications, weighted by frequency of dispensing events.	18
Figure 7. Frequency distribution of the number of medications listed on each Enhanced Medication History document.....	19
Figure 8. Categorization of all Decision Support Reminders, in all categories.....	22
Figure 9. Decision support reminders in all categories.....	23
Figure 10. Decision support reminders in the category of annual laboratory monitoring.....	25
Figure 11. Simplified illustration of the implications of the Generalized Estimating Equations analysis.....	28

Figure 12. Decision support reminders in the category of laboratory testing for patients with diabetes.. 29

Figure 13. Decision support reminders in the category of abnormal laboratory warnings..... 32

Introduction

In this Final Report we describe the implementation and evaluation of the Indiana Network for Patient Care (INPC) Enhanced Medication History (EMH). The EMH system was constructed at Indiana University and Regenstrief Institute under AHRQ Contract HHS2902006000131. The goal of this project was to design, develop and evaluate a method of providing INPC medication data to ambulatory primary care practices, with the intent of enhancing health care quality and safety.

Briefly, when a patient arrives for an ambulatory health care visit, the EMH system carries out processes to assemble and print a Medication History for that patient. Although the processes are complex, they occur within seconds, so that the Medication History prints on a printer at the clinic within a few minutes of the patient's arrival there. Typically, the clinic staff take the Medication History from the printer, and place it on the patient's chart before giving that chart to the physician. The physician reviews the chart, and the Medication History, prior to the encounter with the patient. Often, the physician discusses the Medication History with the patient during the encounter, as part of the general process of Medication Reconciliation. See Figure 1 for a sample Medication History.

Problem Statement

Medication Errors and Adverse Drug Events (ADEs) are a major problem across the United States. Several expert bodies have attempted to provide estimates of the national scale of this problem. The Institute of Medicine estimated that at least 1.5 million preventable ADEs occur each year in the United States.¹ The Center for Information Technology Leadership examined the outpatient setting specifically, and estimated more than 8 million outpatient ADEs per year, of which 3 million are preventable.² Injuries due to drugs have important economic consequences. The cost of drug-related morbidity in the United States exceeded \$177 billion in 2000.³ Field and colleagues studied the costs of ADEs among older adults in the outpatient setting, and estimated that the increased costs associated with ADEs and preventable ADEs were \$1310 and \$1983, respectively.⁴

Although outpatient providers could detect and prevent many of these errors, their limited time with patients (in ambulatory settings), their high workload requirements, and the challenge of managing a large volume of dynamic information can affect their ability to do so. Health information technology can be of great value to physicians and other health care providers to aid them in providing patients with high quality health care—but with a lower rate of errors and adverse events.

In order to prescribe medications in a wise manner, clinicians need to know the list of medications that their patients are taking currently, or in the past. However, primary care providers often do not know which medications have been prescribed by other providers, or are actually being taken by the patient.¹ Some patients maintain their own records, and are able to inform their physician of the list of medications they take; but others cannot.

A medication list is widely regarded as an important tool to promote the quality and safety of health care. The National Quality Forum endorses documentation of a medication list in the outpatient record as an important measure of quality.⁵ A computerized medication list can be compared against a problem list and detect potential medication error.⁶ Researchers studying

medication discrepancies concluded that better methods of ensuring an accurate medication history are needed.⁷ In this study, the most common medication discrepancy was omission of a regularly used outpatient medication.

The example of Hurricane Katrina provided evidence that an aggregated medication list is feasible, and is of great utility to clinicians. Pharmacy data was pooled together from retail pharmacies, pharmacy benefit managers, state Medicaid claims, and VA records. Pharmacists and physicians were able to access a medication history, and thus avoid harmful prescription errors and coordinate care.⁸

Having an accurate medication history available at every patient encounter would enable physicians to provide better care in many ways. One of the deficits that could be improved is the incomplete monitoring (laboratory testing) of patients in the ambulatory setting. Some patients who take a medication on a chronic basis do not get regular lab testing as frequently as is recommended by guidelines. For example, in a chart review of 400 patients using levothyroxine, only 56 percent of patients had the minimum recommended monitoring of thyroid levels.⁹ In another study of 99 outpatients taking amiodarone, only 9 patients received all of the recommended monitoring.¹⁰ These researchers concluded that monitoring practices vary significantly, that few patients receive all of the recommended monitoring, and that patient safety might be improved with a better understanding of monitoring processes.

Therefore, we are seeking to develop ways to provide medication information to support physicians working in the outpatient setting. The Indiana Network for Patient Care has medication data from various sources. However, not all outpatient clinicians can benefit from this information, especially in settings which have limited access to electronic health records. Clinicians working in different settings may require different tools to make use of medication history information.

Simply providing clinicians with a patient's medication history could have various benefits, and address various problems. However, we chose to focus on the problems of laboratory monitoring and abnormal laboratory tests—problems which can be closely linked to a patient's chronic use of medications. We envisioned a Medication History that could be enhanced with relevant laboratory test results, and relevant decision support reminders. We hypothesized that such an "Enhanced Medication History" could cause a measurable improvement in health care quality and safety.

More precisely, we sought to provide medication and laboratory information, and measure an effect on quality and safety, while respecting several important constraints:

1. **Paper-based setting.** Many clinicians still work in outpatient settings or community health clinics that have limited access to health information technology, and where paper-based processes predominate. We sought to develop a process that could be useful in such paper-based settings.
2. **Adaptable to electronic health records.** We also sought a process that could readily adapt to modern electronic health record technology. We anticipate that the next few years will see many clinicians making the transition from paper to electronic systems. We needed a process that could serve outpatient clinicians (1) while they use paper and (2) while they use electronic information systems.
3. **Minimize workflow disruption.** It was crucial not to disrupt the existing clinic workflow. We realize that clinicians in the outpatient setting are busy and operate under conditions of

limited time and resources. We needed to develop a process that could provide benefit—while fitting into the existing workflow.

4. **Aggregated from multiple sources.** Information collected from multiple sources can make a patient’s profile more complete than information from a single source. However, different sources store electronic information in different formats. In the Indiana Network for Patient Care, we are working on the challenges of aggregating information from multiple sources and presenting it to clinicians in a unified and coherent format.
5. **Limited categories of information.** Decision support reminders often require knowledge of a patient’s list of diagnoses—a common feature of electronic health records. However, clinicians working in an environment without electronic health records may not have access to an electronic list of diagnoses codes. We focused on those decision support reminders which could be evaluated based on only three categories of information: (1) Medications; (2) Laboratory tests; (3) Age. Such categories of information are more likely to be available in electronic form across clinical settings.

Research Hypothesis

Simply providing Medication Histories to the clinicians working at a community health center is an important intervention, potentially capable of improving health care quality and safety. However, the focus of our research was on providing “**Enhanced**” Medication Histories: lists of medications **supplemented** by laboratory data and decision support reminders. Our objective was to demonstrate that such a project would be feasible, and that it would improve health care quality and safety.

Our research hypothesis was that the number of decision support reminders would decrease over time, because of the intervention of an Enhanced Medication History—which supports the clinician with extra information, previously not available. Reminders, by themselves, are not a negative item: they are simply a restatement of facts. However, the count of reminders can be used as a proxy for the count of negative conditions. Reminders call a clinician’s attention to a problem of health care quality and safety. For a given patient, if the number of problem conditions decreases, the number of reminders decreases. (Of course, this assertion only holds true if reminders are not modified while the study is in progress.) If we can measure a decrease in the count of reminders, between a patient’s earlier clinic visit, and the same patient’s later clinic visit, then we can infer that the quality and safety of that patient’s health care is improving.

Indiana Network for Patient Care

The Indiana Network for Patient Care (INPC) is a community-wide electronic medical record that was developed in the 1990s, and began to operate in 1995.¹¹ The Regenstrief Institute has developed and implemented all of the software and systems that underpin the INPC, and operates the INPC on behalf of its participants. The participants of the INPC include all five of the major hospital and health care systems in Indianapolis, as well as hospitals in surrounding counties. The participants of the INPC also include several large physician practices, two independent commercial laboratories, public health agencies, payors, and the Indiana State Medicaid program. The number of participants grows as new institutions are added.

The INPC stores over 900 million discrete data items, representing more than 6.1 million residents of Indiana and neighboring states. Important categories of data include: laboratory results, radiology, pharmacy, transcription, coded diagnoses and procedures, inpatient and outpatient encounters.

The INPC is a centrally managed, federated clinical data repository. Thus each institution's data is physically located on separate digital storage media. However, this data is managed in a uniform, standardized way by the Regenstrief Medical Record System. Each patient's data is protected in accordance with HIPAA guidelines for privacy and security. Such a uniform, standardized approach allows a physician to view a patient's previous care information from all participating institutions as a single virtual medical record.

Figure 1. De-identified sample "Enhanced Medication History"

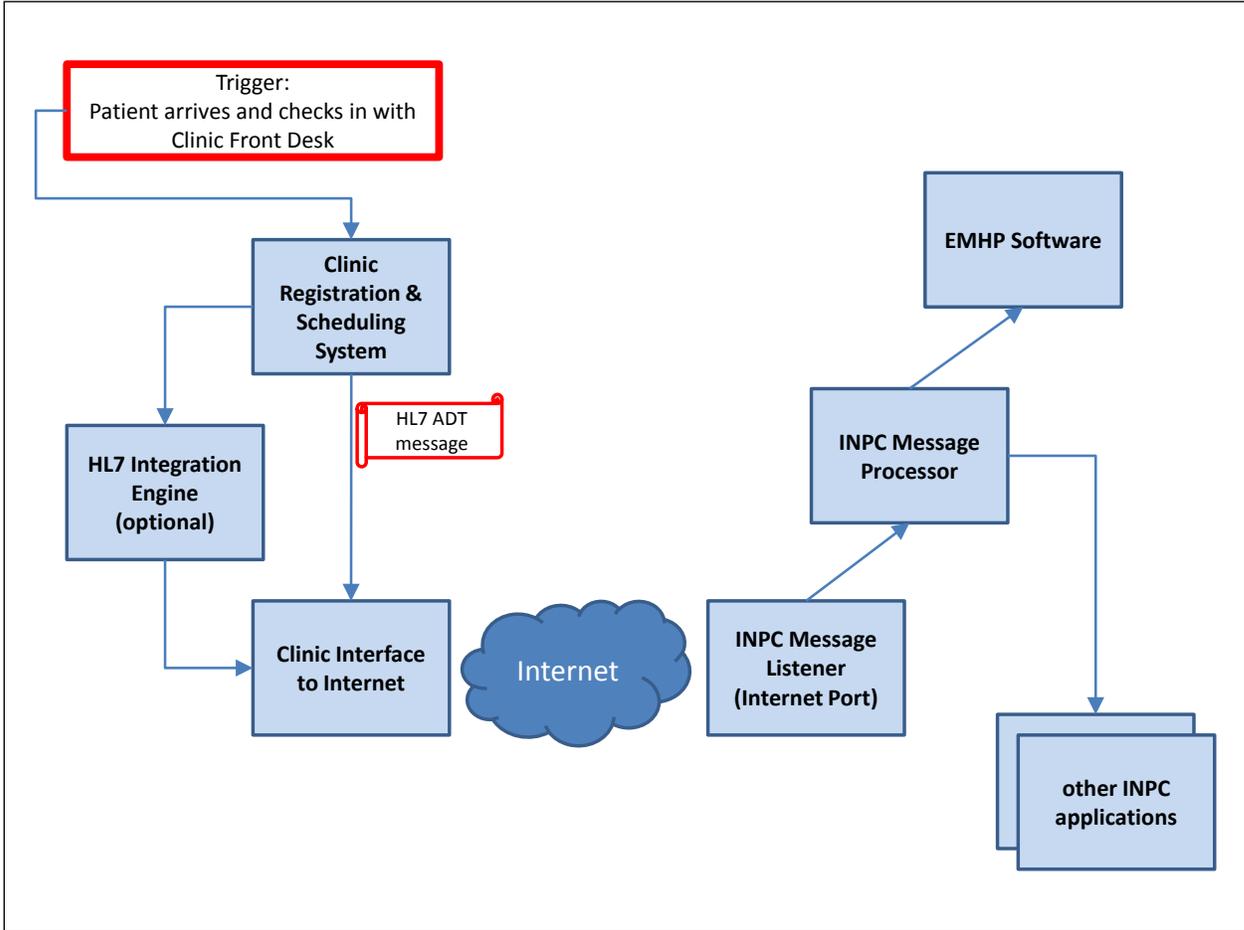
INPC Medication History for: SAMPLEPATIENT, JOHN THE (1234567) for testing purposes						
Enhanced Medication History: June 23, 2009						
Pt: SAMPLEPATIENT, JOHN THE		MR#: 1234567	Gender: M	DOB: 1901-Jan-01		
AMLODIPINE (AMLODIPINE BESYLATE)						
2009-May-07	Amlodipine 10 MG Oral Tablet	\$60	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET BY MOUTH DAILY
2009-Apr-07	Amlodipine 10 MG Oral Tablet	-	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET BY MOUTH DAILY
2009-Mar-16	Amlodipine 10 MG Oral Tablet	\$60	at HALORENS DOWNTOWN	OOOHEALTH, CHARLES		-
2009-Feb-02	Amlodipine 10 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Oct-31	Amlodipine 10 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Jul-31	Amlodipine 10 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
FUROSEMIDE (FUROSEMIDE)						
2009-May-28	Furosemide 20 MG Oral Tablet	\$90	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET BY MOUTH EACH MORNING
2009-Apr-08	Furosemide 20 MG Oral Tablet	\$60	at Primary Care	SPECIALIST, JOE		*sig: TAKE 1 TABLET BY MOUTH EACH MORNING
2009-Jan-18	Furosemide 20 MG Oral Tablet	\$60	at CVS AT THE MALL	OOOHEALTH, CHARLES		-
2008-Nov-06	Furosemide 20 MG Oral Tablet	\$60	at PRIMARY CARE CENTER PHARM	SUROICH,		-
GABAPENTIN (GABAPENTIN)						
2008-Dec-07	Gabapentin 300 MG Oral Capsule	\$90	at Primary Care	COVERING, FRANK		*sig: TAKE 1 CAPSULE BY MOUTH 3 TIMES A DAY
2008-Oct-31	Gabapentin 300 MG Oral Capsule	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH,		-
2008-Oct-01	Gabapentin 300 MG Oral Capsule	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH,		-
GLIPIZIDE SR (GLIPIZIDE XL)						
2009-May-28	Glipizide 10 MG 24 Hour Extended Release Tablet	\$180	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 2 TABLETS BY MOUTH DAILY
2009-Feb-17	Glipizide 10 MG 24 Hour Extended Release Tablet	\$180	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Nov-16	Glipizide 10 MG 24 Hour Extended Release Tablet	\$180	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Aug-12	Glipizide 10 MG 24 Hour Extended Release Tablet	\$180	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
LOSARTAN (COZAAR)						
2009-May-28	Losartan 100 MG Oral Tablet	\$90	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET BY MOUTH DAILY
2009-Apr-23	Losartan 50 MG Oral Tablet	-	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 2 TABLETS BY MOUTH DAILY
2009-Mar-09	Losartan 50 MG Oral Tablet	\$60	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Oct-31	Losartan 50 MG Oral Tablet	\$120	at HALORENS DOWNTOWN	OOOHEALTH, CHARLES		-
2008-Jul-31	Losartan 50 MG Oral Tablet	\$180	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
METOPROLOL (METOPROLOL TARTRATE)						
2009-May-28	Metoprolol 50 MG Oral Tablet	\$270	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 AND 1/2 TABLET BY MOUTH 2 TIMES A DAY
2009-Apr-28	Metoprolol 50 MG Oral Tablet	\$270	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2009-Feb-17	Metoprolol 25 MG Oral Tablet	\$540	at HAL-MART ON MAIN STREET	OOOHEALTH, CHARLES		-
2008-Nov-16	Metoprolol 25 MG Oral Tablet	\$540	at CVS AT THE MALL	OOOHEALTH, CHARLES		-
2008-Aug-12	Metoprolol 25 MG Oral Tablet	\$540	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
NITROGLYCERIN SL (NITROQUICK)						
2008-Oct-01	Nitroglycerin 0.4 MG Sublingual Tablet	\$100	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET UNDER THE TONGUE AS NEEDED FOR CHEST PAIN may repeat 1-2 times
PIOGLITAZONE (ACTOS)						
2009-May-07	Pioglitazone 15 MG Oral Tablet	\$60	at Primary Care	SPECIALIST, JOE		*sig: TAKE 1 TABLET BY MOUTH DAILY
2009-Apr-07	Pioglitazone 15 MG Oral Tablet	\$60	at HALORENS DOWNTOWN	OOOHEALTH, CHARLES		-
2009-Feb-02	Pioglitazone 15 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	COVERING, FRANK		-
2008-Oct-31	Pioglitazone 15 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Jul-31	Pioglitazone 15 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
SIMVASTATIN (SIMVASTATIN)						
Reminder: Recent CK level greater than 500						
2009-Apr-24	Simvastatin 40 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2009-Apr-08	Simvastatin 40 MG Oral Tablet	-	at Primary Care	OOOHEALTH, CHARLES		*sig: TAKE 1 TABLET BY MOUTH EACH EVENING
2009-Jan-18	Simvastatin 40 MG Oral Tablet	\$90	at HAL-MART ON MAIN STREET	OOOHEALTH, CHARLES		-
2008-Oct-31	Simvastatin 40 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
2008-Jul-31	Simvastatin 40 MG Oral Tablet	\$90	at PRIMARY CARE CENTER PHARM	OOOHEALTH, CHARLES		-
Relevant Lab Results Available in the INPC						
2009-Feb-29	ALT SerPl Qn	27.0 UNITS/L	[7-40]			
2009-Feb-29	CK TOTAL	1999.0 UNITS/L	H [30-135]			
2009-Feb-29	Creatinine SerPl Qn	1.2 mg/dL	H [0.5-1.1]			
2009-Feb-19	Hgb A1c Bld Qn IA	6.7 %	H [4.8-6.0]			
2009-Feb-19	LDL Direct SerPl Qn	85.0 mg/dL	[0-99]			
2009-Feb-19	Potassium SerPl Qn	4.6 mmol/L	[3.5-5.5]			
<p><i>This Medication History may be incomplete or inaccurate. The clinician should always discuss and confirm these medications with the patient. For any questions please contact: Linas Simonaitis, MD (lsimonaitis@regenrief.org) (phone: 423-5535 / 423-5500) or Gary Cravens, MD (gcravens@regenrief.org) (phone: 423-5654 / 423-5500)</i></p>						
Printed on June 23, 2009 at 12:18:37 for testing purposes				Page: 1 of 1		

Development and Implementation

Trigger: Arrival of the Patient

In order to generate and print an Enhanced Medication History, the EMH process requires a trigger. The trigger is the arrival of the patient. When a patient arrives at an ambulatory health clinic, he/she stops at the front desk to register. The front desk staff enters the patient's information into the electronic registration system. The front desk staff continues to use the same workflow as always. From their perspective, no new steps are required. However, when they complete the process of registering the patient, they set in motion a complex sequence of software processes that generate the Medication History. (See Figure 2 illustrating the steps taken to activate the EMH software.)

Figure 2. How the EMH software is activated by the arrival of a patient for a clinic visit



The electronic registration system at the clinic creates an HL7 ADT (Admission, Discharge, Transfer) message at the time of a patient's arrival. This HL7 ADT message is sent from the clinic registration system to the INPC over the internet. Although there are various ways to send

such a message, we found it useful to use the Mirth¹² open source HL7 Integration Engine. The Mirth engine examines all messages produced by this clinic's registration system, applies filters to exclude some messages, and then sends the remaining desirable messages over the internet to the INPC server. The Mirth filters exclude children younger than 18, and exclude messages that indicate an event, other than a patient's arrival for an office visit (e.g., a rescheduled appointment, or arrival for a blood test). We used the Mirth engine in order to make things easier for the Information Technology personnel at the clinic, to remove as much of their workload as possible.

The INPC Server receiving this HL7 ADT message is also receiving hundreds of other HL7 messages each minute. The INPC Server runs a Message Processor which decides what to do with each message. The Message Processor examines a few fields in each HL7 message it receives. If these fields match a predetermined listing, the Message Processor simply routes the HL7 ADT message to the EMH software. Other messages are routed to other systems: for example, public health reports, laboratory results, hospital discharge notifications, and many more, all arrive to the INPC concurrently, and need to be routed to the appropriate software system.

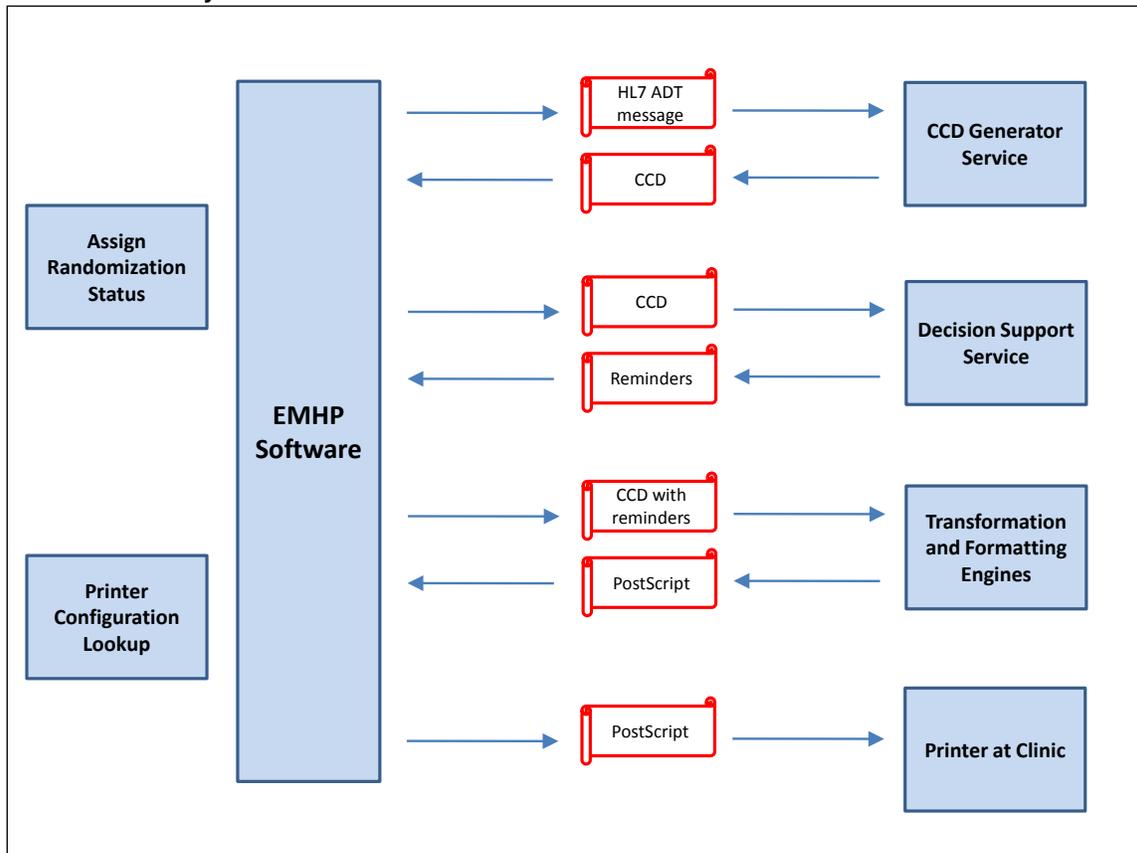
EMH Process Controls Generation of a Medication History

The EMH process (EMHP) is activated by the HL7 ADT message it receives. From this point on, the EMHP takes control. It takes the following steps (each described in more detail below):

1. Obtains a CCD (Continuity of Care Document)
 - a. Populates the CCD with laboratory data
 - b. Populates the CCD with medication data
2. Obtains decision support reminders, and inserts them into the CCD
3. Formats the CCD and prints the Medication History

See Figure 3 for an overview illustration of the steps taken by the EMHP to generate and print an Enhanced Medication History.

Figure 3. Overview illustration of the steps taken by EMHP software to generate and print an Enhanced Medication History



Obtaining the Continuity of Care Document

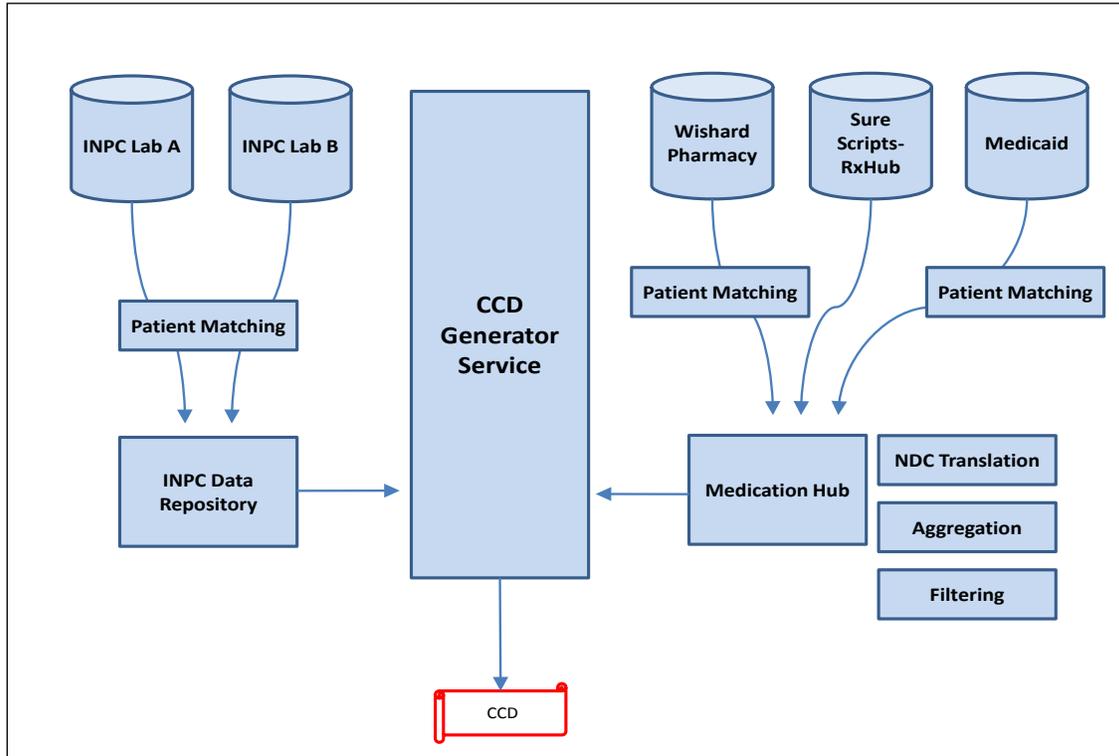
The Continuity of Care Document (CCD) is an HL7 version 3 document, based on the HL7 Reference Information Model. The CCD specification is a standard, developed to allow health care entities to exchange a patient summary clinical document. The CCD standard has been further constrained by the HITSP (Health Information Technology Standards Panel) of the U.S. Department of Health and Human Services. This HITSP construct—commonly referred to as the C32 construct—is the one we used to guide our development of the CCD.¹³

We use the CCD as an “envelope”—a convenient way to store a patient’s demographic, medication, and laboratory information. The EMHP system does not actually exchange the CCD with other institutions. At the end, the EMHP transforms the CCD into a printed document. Nevertheless, it is important to point out that it would be relatively easy for our software to send the CCD electronically to another institution’s Electronic Medical Record.

The EMHP obtains a CCD by calling a CCD Generator Web Service. This is a Web Services interchange. The EMHP sends a SOAP request, which wraps the same HL7 ADT patient arrival message, to the CCD Generator Web Service. The CCD Generator extracts patient demographic information from the HL7 fields, and creates the shell of a CCD with that information. Then the CCD Generator obtains: (1) Laboratory results and (2) Medication histories, and builds the “Laboratory Results” module and the “Medications” module, respectively. The CCD Generator

obtains Laboratory Results by direct query of the INPC database. The CCD Generator obtains Medications by calling the INPC Medication Hub in an HL7 version 2 request/response interchange. See Figure 4 for an overview of how the CCD Generator obtains Laboratory and Medication data.

Figure 4. CCD Generator Service queries the INPC Data Repository for laboratory test data, and calls the Medication Hub for medication dispensing records. Laboratory and medication data is assembled into a CCD, which is returned to the calling application.



Laboratory Results

The CCD Generator connects to the INPC Data Repository and queries it for laboratory results. It does not seek all laboratory results, only the most recent value of each test. For example, a patient may have had blood drawn dozens of times to test the Serum Potassium; but the database query retrieves only the most recent Serum Potassium, whether it was performed days ago, or years ago.

An important feature of the INPC Data Repository is that it stores laboratory test results from multiple institutions. Yet each institution stores its test results using its own medical record system. Therefore, a patient by the name of John Smith may have visited two hospitals in Indianapolis, and have had a Serum Potassium tested at Hospital A, and a Serum Potassium tested at Hospital B. Both Potassium test results are in the INPC Data Repository, but they are stored under different medical record numbers. It may not be immediately obvious that both test results refer to the same John Smith.

The INPC Data Repository relies on a Patient Matching Algorithm to link the different medical record numbers to the same individual. The identifiers from each institution are compared, and if there is a match—i.e., good evidence that two identifiers refer to the same individual—then those identifiers are grouped together. Strong evidence linking two patient records together includes a common medical record number, or social security number. If such a linking identifier is not present, then other evidence is examined: birthdates, names, gender, and geographic address. The algorithm makes adjustments to give stronger weight to matches with uncommon values, and lesser weight to common values. When two patient records contain evidence that they are linked, then the medical record numbers in those patient records are grouped together, to make subsequent queries easier.

This Patient Matching Algorithm is invoked to search through the laboratory test results maintained by all INPC institutions. For each laboratory test, the most recent result is obtained, even though some lab results may be provided by one health system, other lab results may be provided by another health system. All laboratory test results are placed into the CCD.

Medication Hub Obtains Pharmacy Data From Three Sources

The CCD Generator obtains Medications by calling the INPC Medication Hub.¹⁴ In its turn, the Medication Hub calls three other systems to obtain Medication History data:

1. Wishard Pharmacy
2. SureScripts-RxHub
3. Indiana State Medicaid

Wishard Pharmacy is the multisite outpatient pharmacy of Wishard Health Services, which serves the disadvantaged population of Marion County in Indiana. Wishard Pharmacy sends a record of every medication that it dispenses to the INPC repository. The Medication Hub sends an HL7 version 2 request to the INPC repository to obtain Wishard Pharmacy data. The Medication Hub then receives an HL7 version 2 response, with a record of all medications dispensed for that patient by the Wishard Pharmacy in the last 13 months.

This transaction assumes that each patient has a Wishard MRN (Medical Record Number); without it, the Wishard Pharmacy is not able to return any medication history. But a Wishard MRN is not present in the HL7 ADT messages originating from a non-Wishard ambulatory clinic. If the HL7 ADT message does not contain a Wishard MRN, then the Patient Matching Algorithm (described above) is invoked by means of a lookup service. In some cases, a matching Wishard MRN is found for that patient; if so, this Wishard MRN is used in the request to Wishard Pharmacy.

SureScripts-RxHub¹⁵ (now renamed simply SureScripts) was founded by the merger in 2008 of two separate organizations: SureScripts and RxHub. SureScripts had been keeping records of all pharmacy sales transactions in the United States; RxHub had been a consortium of Pharmacy Benefit Managers. We query SureScripts for its pharmacy claims records. The Medication Hub sends a request to the MEDS interface of SureScripts-RxHub. This request does not need to contain any specific medical record number. The identifiers required by SureScripts-RxHub are as follows:

- last name, first name
- date of birth
- gender
- home ZIP code

SureScripts-RxHub will not release any medication history data unless all four of these data fields match.

Finally, the Medication Hub sends a request for medication histories to a third source: Indiana State Medicaid. Indiana State Medicaid data is stored in the INPC repository, and is accessible by a Web services request. Note that Medicaid is not routinely available for all users; however, Medicaid granted special permission for use of its data in this research project. Medicaid stores pharmacy claims for each patient in its databases; however, that data is indexed by a Medicaid identifier, unique for each patient. This Medicaid identifier must be looked up using the same Patient Matching Algorithm as required for the Wishard Pharmacy look-up, and for the Laboratory Results query across INPC institutions.

Some data sources are more current than others. The Wishard pharmacy can provide medication history data the same day that a drug was dispensed. Likewise, the pharmacy claims available through Sure-Scripts RxHub are usually current within a day. On the other hand, our version of the Medicaid database is updated less frequently, only about once a month. Therefore, a patient's medications might not be available in the Medicaid database, even if they were dispensed several weeks previously.

Medication Hub Translates, Aggregates, and Filters Pharmacy Records

Pharmacy records are coded. There is one drug coding system that is ubiquitous in the United States: the FDA National Drug Code (NDC) system. Almost all pharmacy records contain this NDC identifier. Unfortunately, the disadvantage of the NDC is that it is not designed for clinical use. For example, we found at least 227 different NDCs that refer to Amoxicillin 500mg capsules. Each manufacturer, distributor, and repackager uses a different NDC for the same clinical product. Yet the differences in these NDCs are irrelevant, and even detrimental, for most clinical applications.

Therefore, the Medication Hub translates the NDC in each pharmacy record to a common clinical code. The primary clinical code used is the Regenstrief Medical Record System (RMRS) Dictionary Drug Term. The secondary clinical code used is the RxNorm Clinical Drug Code. The Medication Hub was originally designed for use with other Regenstrief Institute applications which use the RMRS Dictionary Drug Term. The RMRS Dictionary Drug Terms are intended to represent medications in the way clinicians order and prescribe medications, and are modified based on feedback from clinicians. For example, there is one RMRS Dictionary Drug Term to represent oral Amoxicillin (as opposed to hundreds of NDCs). The translated clinical code is inserted into the record for that dispensing event.

The Medication Hub groups dispensing records together if they share the same RMRS Dictionary Drug Term. For example, a patient might have been dispensed Amoxicillin on two different dates. On the first date, the pharmacy used one NDC for Amoxicillin; on the second

date, the pharmacy used a different NDC for Amoxicillin. Both of these dispensing events will be grouped together in the Medication Hub output.

The Medication Hub filters out any medication records that are older than 13 months old. We established this cutoff, in order to provide an adequate window on a patient's medication history, but to avoid cluttering medication histories with old data that is no longer relevant. Nevertheless, the 13 month cut-off is configurable and can be changed.

After the Medication Hub retrieves, translates, aggregates, and filters the pharmacy records, it returns them in an HL7 response to the CCD Generator. The CCD Generator populates the CCD "Medications" Module with this medication data, just as the CCD Generator populated the CCD "Laboratory Results" Module with laboratory data.

Decision Support Service

The EMHP software then calls a Decision Support Service. The Decision Support Service parses the CCD to extract "facts" (i.e., data in the CCD which may be used to evaluate a decision support rule). The list of "facts" which we use to evaluate decision support rules is not extensive:

1. Age of patient
2. List of all dispensing events. For each dispensing event:
 - a. Drug dispensed
 - b. Date dispensed
3. List of all laboratory values. For each laboratory value:
 - a. Lab test
 - b. Lab value
 - c. Date tested

These "facts" are then passes to an instance of the Drools Decision Support Engine.¹⁶ Drools is an open-source engine developed by the JBoss community (best known for the development and support of RedHat Linux). Drools is written in Java, integrates easily with our Eclipse development environment, and offers a convenient user interface.

The Decision Support Service evaluates the rules and generates a list of reminders for each patient. Each reminder is indexed by a medication. Therefore, the EMH software can insert each reminder into the CCD document, as a child element of its medication element. Afterwards, when the Medication History is printed, the clinician can view each reminder located immediately adjacent to its associated medication.

Formatting and Printing a Readable Document

The processes described above generate a CCD for each patient visit; the CCD contains medications, lab test results, and decision support reminders. However, the CCD is an XML file, and is almost unreadable by human eyes. Therefore, the controlling EMHP software formats the XML to produce a readable document.

The EMHP software calls the Saxon (version 9) XSL Transformation Engine (free and open source, available through <http://saxon.sourceforge.net>) and the Apache FOP (version 0.94) Formatting Engine (free and open source, available through <http://xmlgraphics.apache.org/fop/>).

The Saxon Transformation Engine applies an XSLT stylesheet to the CCD document to generate a tree of formatting objects; the Apache FOP Formatting Engine converts this tree into a PostScript document.

Depending on the patient's randomization status, one XSLT stylesheet is used for Control patients, and another XSLT stylesheet is used for Intervention patients. The Control stylesheet creates a PostScript document without any medications, labs, or reminders. Its only usefulness is to reassure the clinic personnel that the patient visit was processed and that no failures occurred.

The Intervention stylesheet is more complex, because it produces a readable medication history. All dispensing records are grouped by RMRS Dictionary Drug Term, and then alphabetized by the name of that drug term. If any reminders exist, these are displayed underneath the drug name. For each grouping (i.e., for each drug name), the dispensing events themselves are sorted in reverse chronological order. Each dispensing event includes the following fields (not all fields are always available):

- Date dispensed
- RxNorm Clinical Drug name
- Quantity dispensed
- Pharmacy where dispensed
- Prescriber name
- Instructions (“SIG”) for how to take the drug

Refer back to Figure for a de-identified sample illustration.

The PostScript document is readable—when it is sent to a printer and printed. The above steps have described how each patient visit triggers creation of a PostScript document. Intervention patients have a document listing medications. Control patients have a document without medications. Nevertheless, all patients have a document which must now be printed.

The EMHP software accomplishes printing by calling a standard Java “print” routine. The most difficult aspect of printing is specifying which printer should be invoked. The EMHP software is designed to be scalable, and must be able to print to different printers at different remote locations and in different health care system. We constructed a printer configuration look-up table to store the name of which printer to use. The EMHP software extracts the clinic identifier and the visit location from each arrival message, and uses the composite key to look up the name of the printer to use.

Implementation in the Clinic

The Enhanced Medication Histories became operational at a community health clinic in Indianapolis in December, 2008. Originally the Histories were delivered to one site; a second site for the same community health clinic network was added in March, 2009. Histories were delivered with the intent of an evaluation period of 1 year (52 weeks). However, 46 weeks into the project (October 2009) the project had to be stopped. Why? The community health clinic switched to a completely different electronic registration system. The new registration system was no longer able to send registration messages to the INPC to trigger the creation of Medication Histories. Although it may be possible for the new registration system to undergo the modifications needed to send registration messages in the future, implementing such a change would have required development work which could not be completed for several more months. Therefore, we considered the research study completed at the time the registration messages stopped, even though the project could not run for the full 52 weeks.

Study Design

In order to evaluate the primary research hypothesis, we needed a randomized controlled trial. Our primary hypothesis was as follows: This intervention (the Enhanced Medication History) would lead to a measurable effect on quality and safety. Our proxy measurement of quality and safety is the count of reminders. This proxy is only valid, if the reminder rules do not undergo modification over the course of the study. (We did not modify them.) Therefore, we hypothesized that the count of reminders would slowly decrease with the passage of time, as patients returned for follow-up visits and their care improved. On an initial visit, we would expect patients to have more problems of quality and safety—and more reminders on their medication history. On a subsequent visit, we would expect patients to have fewer problems of quality and safety—and fewer reminders on their medication history.

In order to test this hypothesis, we needed to assign some patients to intervention status, and other patients to control status. Intervention patients had an Enhanced Medication History printed, and given to the physician, at the time they arrived for each clinic visit. Control patients had a sheet printed, which included the patient's name, but did not include any medications—only a note that this is a control patient. Randomization status was assigned for each new patient (new to the study, not necessarily new to the clinic). As that patient returned for follow-up visits, his or her randomization status was maintained. Intervention patients continued to have Enhanced Medication Histories printed; control patients continued to have uninformative sheets printed.

If statistical analysis had been our only consideration, we would have chosen a randomization ratio of 50 percent intervention, and 50 percent control, in order to maximize the statistical power. However, in a real clinical setting, we needed to contend with other considerations. The physicians in this clinic were hoping to receive as much information as possible. It was unacceptable for them to receive a medication history only 50 percent of the time, and to receive an uninformative piece of paper the other 50 percent of the time. An 80 percent: 20 percent ratio was the best practical compromise. Medication Histories were provided for the majority of patients, allowing them to be used practically in the clinic workflow. But a 20

percent assignment of patients to control status still allowed statistical tests to be performed, in order to measure whether patients in the Intervention group had any demonstrable benefit.

As stated above, the duration of the intervention had to be stopped at 46 weeks. We hypothesized that—even within such a short time interval—there would be sufficient numbers of patients who came to the clinic on two separate occasions. We needed to evaluate a patient’s first visit, and a patient’s last visit, in order to answer the question of whether any benefit can be demonstrated over time. Those patients who only had one clinic visit over the course of the 46 week study period could contribute valuable baseline data. However, they could not contribute data to demonstrate a change over time. Therefore, they were excluded. Statistical analysis (see below) was limited to those patients with at least a first visit and a subsequent visit.

Patient Demographics

Medication Histories were generated for a total of 4449 distinct patients. However, in order to permit a randomized controlled trial, 80 percent of patients were randomized to an Intervention status, and 20 percent of patients were randomized to a Control status. Randomization status was assigned at the time of the first visit, and was maintained for each patient who returned for subsequent visits. See Table 1 for exact description of participating patients. Intervention and Control groups appear comparable with respect to age and gender.

Table 1. Patient demographics.

	Intervention	Control	Total
Number of patients	3556 (79.9%)	893 (20.1%)	4449 (100%)
Age (years)	42.1 ±16.3	42.0 ±16.8	42.1 ±16.4
% Female	72.9% (n=2594)	70.1% (n=626)	72.4% (3220)

Patient Visits

The proper unit of analysis was the patient visit, because a new Enhanced Medication History was created for each visit. A total of 10498 visits were analyzed. (See Table 2.) Some patients had only one visit over the course of the 46 week study. Other patients returned a second time, or more, over the 46 weeks. (See Table 3).

Table 2. Total number of clinic visits over the course of the 46 week study.

	Intervention	Control	Total
Number of visits	8369 (79.9%)	2129 (20.3%)	10498 (100%)

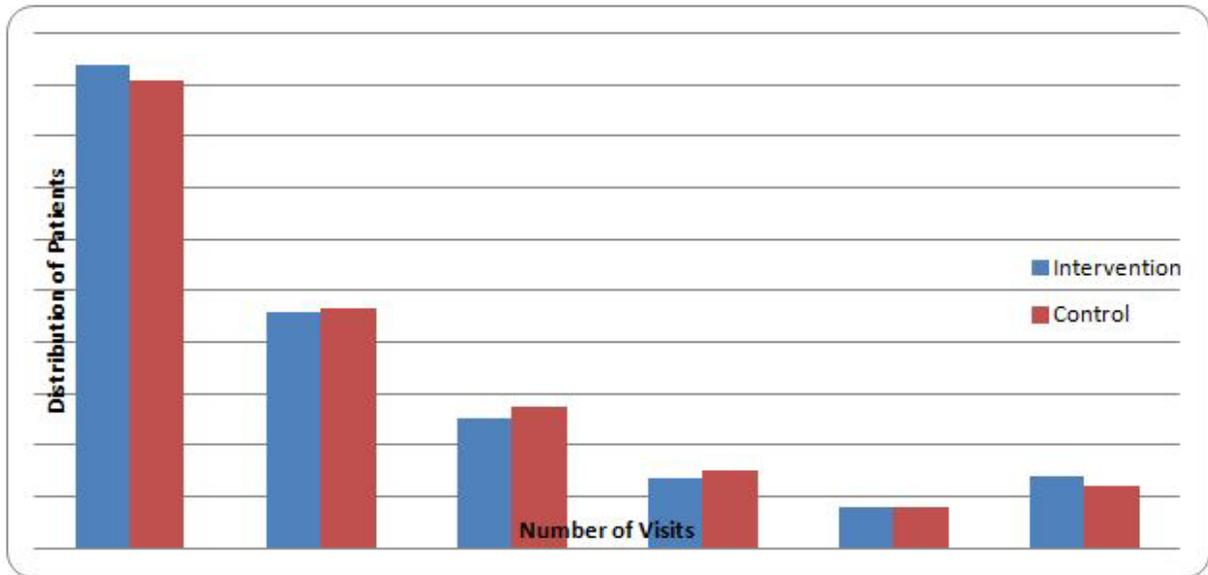
Table 3. Distribution of Patients with respect to Number of Visits over the 46 week study time period. Most of the subsequent analysis is limited to those patients with 2 or more visits: the row with asterisks.

Number of patients...	Intervention	Control	Total
...with 1 visit	1669	405	2074
percentage	(46.9%)	(45.4%)	(46.6%)
...with 2 visits	818	207	1025
percentage	(23.0%)	(23.2%)	(23.0%)
...with 3 visits	444	123	567
percentage	(12.5%)	(13.8%)	(12.7%)
...with 4 visits	237	68	305
percentage	(6.7%)	(7.6%)	(6.9%)
...with 5 visits	141	35	176
percentage	(4.0%)	(3.9%)	(4.0%)
...with 6 or more visits	247	55	302
percentage	(6.9%)	(6.1%)	(6.8%)
...with 2 or more visits*	1887*	488*	2375*
percentage	(53.1%)	(54.6%)	(53.4%)
...with any visits	3559	893	4449
percentage	(100%)	(100%)	(100%)

This study focused on those patients who had a return visit: who had two or more visits over the course of the 46 week study. The essential research hypothesis was that the number of reminders (the number of indicators of low quality) would decrease over time. In order to observe any change over time, at least two visits were necessary. Although patients with only one visit might benefit from the intervention (the Enhanced Medication History) and could provide useful baseline data, they could not contribute data which might indicate a downward trend. Therefore, as will be seen later in this report, the analysis of many of the reminders will be limited to those 2375 patients who had two or more visits. (Note the row with asterisks in Table 3.)

A large group of patients—more than half—had multiple visits over the 46 week study, which substantiates the idea that these patients in these clinics represent a good population for observing a trend over time. See Figure 5 for the distribution of patients with respect to number of visits. The intervention and control groups appear similar in this distribution.

Figure 5. Distribution of Patients with respect to Number of Visits over the 46 week study time period. More than half of patients returned for a second visit.



Because the objective of this study was to observe a trend over time, an important factor is the time interval between a patient’s first visit, and the same patient’s last visit. The longer this time interval, the more likely it is that an intervention targeting preventive care or chronic conditions would have a measurable impact. During this study, we observed a median time interval of greater than 3 months. (See Table 4.) Calculation of a median time interval excludes those patients who simply had one visit.

Table 4. Time intervals separating the first visit from the last visit

Separation between First and Last Visit	Intervention	Control	Total
Median (months)	3.25	3.28	3.25
Average (months)	3.58	3.64	3.60

Medications

The Medication History was a document listing all dispensing events during the previous 13 months. Whether or not it was printed (depending on randomization status) such a document was created for all patients. However, simply listing all dispensing events without any categorization or sorting would have led to a chaotic and unhelpful display. Therefore, all dispensing events were translated to a corresponding code. The Indiana Network for Patient Care relies on the Regenstrief Institute’s Terminology Dictionary to code medical concepts: not only medications, but also diseases, tests, procedures. Therefore, all dispensing events were grouped according to their corresponding Dictionary Term, and sorted alphabetically.

A total of 55901 dispensing events were processed over the course of this study. For each of those dispensing events, the National Drug Code (NDC) was translated to a Dictionary Term; 803 unique Terms were used. See Table 5 for a listing of the 10 most frequently occurring medications.

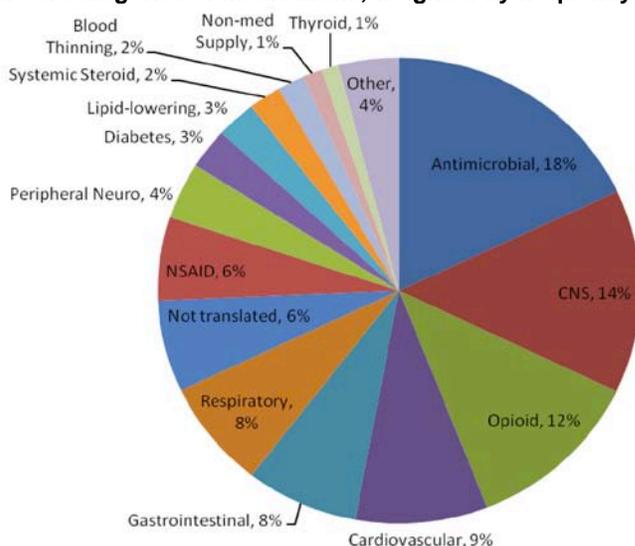
Table 5. Top ten most frequently occurring medications, as a percentage of all dispensing events

Drug Term	Frequency
Not-translated drug order	2600 (4.6%)
Hydrocodone 5/Acetaminophen 500	2394 (4.3%)
Ibuprofen	1337 (2.4%)
Albuterol HFA Inhaler	931 (1.7%)
Lisinopril	908 (1.6%)
Cephalexin	854 (1.5%)
Amoxicillin	839 (1.5%)
Cyclobenzaprine	812 (1.5%)
Prednisone	755 (1.4%)
Naproxen	752 (1.3%)
Sum of all 803 Drug Terms	55901 (100.0%)

The most common term, “Not-translated drug order”, represents those Dispensing Events (4.6 percent of the total) for which the NDC could not be translated to a Dictionary Drug Term. Unfortunately, such medications could not be processed by the Decision Support Engine. (All rules used by the Decision Support Engine rely on Regenstrief Dictionary Terms.) It is possible that some of those medications were eligible for decision support reminders; but without a successful translation to a specific Dictionary Term, no reminder could be generated. The converse is reassuring: more than 95 percent of medications could be successfully translated to Dictionary Terms, and could be used as data for the Decision Support Engine.

In an analysis limited to the top 100 most frequently occurring medications, drug categories were assigned to each medication. The distribution of drug categories may be seen in Figure 6. Note that this distribution has limited validity, because it is based on only 100 medications, and because some medications could be assigned to multiple categories. However, it is adequate to represent the diversity of medications used in the outpatient clinics, and to indicate the relative importance of some medications (especially antimicrobials and opioids).

Figure 6. Categories of medications, weighted by frequency of dispensing events.

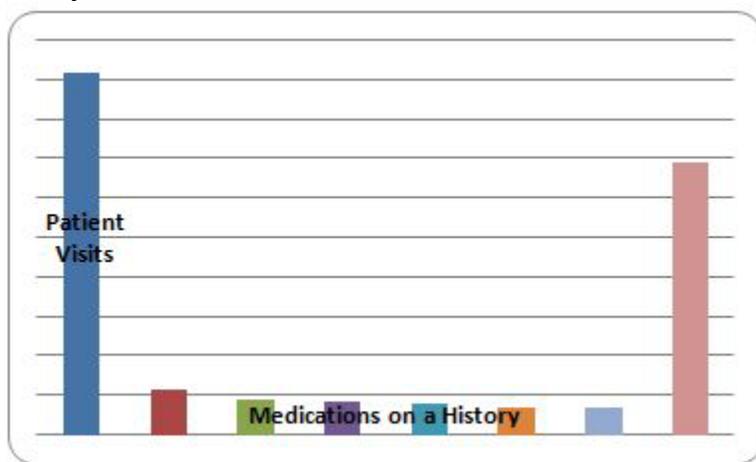


Note: Analysis is limited to the 100 most frequent medications.

The number of medications on each Medication History varied greatly. When analyzing all 10498 patient visits, no medications were reported on 44 percent of the Medication Histories. (See Figure) Such a large number of Histories without medications may reflect clinical reality: not all patients take medications. But it may also reflect the fact that our data sources were incomplete, and limited to Medicaid, SureScripts claims, and Wishard Health Services. Unfortunately, it weakens the analysis of clinical reminders; each reminder is linked to a medication: if no medication is available, then no reminder is generated.

The remaining 56 percent of Medication Histories had at least medication, but—as the histogram in Figure 7 shows—the number of medications varied: there was no preponderance of Histories with only one medication. While 5 percent of Histories had one medication, 3 percent of Histories had six medications, and the frequency distribution remained broad.

Figure 7. Frequency distribution of the number of medications listed on each Enhanced Medication History document



Decision Support Reminders

In order to provide added value, a Decision Support Engine was incorporated into the Enhanced Medication History Process. During the creation of each Medication History, the Decision Support Engine examined each medication to determine whether any rules were applicable to it. If so, a Decision Support Reminder was generated. Each reminder was attached to a specific medication, and was printed under the name of that medication. In other words, there were no reminders of a general nature.

A central focus of this research study was to examine what kind of Decision Support Reminders could be provided for a patient, based on only a few selected categories of data for that patient. Computerized information systems typically have access to coded data in some categories, but do not have access to other valuable information, such as that hidden in dictated progress notes. Some categories of coded data which are widely available for many patients in central Indiana are—

- Patient demographics
- Laboratory tests
- Medication dispensing records

On the other hand, only a few academic medical centers and integrated health systems manage the detailed diagnosis lists and visit notes that can be generated from Computerized Provider Order Entry applications. Wishard Health Services (the primary teaching hospital for Indiana University School of Medicine) is an example of one such academic medical center that can generate decision support reminders based on fairly complete information about patients, including diagnoses. However, beyond Wishard Health Services, many other inpatient and outpatient care settings in Indiana, and in the rest of the country, do not have such complete information. Therefore, our goal was to examine what decision support could be provided using only limited categories of data (demographics, laboratory tests, and dispensing records) without relying on other popular categories of data (especially diagnoses). We believe that such research could have broader generalizability to outpatient care settings beyond the large medical centers.

Decision Support Rules are difficult to write in the absence of knowledge of a patient's diagnoses. For example, rules to monitor the use of inhaled corticosteroids in asthma require the computer to know that a patient has asthma. Rules to monitor the use of beta blockers after myocardial infarct require the computer to know that a patient has a myocardial infarct. The range of Decision Support rules is decreased, when diagnosis information is not reliably available.

Nevertheless, some useful categories of Decision Support remain possible, even in the absence of diagnostic information. One such category is the recommendation for annual laboratory monitoring for those patients taking medications in a few select groups, as defined by the National Committee for Quality Assurance (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS) specifications.¹⁷ This requires only knowledge about (1) medications; and (2) dates of the most recent laboratory tests.

A second category is the diabetes guidelines, also specified by NCQA HEDIS. At first glance, it would appear that diabetes guidelines require knowledge that a patient has the diagnosis of diabetes. However, even the HEDIS guidelines allow for patients who may not have a diagnosis of diabetes, but who are taking diabetes medications, to be included in the denominator. Therefore it is possible to define some quality measures, relying only on knowledge about (1) diabetes medications and (2) laboratory tests.

A third category is abnormal laboratory warnings. These rely on knowledge of (1) medications and (2) values of the most recent laboratory tests. A fourth category is that of drugs to avoid in the elderly, based on HEDIS guidelines on which medications are not appropriate in elderly patients. The only data necessary to evaluate such rules are (1) patient's age and (2) medications. A fifth category is that of Drug-Drug Interactions. The only data necessary to evaluate such rules are knowledge of (1) medications.

Decision Support Reminders: Specifications

Category 1. Annual Lab Monitoring for Patients on Persistent Medications

If a patient has had a medication in the following groups dispensed recently (defined as 6 months), and if one of the following laboratory tests has not been performed (within the past 12 months), then a reminder is printed. Following is the medication group and the laboratory test.

- Digoxin—Potassium or Creatinine
- ACE-I / ARB—Potassium or Creatinine

- Diuretic—Potassium or Creatinine
- Anticonvulsant—serum drug level
- Levothyroxine—TSH
- Statin—LDL

Category 2. Lab Testing for Patients with Diabetes

If a patient has diabetes (defined as a diabetes medication dispensed within the past 6 months) and has one of the following lab conditions, then a reminder is printed. Note that Metformin use is not sufficient to diagnose diabetes, because of the risk of falsely including patients using Metformin for other illnesses. Note that only patients within the age range of 18 to 75 are included, as per the HEDIS guidelines.

- Diabetes—HgbA1C: no test within the past 12 months
- Diabetes—poor control of HgbA1C (>9.0)
- Diabetes—LDL: no test within the past 12 months
- Diabetes—poor control of LDL (≥ 100)

Category 3. Abnormal Laboratory Warnings

If a patient has one of the following abnormal laboratory conditions (based on the most recent test available within the past 12 months) and has one of the following medications dispensed within the past 6 months, then a reminder is printed. Following is the laboratory test and the medication group.

- High Potassium (>5.5)—ACE-I or ARB
- High Potassium (>5.5)—Potassium-sparing diuretic
- High Potassium (>5.5)—Potassium supplement
- Low Potassium (<3.5)—Digoxin
- Low Potassium (<3.0)—Potassium-wasting diuretic
- High Creatinine (>1.4)—Metformin
- High Creatinine (>2.0)—NSAID
- High SGPT (>150)—Statin, Fibrate, Glitazone, Nefazadone, Niacin
- High CK (>500)—Statin, Fibrate
- High TSH (>6)—Levothyroxine
- Low TSH (<0.3)—Levothyroxine

Category 4. Drugs To Be Avoided in the Elderly

- Patients (>65 years in age) who were dispensed (within the past 6 months) one medication from the HEDIS list of Drugs to be Avoided in the Elderly
- Patients (>65 years in age) who were dispensed (within the past 6 months) two (or more) medications from the HEDIS list of Drugs to be Avoided in the Elderly

Category 5. Drug-Drug Interactions

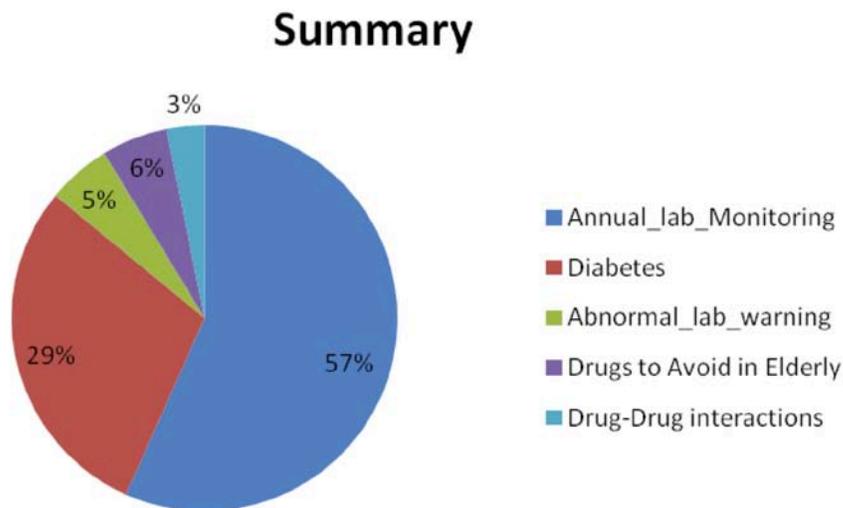
Patients with a Drug-Drug Interaction (from the table of Drug-Drug Interactions), where: the first drug was dispensed within the past 6 months; the second drug was dispensed within the past

6 months; and both drugs were dispensed within 3 months of each other. The table of Drug-Drug Interactions is derived from the Regenstrief Gopher CPOE system knowledge base, but is limited to only the interactions of highest clinical significance. Thus 693 separate Drug-Drug Interactions are listed.

Decision Support Reminders: Overall Counts

Taking the total over all 4449 patients, for all 10498 visits, 2934 Reminders were generated over the course of the 46-week study period. These Reminders can be categorized as follows. (See Figure 8)

Figure 8. Categorization of all Decision Support Reminders, in all categories

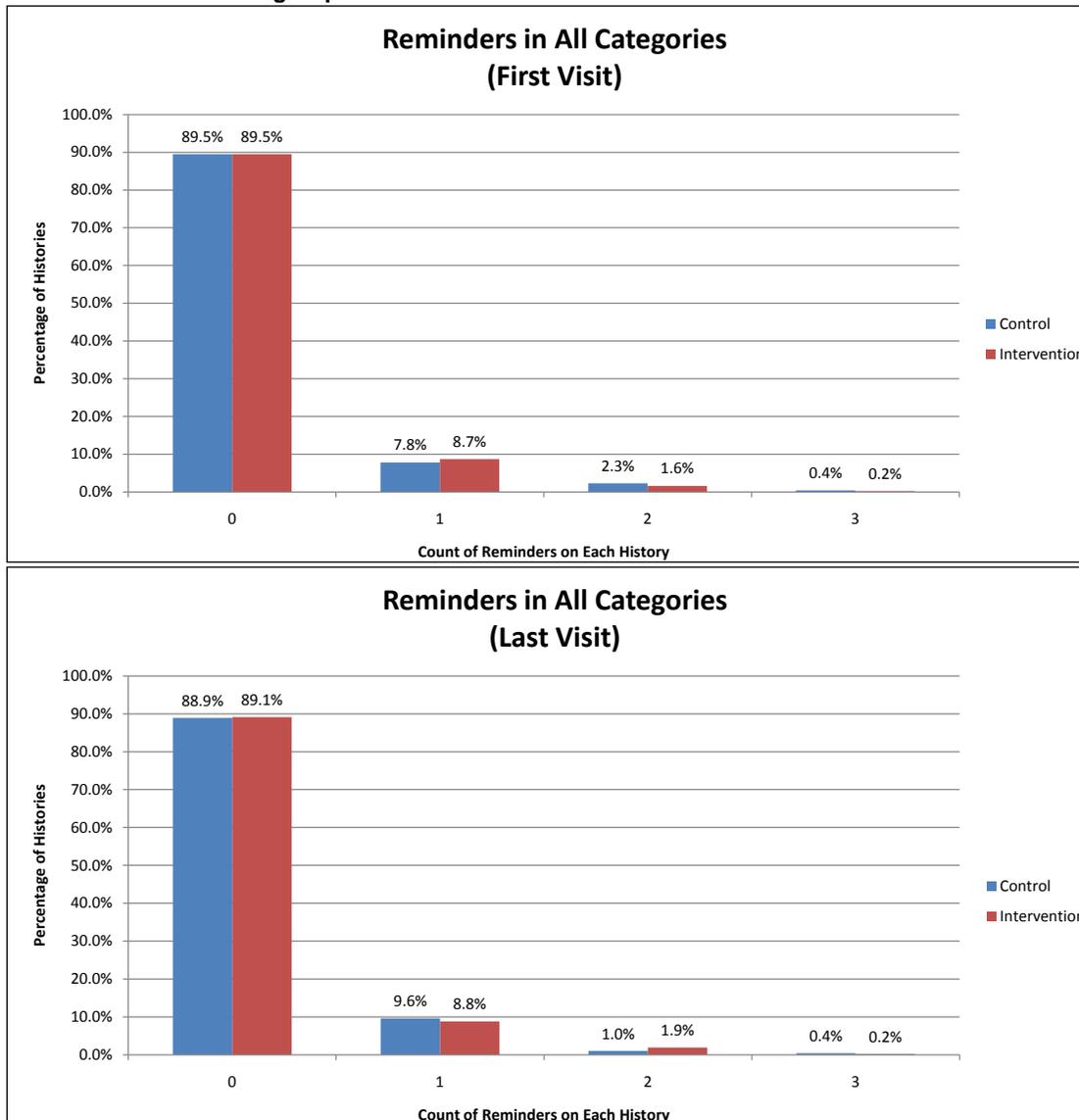


The categorization is slightly unexpected, because we expected roughly similar counts of reminders to be generated in each of the five broad categories. In particular, the number of Drug-Drug Interactions is not large; whereas in the academic medical center Gopher CPOE system, Drug-Drug Interactions are a common source of decision support reminders.

We examined the occurrence of these reminders on a per-patient basis. Taking all patients, the average number of reminders per patient was 0.66, and the median number of reminders per patient was 0. Excluding those patients with zero reminders (many of which had histories with no medications), the average number of reminders per patient was 5.35, and the median number of reminders per patient was 3.

Next, we examined the occurrence of these reminders on a per-visit basis. Our analysis was limited to those 2375 patients (1887 in the intervention group, 488 in the control group) with 2 or more visits. We were most interested in patients with more than one visit, because our objective was to search for a trend over time. Breaking down by First Visit vs. Last Visit, breaking down by Control vs. Intervention, across all categories of reminders, the reminders are distributed as follows (see Figure 9)

Figure 9. Decision Support Reminders in all categories. Breakdown by First Visit vs. Last Visit; and by Control vs. Intervention groups



Even though the above analysis takes all categories of reminders, some general observations are possible:

- Control and Intervention groups are similar at baseline, which is desirable for scientific studies.
- Control and Intervention groups are similar at the last visit, which implies lack of an observable treatment effect.
- Frequency distributions are similar for the First Visit, and for the Last Visit, which implies absence of a change over time.
- About 89 percent of visits do not generate a reminder. Reminders are printed in the remaining 11 percent of visits.
- When a reminder is printed, usually there is only one reminder per Medication History.

Making such broad observations has limited validity, because reminders in all categories are grouped together. It is possible that a treatment effect with one category of reminder (e.g., Drugs to Avoid in the Elderly) is diluted by lack of a treatment effect with another category of reminder (e.g., Drug-Drug Interactions). Nevertheless, the overall counts of reminders are smaller than anticipated.

All of the reminders are generated for conditions where quality or safety are problematic, and could be improved. Therefore, reminders are a proxy for a negative condition. Counting reminders is a convenient way to count the number of negative conditions (e.g., the number of patients taking Digoxin with abnormally low Potassium lab values). Our hypothesis is that with a good intervention (the Enhanced Medication History), the reminders should decrease over time, because the negative conditions should decrease over time. However, this hypothesis is only reasonable when examining each category of reminder separately.

The core of this research study is the subgroup analysis. Instead of asking the broader question, “Does the intervention improve all categories of health care quality and safety”, we ask five more specific questions:

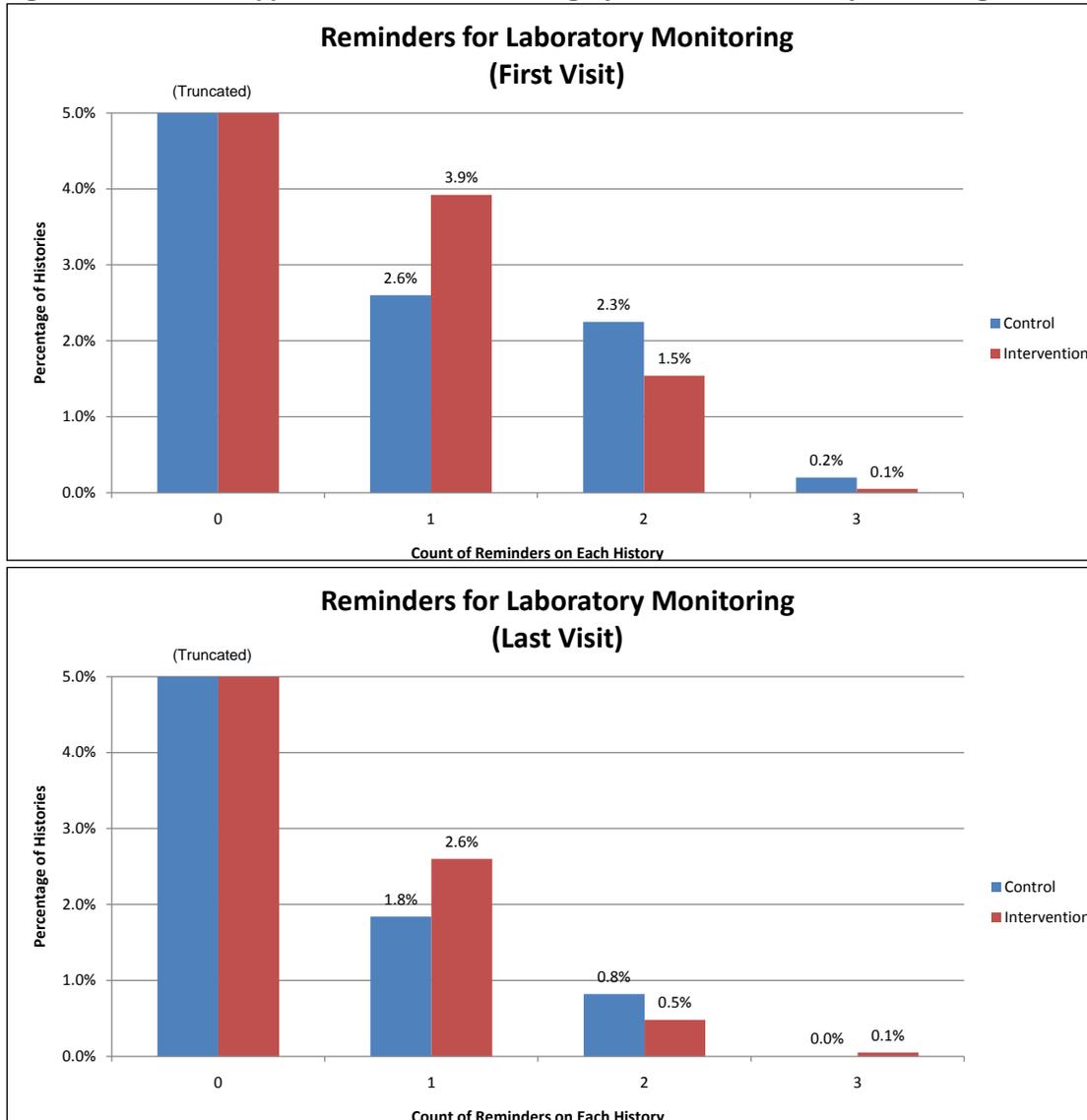
1. Does the intervention improve laboratory monitoring recommended for chronic medication use?
2. Does the intervention improve diabetes care?
3. Does the intervention decrease the use of drugs in the presence of abnormal labs?
4. Does the intervention decrease the drugs to be avoided in the elderly?
5. Does the intervention decrease drug-drug interactions?

The following analyses are limited to those 2375 patients (1887 in the intervention group, 488 in the control group) with 2 or more visits.

Category 1 of Decision Support Reminders: Laboratory Monitoring Recommended for Chronic Medication Use

First, let us view the distribution of all reminders in this category. (See Figure 10.)

Figure 10. Decision Support Reminders in the category of Annual Laboratory Monitoring.



Note: Analysis of 1887 Intervention patients and 488 Control patients. The top graph shows the distribution of reminders during the first visit for each patient. The bottom graph shows the distribution of reminders during the last visit for each patient. The percentage of histories with zero reminders has been truncated in order to fit on the display.

As seen in Figure 10 there does not seem to be any overall difference between intervention and control at first visit, which is desirable in a scientific comparison. However, there does not seem to be any difference at last visit, which suggests lack of a treatment effect. But this is merely a visual impression.

Next, we break down the reminders in the category of Recommended Laboratory Monitoring into individual medication groups (see Table 6 through Table 11).

Table 6. Annual Lab Monitoring reminder rates, restricted to ACE-Inhibitors/Angiotensin Receptor Blockers

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	49	59	166	211
Medication dispensed for patient, AND reminder generated	16	6	54	26
Reminder rate	32.7% (=16/49)	10.2%	32.5%	12.3%

Table 7. Annual Lab Monitoring reminder rates, restricted to Digoxin

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	4	5	8	9
Medication dispensed for patient, AND reminder generated	1	0	2	1
Reminder rate	25%	0%	25%	11%

Table 8. Annual lab monitoring reminder rates, restricted to Diuretics

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	53	74	171	220
Medication dispensed for patient, AND reminder generated	18	10	72	36
Reminder rate	34.0%	13.5%	42.1%	16.4%

Table 9. Annual lab monitoring reminder rates, restricted to Anticonvulsants

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	3	3	10	12
Medication dispensed for patient, AND reminder generated	3	1	7	7
Reminder rate	100%	33%	70%	58%

Table 10. Combined rate of annual lab monitoring for all four above medication groups (ACE-I/ARB, Digoxin, Diuretic, Anticonvulsant)

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	70*	93	261	320
Medication dispensed for patient, AND reminder generated	25	13	104	59
Reminder rate	35.7%	14.0%	39.8%	18.4%

*(Note that this is not simply a sum of the above 4 tables, because many patients take both ACE-I and Diuretic medications at the same time)

Table 11. Combined rate of annual lab monitoring for all medication groups (ACE-I/ARB, Digoxin, Diuretic, Anticonvulsant, Statin, Levothyroxine)

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	53	74	171	220
Medication dispensed for patient, AND reminder generated	18	10	72	36
Reminder rate	34.0%	13.5%	42.1%	16.4%

Note that in each medication group, the reminder rate between the First Visit and the Last Visit decreases for intervention patients. An initial impression may be that there is a strong treatment effect: over time, the number of negative conditions is decreasing. However, this is a wrong impression. A similar decrease in reminder rate can be seen for control patients as well. We must ask the question: is there a statistically significant difference between the intervention and control patients?

(The combined rate is calculated for 4 medication groups (ACE-I/ARB, Digoxin, Diuretic, Anticonvulsant), and then calculated again with the addition of Statin and Levothyroxine medications. The rationale is that, strictly speaking, only the first 4 groups are specified by NCQA HEDIS guidelines.)

Finally, we perform a quantitative test of the hypothesis: does the intervention truly cause a statistically significant improvement in quality metrics (i.e., a decrease in the reminder rate) for the category of Recommended Lab Monitoring? Let us rephrase the hypothesis: we hypothesize that the odds of a reminder decrease faster in the intervention group than in the control group. (The odds of a reminder on a history are: $\text{Probability}[\text{reminder}] / 1 - \text{Probability}[\text{reminder}]$.) We carry out logistic regression analysis to study the additive effects of the explanatory variables (intervention/control status, and time in weeks) on the log of the odds.

There were 310 visits with a reminder in this category. There were 673 visits during which a patient was eligible, but there was no reminder in this category. There were 592 patients for those $(310 + 673 =)$ 983 visits. Not every patient had a first visit and last visit in which he/she was eligible: e.g., some patients were only eligible during their last visit.

Applying generalized estimating equations, and using the more robust “Sandwich estimator” of standard error, we estimate the parameters for the explanatory variables. The output of the GENMOD procedure is shown on Table 12 as follows:

Table 12. Parameter estimates from the Generalized Estimating Equations analysis. Effect of randomization status and of time on the odds of reminders. Restricted to reminders in the category of Laboratory Monitoring

Parameter	Parameter Estimate	Lower Confidence Limit	Upper Confidence Limit
Intercept	-0.480	-0.687	-0.273
Control (Control Flag = 1)	0.068	-0.385	0.521
Intervention (Control Flag = 0)	0	0	0
Time (Weeks)	-0.029	-0.041	-0.016
Control (Control Flag = 1)	-0.020	-0.050	0.010
Intervention (Control Flag = 0)	0	0	0

What do these parameters mean?

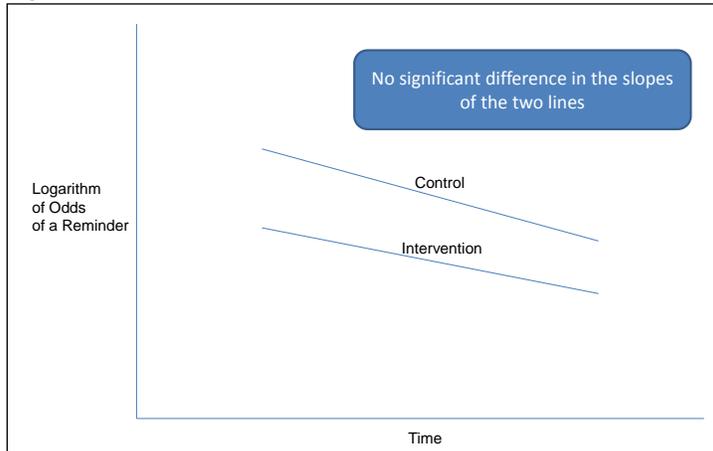
- Odds of a reminder in the intervention group at baseline: $e^{-0.480}$

- Odds of a reminder in the control group at baseline: $e^{-0.480 + 0.068}$
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.385}, e^{0.521})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at baseline.
- Odds of a reminder in the intervention group at week X: $e^{-0.480 - 0.029(x)}$. As time passes, odds of a reminder decrease.
- Odds of a reminder in the control group at week X: $e^{-0.480 + 0.068 - 0.029(x) - 0.020(x)}$. As time passes, odds of a reminder decrease.
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.050}, e^{0.010})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at unit time X.

The most important finding provided by the Generalized Estimating Equations analysis is bolded in Table 12. The 95% Confidence Interval crosses zero. The number of reminders in the intervention group decreases with time. The number of reminders in the control group decreases with time. But there is no significant difference between the intervention group and the control group.

Because not all readers are familiar with logistic regression, it may help some readers to visualize the following chart (Figure 11). Both intervention and control groups demonstrate improved quality with time. But the Intervention group does not have any special advantage: the slope of the two lines are not significantly different.

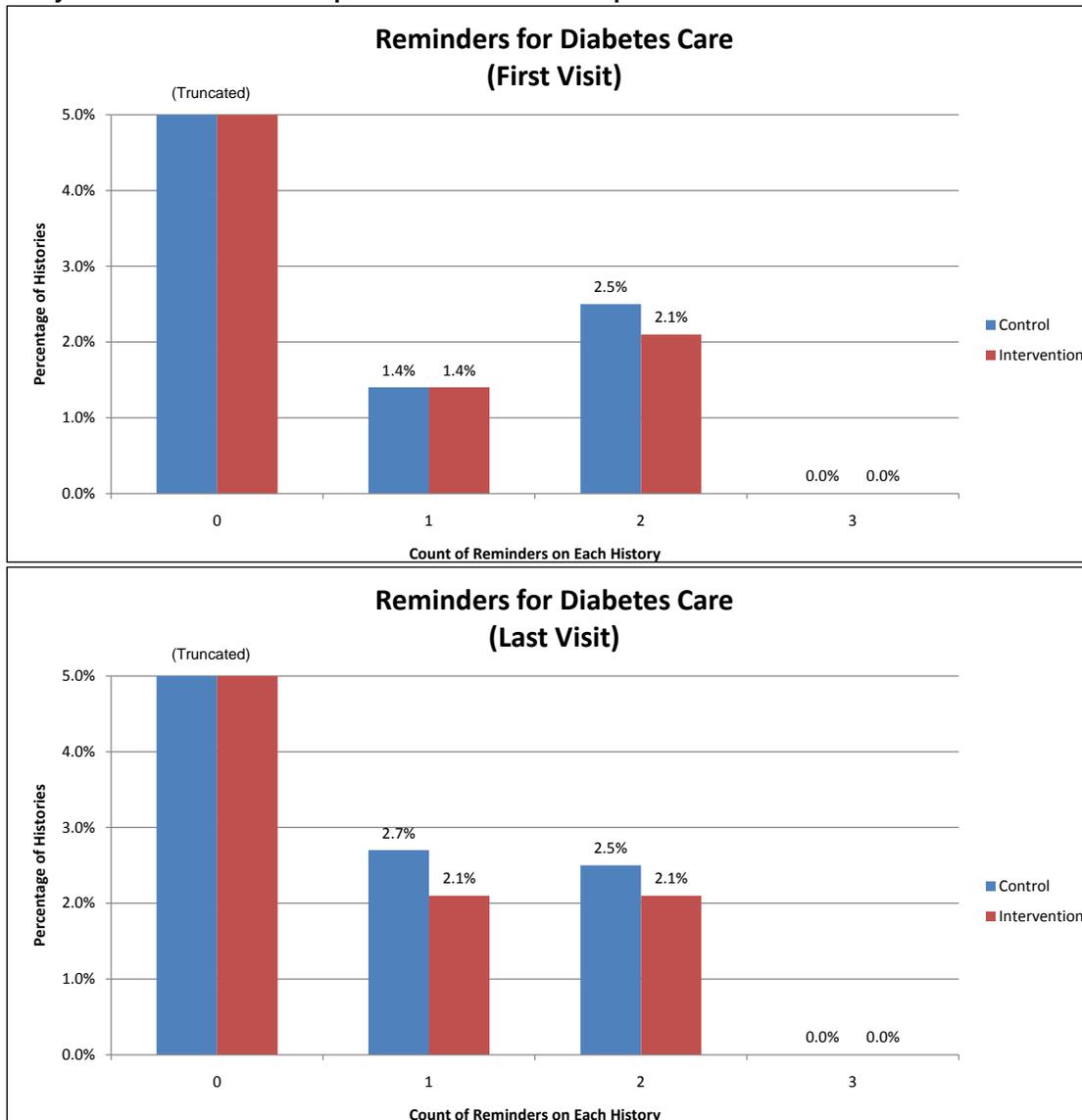
Figure 11. Simplified illustration of the implications of the Generalized Estimating Equations analysis



Category 2 of Decision Support Reminders: Laboratory Testing for Patients with Diabetes

First, let us view the distribution of all reminders in this category. (See Figure 12.)

Figure 12. Decision Support Reminders in the category of Laboratory Testing for Patients with Diabetes. Analysis of 1887 Intervention patients and 488 Control patients.



Note: The top graph shows the distribution of reminders during the first visit for each patient. The bottom graph shows the distribution of reminders during the last visit for each patient. The percentage of histories with zero reminders has been truncated in order to fit on the display.

As seen in Figure 12, there does not seem to be any overall difference between intervention and control groups, neither on first visit, nor on last visit. But this is just a visual impression.

Next, we break down the reminders in the category of Laboratory Testing for Patient with Diabetes into individual reminders. (See Table 13 through Table 16.)

Table 13. Reminder rates for Poor Control of HgbA1C (>9.0%)

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	23	29	72	91
Medication dispensed for patient, AND reminder generated	4	6	12	13
Reminder rate	17.4%	20.7%	16.7%	14.3%

Table 14. Reminder rates for No HgbA1C testing within 12 months

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	23	29	72	91
Medication dispensed for patient, AND reminder generated	13	16	45	54
Reminder rate	56.5%	55.2%	62.5%	59.3%

Table 15. Reminder rates for Poor Control of LDL (>100)

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	23	29	72	91
Medication dispensed for patient, AND reminder generated	6	6	18	20
Reminder rate	26.1%	20.7%	25%	22.0%

Table 16. Reminder rates for No LDL testing within 12 months

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Medication dispensed for patient	23	29	72	91
Medication dispensed for patient, AND reminder generated	8	9	30	30
Reminder rate	34.8%	31.0%	41.7%	33.0%

As in the category of Annual Lab Monitoring, so in this category of Laboratory Testing for Patients with Diabetes, there is a similar phenomenon. For all four reminders in this category, there is a decrease in the reminder rate between the First Visit and the Last Visit for Intervention Patients. However, there is also a decrease for Control Patients. Again, it is not clear whether any significant difference exists between intervention and control patients.

Note that in all four of the above tables, the first data row is identical, because eligibility for each of the four rules is determined identically. A patient is defined as having diabetes (and so is eligible for the rule) if the patient was dispensed a medication used for treating diabetes (with the exception of Metformin, which is used for treatment of additional diseases). Applying this definition to all 4449 patients, 269 (6.0 percent) have diabetes. Although the prevalence of diabetes in this country is difficult to measure precisely, and varies based on estimation method, one figure published by the National Diabetes Information Clearinghouse is 10.7% of all patients of age 20 years and older.¹⁸ Thus our method of defining diabetes may lack sensitivity, and may

miss some patients who have the disease, but do not take the medication—or who rely on diet alone for control of the disease.

Finally, we perform a statistical test of the hypothesis: does the intervention truly cause a statistically significant improvement in quality metrics (i.e., a decrease in the reminder rate) for the category of Laboratory Testing for Patients with Diabetes?

There were 145 visits with a reminder in this category. There were 70 visits during which a patient was eligible, but there was no reminder in this category. There were 144 patients for those (145 + 70 =) 215 visits.

Applying generalized estimating equations, and using the more robust “Sandwich estimator” of standard error, we estimate the parameters for the explanatory variables. The output of the GENMOD procedure is shown in Table 17 as follows:

Table 17. Parameter estimates from the Generalized Estimating Equations analysis. Effect of randomization status and of time on the odds of reminders. Restricted to reminders in the category of Laboratory Testing for Patients with Diabetes.

Parameter	Parameter Estimate	Lower Confidence Limit	Upper Confidence Limit
Intercept	0.852	0.364	1.340
Control (Control Flag = 1)	0.102	-0.862	1.065
Intervention (Control Flag = 0)	0	0	0
Time (Weeks)	-0.014	-0.038	0.011
Control (Control Flag = 1)	-0.001	-0.042	0.040
Intervention (Control Flag = 0)	0	0	0

What do these parameters mean?

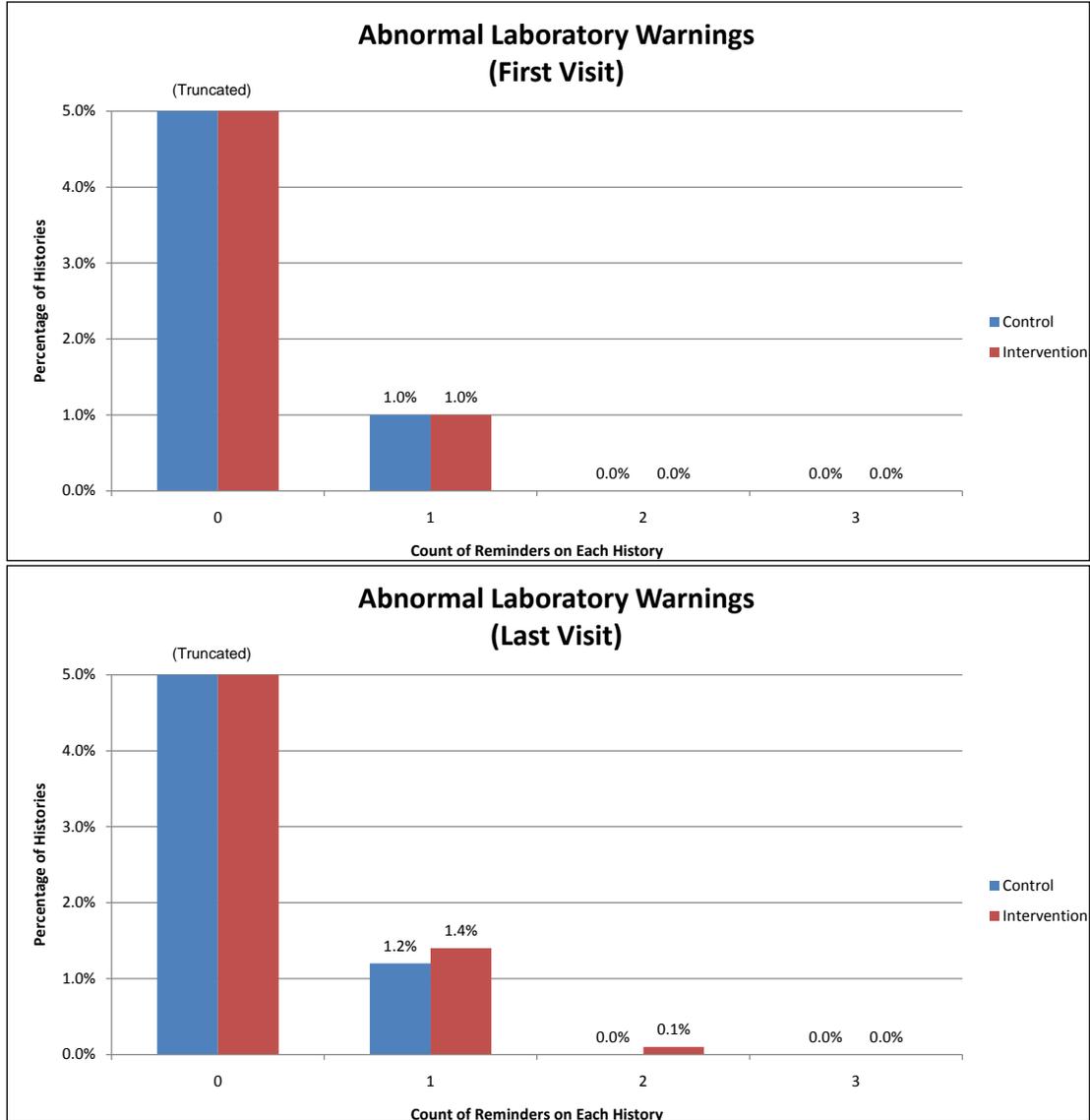
- Odds of a reminder in the intervention group at baseline: $e^{0.852}$
- Odds of a reminder in the control group at baseline: $e^{0.852 + 0.102}$
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.862}, e^{1.065})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at baseline.
- Odds of a reminder in the intervention group at week X: $e^{0.852 - 0.014(x)}$. As time passes, odds of a reminder decrease.
- Odds of a reminder in the control group at week X: $e^{0.852 + 0.102 - 0.014(x) - 0.001(x)}$. As time passes, odds of a reminder decrease.
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.042}, e^{0.040})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at unit time X.

The most important finding provided by the Generalized Estimating Equations analysis is bold in Table 17. The 95% Confidence Interval crosses zero. The number of reminders in the intervention group decreases with time. The number of reminders in the control group decreases with time. But there is no significant difference between the intervention group and the control group.

Category 3 of Decision Support Reminders: Abnormal Laboratory Warnings

First, let us view the distribution of all reminders in this category. (See Figure 13) As with the previous categories, there is no visual impression of a difference between intervention and control groups, neither on the first visit, nor on the last visit.

Figure 13. Decision Support Reminders in the category of Abnormal Laboratory Warnings



Note: Analysis of 1887 Intervention patients and 488 Control patients. The top graph shows the distribution of reminders during the first visit for each patient. The bottom graph shows the distribution of reminders during the last visit for each patient. The percentage of histories with zero reminders has been truncated in order to fit on the display.

We will not break down this category into an full analysis of individual reminder rates, to avoid too many tables. But we can examine the overall distribution of individual reminders. (See Table 18.)

Table 18. Abnormal Laboratory Warning reminders across all 4449 patients, across all 10498 visits, in sorted order of decreasing frequency

Warning	Count of Visits, with Reminder Generated (i.e., medication dispensed for patient, AND abnormal lab)	Count of Visits, Eligible for Rule (i.e., medication dispensed for patient)	Reminder Rate
TSH high, on Levothyroxine	57	431	13.2%
TSH low, on Levothyroxine	31	431	7.2%
Potassium high, on ACE-I/ARB	31	1179	2.6%
Creatinine high, on Metformin	16	548	2.9%
CK high, on Statin or Fibrate	7	1212	0.6%
SGPT high, on Statin, Fibrate, Glitazone, Nefazadone, or Niacin	4	1254	0.3%
Potassium low, Potassium-wasting Diuretic	3	1037	0.3%
Potassium high, Potassium-sparing Diuretic	2	242	0.8%
Creatinine high, on NSAID	2	1279	0.2%
Potassium high, on Potassium supplement	0	246	0
Potassium low, on Digoxin	0	77	0

There are valuable lessons here. Some conditions are of such low prevalence (e.g., patient on Digoxin, and Potassium low) that it is practically fruitless to study them in the outpatient clinic setting—unless a larger population, or a different population, is available. But other conditions may still be amenable to interventions (e.g., patient on Levothyroxine, but still Hypothyroid).

Finally, we perform a statistical test of the hypothesis: does the intervention truly cause a statistically significant improvement in quality metrics (i.e., a decrease in the reminder rate) for the category of Abnormal Laboratory Warnings?

There were 59 visits with a reminder in this category. There were 1300 visits during which a patient was eligible, but there was no reminder in this category. There were 865 patients for those (59 + 1300 =) 1359 visits.

Applying generalized estimating equations, and using the more robust “Sandwich estimator” of standard error, we estimate the parameters for the explanatory variables. The output of the GENMOD procedure is shown in Table 19.

Table 19. Parameter estimates from the Generalized Estimating Equations analysis. Effect of randomization status and of time on the odds of reminders. Restricted to reminders in the category of Abnormal Laboratory Warnings

Parameter	Parameter Estimate	Lower Confidence Limit	Upper Confidence Limit
Intercept	-3.330	-3.786	-2.874
Control (Control Flag = 1)	0.024	-1.050	1.099
Intervention (Control Flag = 0)	0	0	0
Time (Weeks)	0.020	0.000	0.040
Control (Control Flag = 1)	-0.013	-0.078	0.052
Intervention (Control Flag = 0)	0	0	0

What do these parameters mean?

- Odds of a reminder in the intervention group at baseline: $e^{-3.330}$
- Odds of a reminder in the control group at baseline: $e^{-3.330 + 0.024}$

- 95% Confidence Interval of the effect of randomization status: $(e^{-1.050}, e^{1.099})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at baseline.
- Odds of a reminder in the intervention group at week X: $e^{-3.330 + 0.020(x)}$. As time passes, odds of a reminder may increase. But the Confidence Interval includes e^0 , thus there is no statistical significance to this trend.
- Odds of a reminder in the control group at week X: $e^{-3.330 + 0.024 - 0.020(x) - 0.013(x)}$. As time passes, odds of a reminder decrease.
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.078}, e^{0.052})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at unit time X.

The most important finding provided by the Generalized Estimating Equations analysis is highlighted in bold in Table 19. The 95% Confidence Interval crosses zero. The number of reminders in the intervention group decreases with time. The number of reminders in the control group decreases with time. But there is no significant difference between the intervention group and the control group.

Category 4 of Decision Support Reminders: Drugs to Avoid in the Elderly

In the outpatient clinics we studied, the average age was 42, and elderly patients did not form a large group. But as may be seen from Table 20 and 21, drugs from the HEDIS list of “Drugs to Avoid in the Elderly” are often used by elderly patients. Based on these rates, the use of inappropriate medications by the elderly is an important area to continue to address.

Table 20. Reminder rates for elderly patients taking at least one drug from the list of “Drugs to Avoid in the Elderly”

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Eligible for rule (over age 65, and at least one medication)	4	6	19	37
Reminder generated	3	4	16	35
Reminder rate	75%	67%	84%	95%

Table 21. Reminder rates for elderly patients taking at least two drugs from the list of “Drugs to Avoid in the Elderly”

	Control Patient First Visit	Control Patient Last Visit	Intervention Patient First Visit	Intervention Patient Last Visit
Eligible for rule (over age 65, and at least two medications)	3	5	2	7
Reminder generated	2	3	1	6
Reminder rate	67%	60%	50%	86%

Only a few of the medications on the list of “Drugs to Avoid in the Elderly” are responsible for the majority of reminders being generated. This suggests that those few medications are especially important targets for future interventions. Table 22 lists the top 10 most frequent “Drugs to Avoid in the Elderly.”

Table 22. Top 10 most frequent Drugs to Avoid in the Elderly.

Medication Name	Count of Reminders
Cyclobenzaprine	34
Propoxyphene/Acetaminophen	28
Nitrofurantoin SR	23
Promethazine	21
Diazepam	18
Hydroxyzine	11
Nitrofurantoin	9
Methocarbamol	8
Dicyclomine	7
Conjugated Estrogen	6

(Note that these medications are taken from all visits made by elderly patients—not limited to first and last visits)

Finally, we perform a statistical test of the hypothesis: does the intervention truly cause a statistically significant improvement in quality metrics (i.e., a decrease in the reminder rate) for the category of Drugs to Avoid in the Elderly?

There were 58 visits with a reminder in this category. There were 8 visits during which a patient was eligible, but there was no reminder in this category. There were 47 patients for those $(58 + 8 =)$ 66 visits.

Applying generalized estimating equations, and using the more robust “Sandwich estimator” of standard error, we estimate the parameters for the explanatory variables. The output of the GENMOD procedure is on Table 23 as follows:

Table 23. Parameter estimates from the Generalized Estimating Equations analysis. Effect of randomization status and of time on the odds of reminders. Restricted to reminders in the category of Drugs to Avoid in the Elderly

Parameter	Parameter Estimate	Lower Confidence Limit	Upper Confidence Limit
Intercept	1.704	0.588	2.819
Control (Control Flag = 1)	-0.773	-2.874	1.329
Intervention (Control Flag = 0)	0	0	0
Time (Weeks)	0.042	-0.025	0.109
Control (Control Flag = 1)	-0.052*	-0.127*	0.022*
Intervention (Control Flag = 0)	0	0	0

*The most important finding provided by the Generalized Estimating Equations analysis

What do these parameters mean?

- Odds of a reminder in the intervention group at baseline: $e^{1.704}$
- Odds of a reminder in the control group at baseline: $e^{1.704-0.773}$
- 95% Confidence Interval of the effect of randomization status: $(e^{-2.874}, e^{1.329})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at baseline.
- Odds of a reminder in the intervention group at week X: $e^{1.704 + 0.042(x)}$. As time passes, odds of a reminder decrease.
- Odds of a reminder in the control group at week X: $e^{1.704-0.773 + 0.042(x)-0.052(x)}$. As time passes, odds of a reminder decrease.
- 95% Confidence Interval of the effect of randomization status: $(e^{-0.127}, e^{0.022})$. The 95% Confidence Interval includes e^0 . Therefore there is no significant difference between intervention and control at unit time X.

The most important finding provided by the Generalized Estimating Equations analysis is marked with an asterisk in Table 23. The 95% Confidence Interval crosses zero. The number of reminders in the intervention group decreases with time. The number of reminders in the control group decreases with time. But there is no significant difference between the intervention group and the control group.

Category 5 of Decision Support Reminders: Drug-Drug Interactions

In the category of Drug-Drug Interactions, there were insufficient counts to warrant tests for statistical significance. Of the 488 control patients, 0.8 percent had a Drug-Drug Interaction reminder on first visit; 1.0 percent had a Drug-Drug Interaction reminder on last visit. Of the 1887 intervention patients, 0.2 percent had a Drug-Drug Interaction reminder on first visit; 0.4 percent had a Drug-Drug Interaction reminder on last visit.

Although the Decision Support Engine contained rules enabling detection of 693 Drug-Drug Interactions, only 18 of those Interactions were observed over the course of this research study. See Table 24, which lists all Interactions observed (across all patients, for all visits), in descending order of frequency. One possible lesson to learn from such data is that some combinations of medications occur with sufficient frequency in the outpatient setting, that clinicians probably have good rationales to justify using them together. Therefore, simply warning against such combinations any time that they occur is not a good strategy, and may lead to reminders that are ignored. Instead, it may be more fruitful to tailor those rules to recognize especially high doses, or insufficient monitoring of the use of these drugs.

Table 24. Drug-Drug Interactions (across all patients, all visits)

Count of Reminders	Drug 1	Drug 2
17	Fenofibrate	Simvastatin
13	Risperidone	Fluoxetine
10	Gemfibrozil	Simvastatin
7	Fenofibrate	Atorvastatin
7	Clonidine	Amitriptyline
6	Risperidone	Sertraline
6	Clonidine	Doxepin
4	Digoxin	Verapamil
4	Spironolactone	Valsartan
3	Digoxin	Amiodarone
3	Spironolactone	Candesartan
3	Fenofibrate	Pravastatin
3	Fenofibrate	Ezetimibe/Simvastatin
2	Spironolactone	Losartan
2	Risperidone	Paroxetine
2	Risperidone Injection	Sertraline
1	Gemfibrozil	Pravastatin
1	Fenofibrate	Rosuvastatin

Chart Review: Comparison with the Paper Charts Already in the Clinic

We performed a chart review to better understand the correspondence between the EMHP Medication Histories (based on dispensing data) and the medication history, as written in the patient's chart (usually based on the history taken from the patient, or the prescriptions written by the physician).

The paper clinic charts of 50 patients (first five visits on each of 10 daily sessions; age 18 years and older) were reviewed, and all medications noted in the charts were extracted. Likewise, the EMHP dispensing histories for these patients were reviewed. The generic names of all medications were listed, as far back as 13 months, without distinguishing differences in strength. All medications were assigned to broad categories. DEA Controlled Substances Status was also noted. The counts of medications listed in charts were compared with those in the dispensing histories, first as totals and then by controlled substance status and medication category.

The 50 patients had a total of 306 medications listed in their charts; the EMHP histories provided a total of 247. The EMHP histories covered 166 (54 percent) of the 306 medications noted in the charts. However, they provided an additional 81 medications (1.6 per patient). Controlled substances accounted for 16 (20 percent) of these 81 medications, which was a higher proportion than the controlled substances occurring in charts (11 percent). The distribution of medication categories in EMHP dispensing histories was similar to that of charts, except for the higher proportion of antimicrobials. In the EMHP dispensing histories, 21 percent of medications were categorized as antimicrobials; in the clinic charts, 12 percent of medications were antimicrobials.

Chart review does have serious limitations, because medications handwritten in the chart are not coded. Therefore, some subjective judgment was necessary to decide which of the medications written in the chart overlapped with the medications dispensed. Furthermore, it was not always clear from the chart whether the medications were active within the past 13 months; whereas with dispensing histories, the software imposed a strict 13 month window. Finally, it is common for pharmacists to call back the physician and request a medication switch for formulary reasons; the physician may agree with switching the medication, but no longer has the clinic chart available, and cannot write down the new medication.

In spite of these limitations, comparing the medications listed in the paper chart with the EMHP Dispensing Histories was instructive, and generated the following lessons:

- Our Dispensing Histories are not complete, and miss some medications written in the clinic chart. Our Dispensing Histories are limited to 3 data sources (Medicaid claims, PBM claims, and Wishard transactions) and would probably be more complete if additional data sources could be obtained.
- Dispensing Histories provided added benefit, by informing physicians about medications that were not written in the chart.
- Charts and Dispensing Histories are complementary, each providing medications which the other does not have.
- Dispensing Histories provide more complete information about controlled substances in particular

- Dispensing Histories provide more complete information about antimicrobials in particular

Performance Metrics

In the real-world clinic setting, speed is crucial. Therefore, speed was one of our top three goals. In addition to providing information that was (1) accurate, and (2) useful, we strove to provide it to the point of care (3) quickly.

We had no control over the speed at which patients arrived and checked-in at the clinic front desk. The check-in process used the Nightingale Entity practice management system, which is reasonably typical of other electronic registration systems. Evaluating the registration system was beyond the scope of our study.

However, once the patient did complete the check-in process, an electronic HL7 ADT (Admission/Discharge/Transfer) message was generated instantly. These ADT messages were placed in holding queue, with a maximum wait time of 60 seconds (and therefore a median wait time of 30 seconds). At the end of each 60 second period, all messages in the queue were transmitted to our Enhanced Medication History processor.

We performed an analysis of performance metrics for the entire EMHP system, for a convenience sample of 2217 sequential medication histories. (Time measurements began when the EMHP software received the ADT trigger, and ended when the EMHP software sent the completed report to the printer. All times are in seconds.)

Average time to generate EMHP report—12.58 s
Median time—9.17 s
Minimum—2.00 s
Maximum—516.14 s

We also performed a separate analysis of performance metrics for only the Decision Support Component (for the same sample of 2217 histories).

Average time for decision support component—0.50 s
Median time—0.09 s
Minimum—0.00 s
Maximum—369.59 s

As the above time measurements indicate, the average times are skewed by some Medication Histories which required a very long time to process. But the median times are a better representation of the fact that—in many cases—our software required only a few seconds to create a Medication History.

What do these time measurements mean for the more important question of clinic workflow? One of our research assistants made time measurements with a stopwatch for a convenience sample of 20 reports. He observed the time that the patient completed the front desk registration process, observed the time that the report came out of the printer, and measured the time interval with a stopwatch. Although observations such as these are not precise, we believe that they can be reported with at least a minute's precision, as follows:

- 18 of 20 reports were printed within 2 minutes.
- The remaining 2 reports were printed within 3 minutes.

Practically speaking, these times were fast enough, so that the report finished printing while the patient left the registration desk, and took a seat to wait in the waiting room. For the most part, although there were exceptions, the clinic registration staff reported that the printing was fast enough to allow the Medication Histories to be taken off the printer and included on the patient's medical chart, well before the chart was given to the physician.

Physician Survey

During discussions and conversations with clinicians, the general consensus was that they were pleased with the Medication Histories. General themes were that the information was easy to understand, and was usually available in time for the actual encounter between clinician and patient. Physicians emphasized that the medication histories were especially helpful to reveal medications which the patient had not reported taking—notably controlled substances such as opioids. They believed that the EMHP Medication Histories (which list medications dispensed by pharmacies) were a useful complement to the Medications noted in the patient’s clinic chart (which list medications prescribed by physicians).

We sought to formally quantify (by means of a written survey) some of these opinions. A written survey was given to physicians after at least 3 months of experience with the Medication Histories. For all questions except one, physicians were given a statement about the Medication Histories, and were asked to rate whether they agreed or disagreed with the statement. The following 5-point scale was used:

- 1—strongly disagree
- 2—mildly disagree
- 3—no opinion
- 4—mildly agree
- 5—strongly agree

Nine physicians were approached, and seven of the nine completed the written survey. Table 25 presents the questions asked, along with the Mean and Standard Deviation of the responses, and the visual representation of the mean response, rounded to the nearest integer rating.

Table 25. Results of written survey, based on 7 (of 9) physician responses

	Mean ± S.D.	strongly disagree	mildly disagree	no opinion	mildly agree	strongly agree
The Medication Histories are complete lists of what a patient is taking	2.7 ± 1.3	1	2	3*	4	5
The Medication Histories help me discover drugs, which I previously did not know the patient was taking	4.7 ± 0.5	1	2	3	4	5*
The Medication Histories help identify overuse of controlled substances	4.3 ± 0.5	1	2	3	4*	5
The Medication Histories help identify overuse of other drugs (not including controlled substances)	3.5 ± 1.0	1	2	3	4*	5
The Medication Histories help identify underuse of drugs (e.g., patients not filling their prescriptions)	3.9 ± 1.3	1	2	3	4*	5
It is useful to display relevant lab test results at the bottom	3.1 ± 1.6	1	2	3*	4	5
I have noticed decision support reminders (short statement which sometimes appears below the name of a drug)	2.9 ± 1.2	1	2	3*	4	5
The decision support reminders provide useful advice	3.1 ± 0.9	1	2	3*	4	5
The decision support reminders have prompted me to change or discontinue a prescription	2.3 ± 0.5	1	2*	3	4	5
The decision support reminders have prompted me to order a lab test	3.1 ± 0.9	1	2	3*	4	5
Patients look at the Medication Histories	1.9 ± 0.9	1	2*	3	4	5

	Mean ± S.D.	strongly disagree	mildly disagree	no opinion	mildly agree	strongly agree
I show the Medication Histories to patients	2.3 ± 1.3	1	2*	3	4	5
The Medication Histories help patients remember their medications	1.7 ± 1.0	1	2*	3	4	5
The Medication Histories are available , at the time when I need them	3.6 ± 1.1	1	2	3	4*	5
In my experience, the Medication Histories are useful for me	3.9 ± 0.4	1	2	3	4*	5
Overall, the Medication Histories are a useful resource for patient care	3.7 ± 0.8	1	2	3	4*	5
The Medication Histories contain many errors	2.7 ± 0.8	1	2	3*	4	5
The Medication Histories list erroneous medication names	1.7 ± 0.8	1	2*	3	4	5
The Medication Histories list erroneous dose strengths	1.7 ± 0.8	1	2*	3	4	5
The clinic chart provides additional drugs , which the Medication Histories fail to include	4.4 ± 0.5	1	2	3	4*	5
The patient provides additional drugs , which the Medication Histories fail to include	4.3 ± 1.1	1	2	3	4*	5
The clinic chart provides corrections to drugs, which the Medication Histories list inaccurately	3.3 ± 1.0	1	2	3*	4	5
The patient provides corrections to drugs, which the Medication Histories list inaccurately	2.6 ± 0.8	1	2	3*	4	5

The Mean (and Standard Deviation) rating of agreement with each question is presented in the second column. The * represents the Mean rating (rounded to the nearest integer).

What may be summarized and interpreted from the physician survey results? In general, the written responses seem to corroborate the spoken comments:

1. Overall, the Medication Histories are useful
2. Medication Histories are available in time for the visit
3. The Medication Histories are not complete, but they complement the information derived from the chart, and given by the patient
4. Medication Histories are especially useful to reveal the use of medications, which the physician did not know that the patient was taking

The written responses also raised issues, which were not as apparent from the spoken comments:

5. Providing labs results and decision support values has only limited value to the physician
6. The Medication History is not a tool for the patient, but for the physician helping the patient

The 5th point surprised us, because we believed that “enhancing” a medication history with Lab Results and Reminders would be of great value to physicians. Apparently, it has a little value, but not a great as we had hoped. The greatest value of a Medication History is simply: the Medications on it. The 6th point strengthens our belief that one tool does not fit all; designing a tool for the patient is different from designing a tool for the physician. While we will continue to improve the tool we provide for physicians, we should seek a separate process for providing a tool that is useful to patients.

Finally, the written survey did have one more question (in a different format) to explore the question of “when” Medication Histories are used most often. Six of seven physicians reported

that Medication Histories are used “during” the visit, for discussion with the patient. One reported that they are used “before” the visit, to prepare to see the patient.

Discussion

In summary, we developed, implemented, and evaluated a new tool: the INPC Enhanced Medication History. Over a 46 week time period, the Enhanced Medication Histories were successfully delivered to health care providers at two sites of a community health clinic. At least nine physicians used the medication histories as they provided care to 4449 patients. Based on their written and verbal evaluations, the physicians considered the medication histories to be a useful tool. Although the medication histories were incomplete summaries of a patient’s medications, the physicians found them to be valuable nonetheless. The Enhanced Medication Histories complemented information from chart notes and patients; and they helped discover previously unknown use of medications.

The Enhanced Medication Histories involved a complex sequence of software processes. Medication dispensing data was aggregated from three diverse sources and presented in a unified format. Yet the entire process—from the initial arrival of the patient, to the final delivery of the printed report—required less than two minutes. Furthermore, there was minimal disruption to clinic workflow. In fact, the process was triggered automatically, as a by-product of the normal activities of registering a patient. The printed documents were easily integrated into the paper-based process of assembling a clinic chart.

As clinics make the transition from paper-based processes to electronic health records in coming years, most of the Enhanced Medication History system can be reused. The Continuity of Care Document is the vehicle carrying medication and laboratory data. Just as the CCD can be formatted and delivered to a printer, so it can also be delivered to the interface of an electronic medical record.

After performing the statistical analyses described above in this report, we did not detect any significant difference between intervention patients (those with Enhanced Medication Histories) and control patients (those without). There did not appear to be any effect across all five of the categories of decision support reminders we studied. In one category (Laboratory Monitoring Recommended for Chronic Medication Use) health care quality, as measured by the proxy of counting reminders, appears to improve between a patient’s first visit and last visit. However, this benefit is seen both in intervention patients and control patients. Therefore it can not be attributed to the Enhanced Medication History intervention, but must be attributed to the improved care which all patients receive as they return for follow-up visits.

There are several important explanations for lack of a discernable difference, despite the Enhanced Medication History intervention. The most prominent explanation is insufficient sample size. 4449 patients made 10498 visits during the 46 weeks of this study. However, we could only use the medication history data of 2375 of those patients: those who had at least a first visit and a last visit.

Based on sample size calculations (see below), a larger patient population may be needed to detect a treatment effect. When we launched this research study, we worked to enroll several additional outpatient clinics. But we were able to proceed successfully only at the two sites of one Community Health Center organization. We had approached two other clinic organizations, both of whom expressed enthusiasm for this project. However, the vendors of the electronic

registration systems for those clinics were not able to make modifications needed to send out HL7 ADT patient arrival messages. At yet another ambulatory health care center, we did implement the Enhanced Medication History system, and actually started providing medication histories on patient arrival. However, we had to abort the system within a week; and consequently could not incorporate that clinic into this research study.

Furthermore, our choice of a 20 percent allocation of patients to control status (and 80 percent to intervention status) weakened the statistical analysis. But we needed to make a practical decision for such a randomization ratio. Otherwise, with only 50 percent of patients getting medication histories, clinicians perceived little value in participating in the study. With 80 percent of patients getting medication histories, clinicians perceived sufficient value to go ahead with the study.

Other important considerations were the fact that 44 percent of medication histories did not contain any medications. A substantial number of patients might not take any medications on a chronic basis. However, it is also possible that some patients did take chronic medications, yet we failed to provide that information. Incorporating more sources of pharmacy data (beyond the three sources in this study) would probably be necessary to make the medication histories more complete.

Of the 55901 dispensing events—each represented as an NDC code—the majority could be successfully recognized by the decision support engine. However a minority of 4.6 percent dispensing events could not be translated, and thus could not yield accurate reminders. Although such a drop-off in code translation affects all patients—both intervention and control—it does decrease the power of the study.

Despite these limitations, there may be some evidence for a treatment effect. We analyzed the categories of decision support reminders into smaller subcategories. In the subcategory of Laboratory Monitoring Recommended for the Chronic Use of Diuretics (see Table 8), there is a definite improvement in reminder rates in intervention patients: from 42.1 percent on first visit to 16.4 percent on last visit—an improvement of 25.7 percent. The corresponding improvement in control patients is only (34.0 percent - 13.5 percent =) 20.5 percent.

In this subcategory, sample size estimation can be performed, assuming $\alpha/2 = 2.5$ percent, and $\beta = 20$ percent, and yields $n = 788$. In other words, 788 intervention patients (who take diuretics) and 788 control patients (who take diuretics) may be enough to test the hypothesis that the Enhanced Medication History could lead to a detectable improvement in monitoring rates of potassium and renal function. It is more realistic to test a population of all patients (both those who take diuretics and those who do not). In our analysis, 10.9 percent (53 of 488) patients took diuretics and could benefit from such an intervention. Thus 7255 patients (788 divided by 10.9 percent) in a control arm, and 7255 patients in an intervention arm, could suffice for a proper test of the effect of reminders for Laboratory Monitoring Recommended for the Chronic Use of Diuretics.

Lessons Learned

As a result of this project, we have learned lessons which we would like to share with others carrying out similar work:

1. Minimize Disruption To Clinic Workflow

This project could only proceed successfully when we designed it so that the workflow of clinicians would not be disturbed. The Medication History is printed and placed on the clinic chart along with other printed encounter forms. No additional effort is required from clinicians, except to look at the document in their hand. However, there is minor additional effort required from registration staff personnel, who must remove the document from the printer and place it on the correct patient's chart, at the same time that they are assembling the chart.

2. Clinic Liaison Is Necessary

Although workflow disruption was minimal, there were inevitable problems. Therefore, having a clinic liaison was essential. Our clinic liaison drove out to the clinic sites on a regular basis, and spoke briefly to registration staff and to clinicians. In this way we learned of problems earlier, than if we had waited for the clinic personnel to contact us. (Problems included: prolonged delays in printing; patients arriving, but no printout generated; medications very different than those recorded in the patient chart)

3. Organizational Agreements

This project involves multiple organizations sharing data. Data sharing is a complex activity requiring multiple legal agreements and high level of trust and common understanding. This project could only proceed because the organizational agreements to establish and develop the INPC had already been worked out in previous years. Even so, additional approvals had to be obtained to allow this project to proceed.

4. Patient Identifiers

A project to aggregate data from multiple sources can only proceed if there is a mechanism for linking different patient identifiers together. The INPC has invested effort into developing algorithms for linking patient identifiers, which we were able to make use of. Without such a linkage algorithm already implemented, we could not have carried out this project. Although RxHub pharmacy data did not require a specific identifier, the other two sources of pharmacy data did require specific identifiers. Furthermore, laboratory test results from various institutions required various identifiers. The same linkage algorithm was reused in all cases.

5. Patient Arrival Messages

We found that the arrival of a patient to an outpatient clinic is a useful event to trigger the creation of medication histories, and potentially other types of patient information documents as well. It seems that many outpatient clinic settings already have electronic registration systems (in

contrast to electronic medical record systems). Those electronic registration systems can, or could, send out standardized HL7-protocol ADT messages to describe the patient's arrival.

(As long as a registration system can export its data as text, it is possible to format its text as an HL7 message. The real question is the amount of work needed to modify this step. The vendor providing the electronic registration system for this clinic was able to make these modifications with only a few hours of development effort. The vendor for another clinic we had approached estimated that a large and expensive development effort would be needed.)

HL7 ADT messages can be generated as a by-product of the registration process, without requiring any additional effort from clinic personnel. We believe that this is greatly preferable to any other trigger mechanism, which would require an active request on the part of clinic staff and thus disrupt workflow. However, we also experienced the disadvantage of reliance on an automatic trigger: when connectivity is disrupted, and ADT messages stop arriving, no medication history is triggered—even if the clinician is still seeing the patient and requests a medication history.

6. Careful Filtering of Patient Arrival Messages

Careful planning is required beforehand to determine which ADT messages should be used as triggers, and which ADT messages should be ignored. The ADT message format is used to convey other information, not just the fact of a patient's arrival to the clinic. Our initial attempts required testing and fine-tuning to make sure that we could filter out those ADT messages which should not be used to trigger generation of a medication history. This definition required guidance and feedback from clinic management.

For example, ADT messages can be generated to indicate blood draw for lab testing, to indicate documentation of a follow-up phone call, or to indicate that a patient's demographic information has been updated. It requires investigation to determine which data in which fields of the ADT message indicates an event (which should not be ignored) and differentiates it from an event (which should be ignored). Implementing the filter is relatively straightforward, compared to deciding on the semantics of that filter. Although the HL7 standard is well specified, it can be interpreted in different ways by different system developers, requiring an individual approach for each site.

7. Drugs Must Be Identified by a Clinically Usable Coding System

A drug coding system enables aggregation, grouping, sorting, and incorporation of decision support rules. If we had used free-text drug names, this project could not have been possible. However, even if coded, this project would not have been possible if a variety of drug coding systems had been used.

The NDC codes are ubiquitous in pharmacy dispensing data, forcing us to incorporate NDC codes in our strategy. Although they are ubiquitous, we found that they are very inappropriate for clinical use, because they represent distinctions which are not useful for clinicians. For example, there are at least 227 distinct NDC codes to represent Amoxicillin 500mg capsules. No clinical application would be tolerated by clinicians if medications were represented on such a granular level.

Therefore, a crucial element of our process is the translation of NDC codes to clinical codes: in this project, RxNorm Clinical Drugs and Regenstrief Dictionary Drug Terms. For example, each dispensing event is linked to an RxNorm code, and the dispensing events are grouped and

sorted by Regenstrief Dictionary Drug Terms. All decision support rules operate on the level of Dictionary Drug Terms. Our work with drug codes has helped us realize that much research is still needed in the domain of drug codes, in order to improve their use in the clinic setting. Finally, it is important to realize that any translation between coding systems carries the potential for loss of information, if there is any drop-off during the mapping process.

8. Drug strength Is Not Well-Represented

One important realization was that the strength of a patient's dose of medication is not well represented, when compared to the name of a patient's medication. Pharmacy data sources do attempt to represent the strength of a medication dose, and this information appears to be reliable in those cases where a patient takes one tablet/capsule at a time. However, this information appears to be less reliable in those cases where patients take half a tablet, or two tablets—or where they use inhalers, or oral liquids, or topical creams. When we tried to incorporate strength information in our medication histories, we produced displayed strengths which were confusing. We realized that representing strength information is a complex task, and may still require improvements on the part of external data sources and message standards.

However, we were able to represent the strength of medications in a way acceptable to clinicians. We translated NDC codes to RxNorm Clinical Drug codes, and wrote out the text description of the RxNorm code. (For example, “Lisinopril 10 MG Oral Tablet”, instead of “Lisinopril Oral Tablet” and “10 MG”.) In other words, we used the strength information carried in the NDC code, instead of obtaining it from any other field in the pharmacy data record.

9. RxNorm Readability

Initially we hesitated incorporating the generic drug names in the RxNorm database. The RxNorm database contains hundreds of drug names that are over a hundred characters long. To our relief, the generic RxNorm names which we encountered in this project—fairly common drugs used in primary care—were shorter, and usually fit on one or two lines within a printed column. We successfully displayed them to clinical users. Nevertheless, the length of generic RxNorm names requires caution. In some settings (e.g., total parenteral nutrition in the hospital) they could not be used, unless modified.

10. Choice of Grouping Levels

We represented each dispensing event as an RxNorm Clinical Drug (SCD). The choice of SCD comes naturally: RxNorm provides direct translations from NDCs to SCDs (or their brand equivalents). Federal agencies have also chosen the SCD as an appropriate level of granularity.¹⁹

However, it is also important to facilitate a higher grouping level for the benefit of clinicians. For example, clinicians may think of a patient's use of Lisinopril as a continuation of the same drug, even when the dose changes from 10mg to 20 mg. The two different SCDs (for two different strengths) should be grouped together on a medication list. Although we chose to use Regenstrief Terms for this grouping, others could achieve similar grouping using RxNorm SCDFs (Clinical Drug Forms). Other researchers have suggested the IN (Ingredient) as an appropriate choice for representing clinical drug concepts.²⁰

11. Speed Is Paramount

Our INPC Enhanced Medication History process could not afford delay. Delays were unacceptable to the clinic site staff. After registering the patient in the electronic registration system (and thereby generating the ADT message trigger), clinic staff took roughly several minutes to assemble a patient's chart. For the most part, our software could generate and send a medication history to the clinic printer within two minutes. At one clinic site, the registration staff reported that this was more than enough time to allow them to complete their processes and include the medication histories with the patient chart. But at the other clinic site, staff reported that printing of medication histories was just at the limit of tolerability.

12. A Flexible Solution Must Adapt to Paper-Based Clinics

Although we look forward to completely electronic health records, we anticipate another decade of challenging transitions. Most outpatient health care sites still use paper, some to a small extent, others to a large extent. This project demonstrates the utility of a process that gathers electronic information and converts it to a standard CCD format. We transformed the CCD into a printed document, which easily integrates into clinic workflow. While paper is not a perfect solution, it can be considered a user-interface to an information system, just as a computer monitor is a user-interface. When an outpatient clinic does make the eventual transition from paper to an EHR, the CCD is ready for use. The same CCD structure can continue to carry patient data electronically.

References

1. Institute of Medicine. Preventing medication errors. Washington, DC: National Academies Press; 2006.
2. Johnston D, Pan E, Walker J, et al. The value of Computerized Provider Order Entry in ambulatory settings. Center for Information Technology Leadership. Boston, MA: 2003.
3. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc* 2001 Mar-Apr;41(2):192-9.
4. Field TS, Gilman BH, Subramanian S, et al. The costs associated with adverse drug events among older adults in the ambulatory setting. *Med Care* 2005 Dec;43(12):1171-6.
5. National Quality Forum. National Voluntary Consensus Standards for Ambulatory Care—Part 1: A Consensus Report. Washington, DC: NQF; 2008.
6. Carpenter JD, Gorman PN. Using medication list-problem list mismatches as markers of potential error. *Proc AMIA Symp* 2002:106-10.
7. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies at the time of hospital admission. *Arch Intern Med* 2005 Feb 28;165(4):424-9.
8. Markle Foundation. Lessons from KatrinaHealth. June 13, 2006. Available at: <http://www.katrinahealth.org/katrinahealth.final.pdf> . Accessed April 2010.
9. Stelfox HT, Ahmed SB, Fiskio J, et al. An evaluation of the adequacy of outpatient monitoring of thyroid replacement therapy. *J Eval Clin Pract* 2004;10(4):525-30.
10. Stelfox HT, Ahmed SB, Fiskio J, et al. Monitoring amiodarone's toxicities: recommendations, evidence, and clinical practice. *Clin Pharmacol Ther* 2004 Jan;75(1):110-22.
11. McDonald CJ, Overhage JM, Barnes M, et al. The Indiana network for patient care: a working local health information infrastructure. *Health Aff (Millwood)* 2005 Sep-Oct;24(5):1214-20.
12. Mirth Corporation Website. Mirth Connect Webpage. Available at: <http://www.mirthcorp.com/products/mirth-connect>. Accessed April 2010.
13. HITSP Website. Summary Documents Using HL7 Continuity of Care Document (CCD) webpage. Available at: <http://wiki.hitsp.org/docs/C32/C32-1.html>. Accessed April 2010.
14. Simonaitis L, Belsito A, Overhage JM. Enhancing an ePrescribing system by adding medication histories and formularies: the Regenstrief Medication Hub. *AMIA Annu Symp Proc*. 2008 Nov 6:677-81.
15. SureScripts Website. Available at: <http://www.surescripts.com> . Accessed April 2010.
16. JBoss Community Website. Drools Webpage. Available at: <http://www.jboss.org/drools> . Accessed April 2010.
17. National Committee for Quality Assurance. HEDIS 2008 Technical Specifications. Washington, DC: 2007.
18. National Diabetes Information Clearinghouse Website. National Diabetes Statistics, 2007 Webpage. Available at: <http://diabetes.niddk.nih.gov/dm/pubs/statistics/> . Accessed April 2010.
19. Parrish F, Do N, Bouhaddou O, et al. Implementation of RxNorm as a terminology mediation standard for exchanging pharmacy medication between federal agencies. *AMIA Annu Symp Proc* 2006:1057.
20. Phansalkar S, Robinson G, Getty G, et al. Challenges in exchanging medication information: identifying gaps in clinical document exchange and terminology standards. *AMIA Annu Symp Proc* 2009 Nov 15:526-30.