Grant Final Report

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E-prescribing Impact on Patient Safety, Use and Cost

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Abstract

Purpose: To evaluate the effects of a natural experiment in e-prescribing on uptake, and the impact on cost, safety, and quality.

Scope: Approximately 7.4 million filled prescriptions, over 212,000 of which were e-prescriptions, were included in the study. In total we identified over 35,000 clinicians and over 1.5 million patients with a filled prescription claim. Of these 1,198 clinicians wrote one or more e-prescription that was filled by 64,749 patients.

Methods: Pre-post with concurrent controls, using data from the deployment of an e-prescribing program by two large insurers in a northeastern state. We used data on paid medical and pharmacy claims data coupled with data from the e-prescribing vendor to identify filled prescriptions written / not written during our study period (2003 through the first quarter of 2005). We used these data to evaluate prescribing for each physician in our sample before and after they began e-prescribing.

Results: Evaluation of e-prescribing uptake showed steadily increasing use of e-prescribing over the study period. E-prescribing with formulary decision support led to the use of lower-priced medications. Early results also indicated that patients getting e-prescriptions had less severe potential drug-drug interactions among their dispensed medications.

Key Words: E-prescribing technology, patient safety, prescribing habits

Final Report

Purpose

The primary aim of our study was to conduct a pre-post study with concurrent controls to evaluate the effects of e-prescribing on patient safety, use, and cost of prescription medications. We proposed to use or modify current measures of poor apparent prescribing habits, utilization, and selected patient outcomes. To accomplish this aim, we obtained all pharmacy and medical claims from 2003 through the first quarter of 2005, providing pre- and post-intervention data for patients of physicians who began using the e-prescribing technology from Tufts Health Plan (THP) and Blue Cross Blue Shield of Massachusetts (BCBSMA) and, as a concurrent control, for patients of physicians who did not use it during 2004 and the first quarter of 2005.

We addressed the following study questions:

1. At what rate do prescribers adopt e-prescribing? (See Study 1)

2. Do physicians who use the new technology increase their use of generic drug equivalents, prescribe a higher proportion of drugs found on the formulary, and decrease the cost of drugs per prescription? (See Study 2)

3. Do physicians who use e-prescribing experience a lower rate of apparent poor prescribing habits, as measured by potential drug-drug interactions (DDIs)? (See Study 3)

4. Do patients with selected chronic illnesses such as diabetes, heart failure, hypertension or chronic lung disease have fewer claims for emergency department visits and hospitalization if they are being managed by e-prescribing, versus other patients with similar chronic conditions? (See Study 4)

As health plans nationwide begin to redesign their workplace in order to improve patient safety, it is important to understand whether new technological innovations such as e-prescribing make important contributions to patient safety. The results of these studies will have broad generalizability, especially as the technology becomes more widespread.

Scope

Background

Medication errors occur at every step in the medication process— ordering medications, transcribing the orders, preparing the medications, or administering the medications to patients. Medication errors that occur in the early stages of the process are more likely than others to be intercepted before causing harm. Although dosing errors are among the most common of medication errors,[1] drug-drug interactions also are common. A systems-focused, multidisciplinary approach has been useful for preventing serious errors. Computerized-based rules have been effective in preventing mistakes and injury in the inpatient setting, and hold great promise for application in the ambulatory setting.

In October 2003, Tufts Health Plan (Tufts HP), Blue Cross Blue Shield of Massachusetts (BCBSMA) and ZixCorp collaboratively launched a voluntary e-prescribing program in Massachusetts. PocketScript is an e-prescribing system that enables physicians to electronically write and fax both new and refill prescriptions to the pharmacy via a secure fax. The e-prescribing system has a number of features that may affect prescribing practices resulting in improvements in patient safety and reduced cost. 1) When a prescriber enters a prescription, it identifies possible drug interactions and allows the prescriber to change the prescription; 2) It includes suggested dosages for common drugs, and furthermore allows the prescriber to build in prescriber-specific macros for the most commonly prescribed drugs and dosages; 3) formulary information is supplied, identifying the coverage tier (preferred, accepted, requires approval, and not accepted).

Significance

E-prescribing by ambulatory physicians holds promise in terms of reduced cost and increased patient safety by providing real time drug information to the prescriber. Prior to our research, there have been no carefully controlled studies that have examined the patient safety claims of e-prescribing. Demonstrating that medications can be provided at lower cost without a detrimental impact on clinical outcomes has significant policy implications.

Methods

Overall Study Design. The deployment of the e-prescribing program by Tufts HP and BCBSMA provided an opportunity for a natural experiment. During our study period, Tufts HP and BCBSMA enrolled over 1000 physicians into the e-prescribing program. Using claims data from Tufts HP and BCBSMA, we evaluated prescribing for each physician in our sample before and after they begin e-prescribing. Thus we were able to conduct a retrospective pre-post study with concurrent controls.[2] As a check on temporal trends, our use of concurrent controls allowed us to compare users to non-users.

Although prescriber behavior is of ultimate interest, *the primary unit for most of our analyses was the prescription, controlling for physician effects*. This allowed us to avoid the assumption that a given prescriber would exhibit similar behavior no matter which mode of prescribing he or she is using.

Data Sources/Collection. The data sources for this study were the complete medical claims history for Tufts HP and BCBSMA for their insured population between January 2003 and March 2005, and complete pharmacy claims history from October 2003 and March 2005 merged with e-prescription data from ZixCorp between April 2004 (the start of the initiative) and March 2005. All identifiable characteristics were removed from the data before transmission to the research team. Encrypted patient and physician identifiers were created so that records could be linked across the datasets while preserving confidentiality. We received several types of files. By merging the data files, we were able to identify the date on which intervention physicians began e-prescribing and to generate a marker of which filled claims were prescribed electronically.

Interventions. Patients with at least one drug claim during the study period were included. Prescriptions from medication benefit plans that did not use tiered copayment systems were excluded.

Measures. See each sub-study for specific measures

Limitations. 1) We used administrative data to detect poor prescribing practices, recognizing the limitations inherent in using these data. 2) Our study design is non-randomized. Early adopters of e-prescribing may be systematically different from late adopters in ways that could confound the analysis. 3) A certain level of decision support to reduce prescribing errors is inherent in current systems of care, under programs of Drug Utilization Review (DUR). 4) We will not know if physicians in the control group are already using another e-prescribing device. 5) Some prescribers may stop using e-prescribing after they start using it. Therefore, we monitored the number of prescriptions written electronically and if the number dropped significantly, we eliminated claims for that provider from the analysis. 6) Some of the potential cost savings from e-prescribing may have derived from improved communication between the prescriber and the pharmacist.

Study #1: E-Prescribing Adoption

Study Design. Observational analysis of the uptake of e-prescribing during the first year of the e-prescribing program.

Data Sources/Collection. See above.

Interventions. Use of the e-prescribing system.

Measures. We measured both an absolute count of e-prescriptions and a proportional uptake rate. For each prescriber we identified the first date on which they wrote an e-prescription in the ERX data and assigned this as their start date. We then tabulated the number of e-prescriptions

written each month. This method yielded information on the absolute volume of e-prescriptions written. We also calculated a rate of e-prescribing as a proportion of total filled claims, calculated as the number of e-prescriptions divided by the total number of filled prescriptions in the claims data. Ideally this rate would be calculated as the number of electronic prescriptions divided by the total number of prescriptions written. However, the claims data did not include prescriptions written on paper that were never filled, which can lower the denominator for this rate. On the other hand, the claims data included refills of previously written prescriptions, which can markedly increase the denominator for this rate. Accordingly, we regarded this rate as an approximation of the proportion of medications that were e-prescribed.

We began by tabulating the characteristics of clinicians who used the e-prescribing system. Adoption and uptake of the e-prescribing system were measured by the number of prescribers enrolled and the number of e-prescriptions written in each calendar month. We then examined rates of e-prescribing use by month relative to when clinicians wrote their first e-prescription, regardless of calendar month. We categorized uptake volume and rates by the clinician characteristics available in our data.

In order to limit the impact of potential biases introduced by our proxy measure of proportional uptake rates we re-analyzed the data using a subset of medications more likely to be prescribed for short-term relief of symptomatic conditions (antibiotics, pain medications, anti-emetics). We anticipated that for this subset of medications, discrepancies between filled prescriptions and written prescriptions would be smaller, because these medications are more likely to be filled by patients initially, and would also be less likely to have refills (which would inflate the number of filled prescriptions relative to a written prescription).

To evaluate the relative impact of clinician characteristics on the proportional uptake rate of e-prescribing, we developed regression models using generalized estimating equations. The e-prescribing rate was the dependent variable, and all measured prescriber characteristics were included in the model, in addition to the month relative to first use of the e-prescribing system. We assumed an auto-regressive correlation structure to model repeated measures of e-prescribing use by month. A Poisson distribution with a log link was specified in the model to fit the data.

Limitations. Our study is unable to address the causes of incomplete adoption directly; studies including a qualitative component to evaluate how prescribers adopt and use e-prescribing systems are an important priority for future research.

Study #2: E-Prescribing Impact on Cost

Study Design. To understand the effect of e-prescribing with formulary decision support (FDS) we calculated the proportion of prescriptions written in each of three formulary tiers for 6 months before and up to 12 months after the intervention. The individual prescription was the unit of analysis, and we controlled for data clustering at the patient and physician level. Physician use of the e-prescribing system defined the intervention prescriptions, and all prescriptions written by unenrolled physicians served as controls. We applied the estimated impact of e-prescribing with FDS to patient-level data in order to estimate the potential savings per-patient per-month.

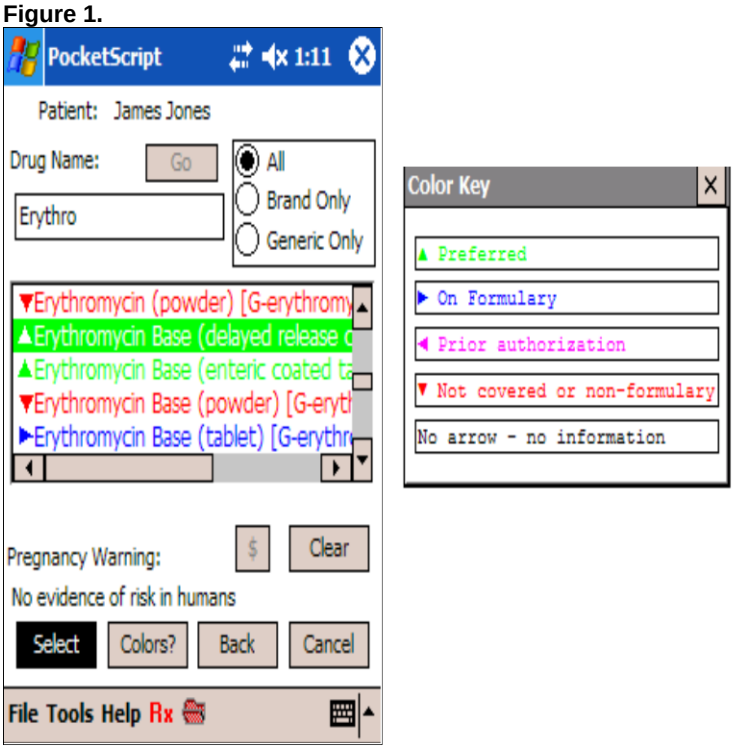
Data Sources/Collection. We obtained data on prescriptions *written* with the e-prescribing system (e-prescribing data) and prescriptions *filled and paid for* by the two participating health

plans (claims data). The e-prescribing data covered 12 months, from April 1, 2004 through March 31, 2005 while the claims data included those 12 months and the 6 preceding months. Patient IDs were linked to enrollment files to obtain age, gender, and insurance plan. The e-prescribing data recorded all e-prescriptions, regardless of whether they were filled or not. Therefore, to identify paid claims written electronically, we linked the two data sources to each other using patient identifiers and drug names, requiring that the prescription fill date was on or after the date of e-prescribing.

Interventions. The e-prescribing software included formulary-based color-coding for drug names (See Figure 1). Tier 1 medications required the lowest copayment and were all generic medications. Medications with preferred formulary status (generally Tier 1) appeared in green text. Non-preferred medications appeared in blue text and those that were not covered appeared in red text. The system did not prevent physicians from prescribing non-preferred medications; the color-coding served only as a reminder.

Measures. Some paid claims (7%) were excluded because the prescriber field could not be linked to a single clinician; this generally occurs when placeholder identifiers are used for trainees or out-of-state prescribers. An additional 3% of claims were excluded due to incomplete or missing data.

Figure 1.



We first examined the data using a simple pre-post descriptive analysis. We calculated the proportion of filled prescriptions that were in each copayment tier and compared the proportion of medications in each tier before and after e-prescribing began. For intervention physicians we

used all filled claims in the 6 months before April, 2004 as baseline data. During the intervention period, we examined the data using two approaches: 1) An "E-prescriptions-Only" analysis including just those prescriptions written electronically (including refills); 2) An "All prescriptions" analysis including all filled claims for each e-prescribing physician on or after the date on which they wrote their first e-prescription, through the end of our data period.

For control physicians we defined the baseline period as above to include all of their filled claims in the 6 months before April 1, 2004, and the intervention period to include those claims during the following 12 months. The same set of prescribing data for the control physicians was used for both the "E-prescriptions-Only" and the "All prescriptions" analyses. We compared the change from baseline period to intervention period across the control and intervention groups, using bootstrapped standard errors. To provide a visual display, we re-categorized the data by "relative months" before and after physicians first wrote e-prescriptions so as to generate a graph depicting Tier 1 prescribing for each group over time.

The descriptive analysis above does not account for the variable time gap between the 'baseline' and 'intervention' periods for the e-prescribing and control groups, which occurred due to the fact that e-prescribing start dates were distributed throughout the study period. The unadjusted analysis also does not account for the fact that, even after enrollment, prescriptions could be written either electronically or on paper. Thus, we developed regression models to quantify more precisely the impact of e-prescribing. In these models we used the individual prescription as the unit of analysis, and modeled the probability that a prescription would be in a given co-payment tier. Since each prescription event has three possible outcomes (i.e. Tier 1, 2, 3) we developed multinomial logistic regression models, using Tier 1 as the reference group.

The basic specification of the multinomial logistic regression model is shown below:

$$\log\left(p(\text{tier}=j) / p(\text{tier}=1) \right) = \beta_{0j} + \beta_{1j}*\text{month} + \beta_{2j}*\text{Intmd\_pre} + \beta_{3j}*\text{Intmd\_post} + \beta_{4j}*\text{ERX}$$

Definitions of the key variables are as follows:

- Intmd_pre indicates that a prescription was written by an intervention MD prior to their first use of the eRx system
- Intmd_post indicates that a prescription was written by an intervention MD at any time after their first use of the eRx system
- ERX indicates that a prescription was actually prescribed electronically; by definition this will be a subset of Intmd_post

The values of these variables in the possible prescribing situations are indicated in the table:

Table 1.

	Intmd_pre	**Intmd_post**	**ERX**
Control MD (regardless of time)	0	0	0
Intervention MD before getting eRx system	1	0	0
Intervention MD after getting eRx system, non-electronic prescription	0	1	0
Intervention MD after getting eRx system, electronic prescription	0	1	1

For the initial calculation, we assumed that e-prescribing with FDS would be used for all prescriptions; we also considered the impact if e-prescribing uptake were not complete. We

assumed that patients filled one prescription/month, a representative utilization rate for privately insured patients. We used prevailing average monthly medication costs for major health plans in our region, corresponding to $28 for Tier 1, $115 for Tier 2, and $139 for Tier 3. We explored the change in financial impact when we varied the drug utilization and cost numbers.

Limitations. Physicians were not randomly assigned to receive the e-prescribing system but were selected by the health insurance plans if they were high-volume prescribers. We controlled for these differences and still found a large impact of e-prescribing with FDS. Nevertheless, there may be residual confounding. Primary care specialties were over-represented in the intervention group – when we restricted the control group to physicians in primary care (results not shown) the control groups had slightly higher Tier 1 prescribing, but the main results were unchanged.

Prescriber identification in the prescriptions claims files did not always correspond to an individual; thus 10% of prescription claims were excluded from our analyses. We re-ran all of the analyses, treating the placeholder prescriber identifiers as if they were individual clinicians, and none of our effect estimates changed. As noted, there are many qualitative factors that could affect whether clinicians choose to prescribe electronically for any given prescription decision, and we did not capture those characteristics.

Study #3: E-Prescribing Impact on Poor Presribing Habits

Study Design. We used filled claims data to identify patients who were potentially exposed to more than one drug at a time ("potential DDIs) for 6 months before and up to 12 months after the intervention. The individual prescription was the unit of analysis, with control for clustering at the patient and physician level. Physician use of the system defined the intervention prescriptions, and all prescriptions written by un-enrolled physicians served as controls.

Data Sources/Collection. We obtained data on prescriptions *written* with the e-prescribing system (e-prescribing data) and prescriptions *filled and paid for* by the two participating health plans (claims data). The e-prescribing data covered 12 months, from April 1, 2004 through March 31, 2005 while the claims data included those 12 months and the 6 preceding months.

The e-prescribing data recorded all e-prescriptions, regardless of whether they were filled or not. Therefore, to identify paid claims written electronically, we linked the two data sources to each other using patient identifiers and drug names, requiring that the prescription fill date was on or after the date of e-prescribing.

Interventions. The e-prescribing system includes warnings based on the medications previously prescribed by the system. Using the Multum database of drug information, the e-prescribing system identifies potential drug-drug interactions and gives prescribers a warning that there may be a safety issue. There are also warnings delivered for dose of a drug.

Measures. For each prescription we used the "days supplied" field or the "quantity dispensed" field to identify the period of time going forward during which the patient can be presumed to be taking the medication in question. We then identified additional filled claims that occurred during that period of time. Any prescriptions filled during that time were matched with the original prescription to form a "co-exposure pair." These pairs constituted the parent

population of potential DDIs. By comparing these potential DDIs to DDIs as identified in commercial drug reference databases, we could measures the rates of these events over time.

Limitations.

1. Since we have only data on drugs that were dispensed, we can only evaluate potential DDIs, we cannot determine whether actual events occurred or whether patients were actually taking the two drugs at the same time. Variable use of the e-prescribing system may lead us to measure the impact of the system with error.

2. We had planned to also evaluate dosing range errors for e-prescribed medications. However, dosing range applications required data elements that were simply not available in filled claims data, such as patient weight, renal function, and other clinical variables. Accordingly, the planned analyses of drug dosing errors could not be performed. Performing such analyses in the future would require more detailed clinical information and would likely have to be done in a setting with a full electronic medical record.

3. Our initial analyses used the First DataBank National Drug Data File as a proxy for identifying potential drug-drug interactions. However, subsequent consultations with experts in the field and a review of the literature showed that First Databank and Multum can have different classification systems for DDIs, which could introduce measurement error into our results. Subsequently, we reached an agreement to obtain a copy of the Multum drug database and will use this to generate revised results in the near future.

Study #4: E-Prescribing Impact among Persons with Chronic Conditions

Study Design. We used a person level, pre-post with concurrent controls study design. The focus was on the impact of being managed by an e-prescribing physician on time to specific care outcomes – hospitalizations, ambulatory care sensitive hospitalization (ACSH) and ED visits among persons with specific chronic conditions.

Data Sources/Collection. Data Source: All medical and pharmacy claims for persons identified as having a chronic illness of interest during the study period.

Analyses File Inclusions/Exclusions. Study participants included all patients identified as having a chronic condition with one or more prescription during the study period. The study period included 12 months of data for these persons between March 2004 and March 2005.

1. Persons with chronic conditions were identified by applying the AHRQ Chronic Condition Indicator Software to 12 months of medical claims data prior to the study period.

2. Data were limited to prescription and medical claims with valid provider identifiers.

3. Data were further limited to persons with one or more prescription claim.

4. Children (age<18) were excluded from the analysis.

Interventions. Use of the e-prescribing system.

Measures. We used survival analysis (Cox) using a time dependent covariate for the date of first Zix e-prescription (treatment). Similar to the cost analysis, the "ever Zix" variable measured the impact of having a high prescribing provider targeted by the Zix collaborative, while the time dependent covariate for first Zix use assessed the independent effect of actual e-prescribing.

The outcome was time to first hospitalization, ACSH, and ED visit for the controls, and time to first hospitalization, ambulatory care sensitive hospitalizations (ACSH), and ED visit before and after becoming a Zix user for the cases. The Analyses controlled for patient age, gender, number of prescriptions filled in pre period, and Charlson co-morbidities.

Identifying Persons with Chronic Conditions.

1. We identified all persons with chronic conditions using the AHRQ Chronic Condition Indicator Software: Persons with chronic conditions were identified as follows:

    - A full year of medical claims (March 2003 to March 2004) was used to identify persons with a chronic condition

    - All claims except laboratory and radiology claims were used to identify persons with chronic conditions. Lab and radiology claims were excluded to avoid rule-out diagnoses.

    - Persons had to have at least 2 ambulatory claims or one inpatient (including nursing home, rehab, SNF…) claim indicative of a chronic condition.

2. We used the AHRQ Clinical Classification Software (CCS) to identify persons with the following specific chronic conditions: CHF, Diabetes Mellitus, COPD, Asthma, and Hypertension. (Note: The Cohen and Krauss (2003) grouping of CCS into pulmonary conditions was not used because the category was too gross and included some diagnoses, such as aspiration pneumonia, which are not chronic conditions.) See http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccsfactsheet.jsp We used a similar method as above to identify specific chronic conditions. Persons had to have at least 2 ambulatory claims with the chronic condition or one inpatient (including nursing home, rehab, SNF…) claim with the specific chronic condition.

Outcomes Assessed in the 12-month Post Period.

1. ED visits.

2. Hospitalizations. All cause and Condition specific ambulatory care sensitive hospitalizations (ACSH).

Limitations. No limitations specific to this study.

Results

Results Common to All Four Studies

The tables below show summary results for patients and prescribers exposed to the e-prescribing system. Results of the specific analyses are given in the appropriate sections.

Patients.

- Intervention: If a patient received one or more e-prescription
- Control: If a patient never received an e-prescription
- Patients receiving e-prescriptions were slightly more likely to be female and were older than patients who did not receive e-prescriptions.

Table 2. Patient characteristics

	Intervention	Control	Total
Patients	Ever got e-prescription	Never got e-prescription	
Overall	N = 64,749	N = 1,466,564	N = 1,531,313
Gender: Male	27,458 (42.4%)	643,375 (43.9%)	670,833 (43.8%)
Gender: Female	37,291 (57.6%)	823,189 (56.1%)	860,480 (56.2%)
Age: zero to 18	8,214 (12.7%)	308,756 (21.1%)	316,970 (20.7%)
Age: 18 to 34	10,203 (15.8%)	320,556 (21.9%)	330,759 (21.6%)
Age: 35 to 54	28,989 (44.8%)	552,989 (37.7%)	581,978 (38.0%)
Age: 55 to 64	11,885 (18.4%)	193,121 (13.2%)	205,006 (13.4%)
Age: 65 and up	5,458 (8.4%)	91,142 (6.2%)	96,600 (6.3%)

Prescribers. The intervention group included all physicians who wrote at least one e-prescription, with all other physicians (whether offered e-prescribing or not) serving as controls. Physicians in the intervention group were slightly younger and were more likely to be female. The specialties of internal medicine, pediatrics, and family practice accounted for about 70% of the intervention group, a higher proportion than in the control physicians. There were a total of 17.4 million filled prescriptions during the entire study period, over 212,000 of which were e-prescriptions.

Table 3. Prescriber characteristics

	Intervention	Control	Total
Prescribers	Ever wrote e-prescription	Never wrote e-prescription	
Overall	N= 1,198	N= 34,453	N= 35,651
Gender: Male	593 (49.5%)	22,495 (65.3%)	23,088 (64.8%)
Gender: Female	460 (38.4%)	10,138 (29.4%)	10,598 (29.7%)
Gender: Missing	145 (12.1%)	1,820 (5.3%)	1,965 (5.5%)
Age: under 35	138 (11.5%)	1,784 (5.2%)	1,922 (5.4%)
Age: 36 to 54	696 (58.1%)	9,017 (26.2%)	9,713 (27.2%)
Age: 55 and up	200 (16.7%)	3,651 (10.6%)	3,851 (10.8%)
Age: Missing	164 (13.7%)	20,001 (58.1%)	20,165 (56.6%)
Specialty*: internal medicine	365 (30.5%)	9,988 (29.0%)	10,353 (29.0%)
Specialty*: pediatrics	300 (25.0%)	3,208 (9.3%)	3,508 (9.8%)
Specialty*: family practice	186 (15.5%)	2,125 (6.2%)	2,311 (6.5%)
Specialty*: other	321 (26.8%)	19,682 (57.1%)	20,003 (56.1%)
Specialty*: missing	137 (11.4%)	110 (0.3%)	247 (0.7%)

* As clinicians may have multiple specialties, categories for specialty are not mutually exclusive. Column percentages do not total to 100%. Control prescribers were identified separately in the two participating insurance plans, so an individual physician may contribute two observations to the control cohort.

Outcome. See each sub-study.

Discussion. See each sub-study.

Conclusions. As the subsequent sections demonstrate, e-prescribing uptake increased over time. E-prescribing with formulary decision support significantly reduced medication cost. Evaluation of whether e-prescribing actually increases drug safety is ongoing, although there is an initial signal that suggests that the most severe potential drug-drug interactions were less frequent for patients getting e-prescriptions. There was not enough e-prescribing for patients with chronic diseases to determine if overall processes of care were improved, but the techniques we developed will allow us to study this in the future.

Significance. These results provide some of the first rigorous data on the actual impact of e-prescribing in community-cased clinical settings.

Implications. As e-prescribing becomes more common nationwide, these results will inform decision makers and should help future researchers studying these questions in other settings.

Study #1: E-Prescribing Adoption

Principal findings. By March 31, 2005 (the end of the study period), the e-prescribing system had enrolled 2,055 prescribers and 1,496 had the system in place. However, over the 12-month study period, only a total of 1,217 clinicians (81%) had actually written one or more e-prescriptions using the PocketScript system.

Outcomes. Table 4 shows the characteristics of providers who used the e-prescribing system during our study period. Primary care specialties accounted for 70% of the e-prescribers, including 30% internists, 24% pediatricians, and 16% family practice. The 19% of e-prescribers in other specialties included gynecologists, cardiologists, and gastroenterologists (demographics were missing for about 11% of participants). More e-prescribers were male than female, and

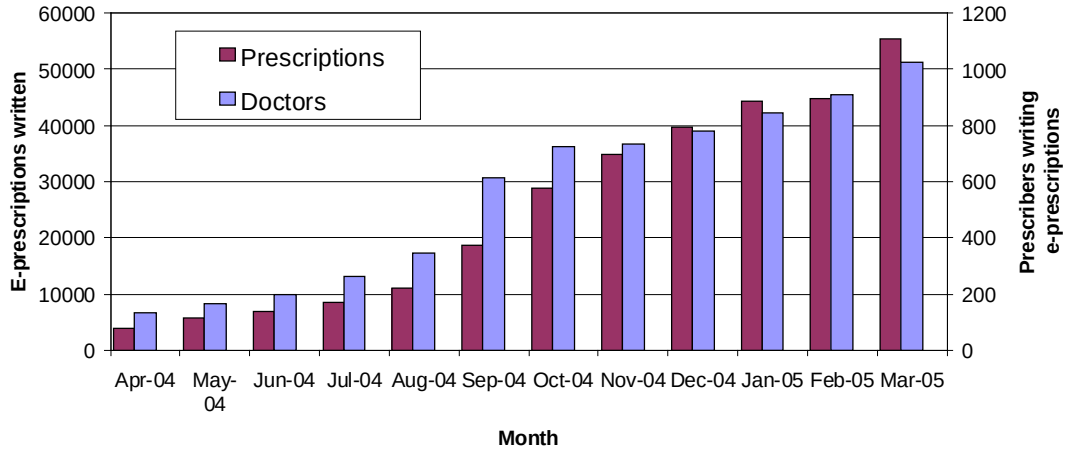
most e-prescribers were between 35 and 54 years of age. Participants were from a variety of practice sizes, with over 60% from practices of 8 clinicians or less. Of the total, 269 e-prescribers were non-physicians.

Table 4. Characteristics of e-prescribers

Characteristic	Number (%)
Specialty: Internal Medicine	366 (30.1)
Specialty: Pediatrics	296 (24.3)
Specialty: Family Practice	188 (15.5)
Specialty: Other	230 (18.9)
Specialty: Missing	137 (11.3)
Gender: Male	595 (48.9)
Gender: Female	461 (37.9)
Gender: Missing	161 (13.2)
Practice size: 1-3	348 (28.6)
Practice size: 4-8	398 (32.7)
Practice size: 9-15	205 (16.8)
Practice size: 16+	266 (21.9)

We also obtained the characteristics of Massachusetts clinicians as a whole. During this study period, 45% were in primary care specialties, and 66% were male. These differences compared with e-prescribers were likely due to the fact that high-volume outpatient prescribers were recruited initially for the eRx Collaborative, skewing the populations towards primary care clinicians. Figure 2 displays the uptake of e-prescribing over the study year in terms of both clinicians using the e-prescribing program in that month and the absolute number of e-prescriptions written by month. Use of the e-prescribing system increased steadily during the study period, with over 55,000 e-prescriptions written in March, 2005.

Figure 2. Clinicians e-prescribing and total e-prescriptions written, by month



The results of multivariable models that control for the independent effects of each of the prescriber characteristics on e-prescribing rates over time are shown in **Table 4** (see below). The

models include the 1,056 e-prescribers for whom information on clinician characteristics was available. The left side of Table 5 shows the results for all prescriptions in the data set while the right side shows the same model with prescriptions limited to acute medications. Model output is presented as relative rates, compared to the index group in each category.

Clinician age had a significant independent relationship with e-prescribing. Relative to prescribers younger than 35, those age 45-54 and 55 and over had a 29% lower e-prescription rate for all medications. The difference was greater when the analysis was restricted to acute medications only. Prescribers in the largest practices (16+) had a 36% higher e-prescribing rate than those in practices of 4-8 clinicians, although this finding was not statistically significant in the analysis restricted to acute medications. There was a trend towards more e-prescribing in 9-15 clinician practices. Pediatricians had significantly higher e-prescribing rates than internists, family practitioners, and other specialists both for all medications and acute medications only. When these other factors were controlled for, there was no difference in e-prescribing rates by clinician gender.

Table 5. Results of multivariate models: Impact of clinician characteristics on relative rate of e-prescribing

Variable	All Medications: Relative ERX rate	All Medications: 95% CI	Acute medications only: Relative ERX rate	Acute medications only: 95% CI
Age: 25-34	ref	-	ref	-
Age: 35-44	0.917	[0.743 – 1.32]	0.860	[0.706 – 1.05]
Age: 45-54	0.711	[0.557 – 0.908]	0.622	[0.499 – 0.775]
Age: 55+	0.714	[0.541 – 0.944]	0.664	[0.510 – 0.863]
Practice size: 1	1.217	[0.935 – 1.59]	0.967	[0.743 – 1.26]
Practice size: 2-3	0.832	[0.610 – 1.14]	0.807	[0.602 – 1.08]
Practice size: 4-8	ref	-	ref	-
Practice size: 9-15	1.280	[0.932 – 1.76]	1.24	[1.02 – 1.49]
Practice size: 16+	1.362	[1.07 – 1.74]	1.17	[0.872 – 1.56]
Specialty: Pediatrics	ref	-	ref	-
Specialty: Internal Medicine	0.619	[0.504 – 0.759]	0.450	[0.380 – 0.533]
Specialty: Family Practice	0.800	[0.638 – 1.00]	0.586	[0.468 – 0.733]
Specialty: Other	0.424	[0.327 – 0.550]	0.389	[0.299 – 0.506]
Gender: Male	ref	-	ref	-
Gender: Female	1.041	[0.880 – 1.23]	1.03	[0.879 – 1.22]

Discussion. We found a slow and steady increase in e-prescribing over the 12 months of this study. This suggests that clinicians may have become somewhat more comfortable with e-prescribing as they continued using it, however, it did not appear that a large proportion of clinicians became exclusive – or even majority – e-prescribers. This lack of full uptake may have multiple causes, such as problems with unusual doses or compounded medications, technical issues with the e-prescribing system, inability to access e-prescribing at all practice locations, or clinician preference for paper prescribing. Some medications, such as controlled substances, require a hard copy with actual prescriber signature and thus cannot be e-prescribed. Clinicians were recruited for the e-prescribing program via office practices, but may have written non-electronic prescriptions when practicing in the hospital or in offices other than their primary practice.

We found higher uptake rates at larger practices; it is possible that larger practices have better access to on-site technology support. Prescribers in smaller practices also increased their

e-prescribing over the course of the study, but it is possible that such practices require additional support in order to adopt technology more fully. Older clinicians wrote e-prescriptions at a significantly lower rate than younger clinicians. Younger prescribers may be more comfortable with technology, or may be less established in their prescribing habits and more willing to adopt new systems, this also is a fruitful topic for additional study. Prior research on the diffusion of innovations has focused on the relative advantage of a new technology and its compatibility with the environment in which it is used as key factors influencing adoption.

We found that pediatricians wrote e-prescriptions at a higher rate than clinicians from other specialties. This result was especially striking when we limited the results to medications written for acute indications. Since chronic medication use is less likely among children, it may be easier to detect the uptake of e-prescribing among pediatric patients, but we cannot exclude the possibility that distinctions between pediatricians and other specialists may be driving the differences that we observed.

Conclusions. Clinician use of e-prescribing increased steadily in the first 12 months of an initiative sponsoring e-prescribing systems. Uptake of e-prescribing was only partial, with younger clinicians and pediatricians more likely to use the system. Research to understand why prescribers vary in their use of e-prescribing and to develop techniques to encourage more wide-spread adoption will be an important priority for future studies.

Significance. This is one of the few published studies with data on e-prescribing use in community-based settings.

Implications. Understanding the variation in e-prescribing uptake will assist in developing future interventions.

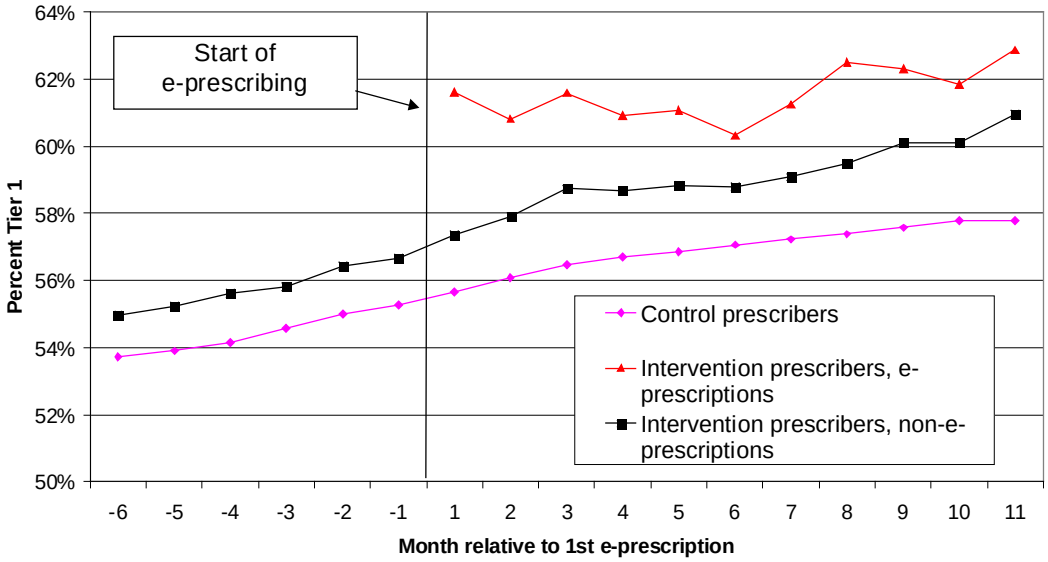
Study #2: E-Prescribing Impact on Cost

Principal Findings. E-prescriptions in the intervention group showed a 6.6% increase in the proportion of Tier 1 drugs (generics) compared to the baseline period, while the control group had an increase of 2.6%. The proportion of drugs in Tier 2 and Tier 3 (brand medications) decreased correspondingly. Multivariate models predicted that e-prescribing would correspond to a 3.3% increase (95% CI 2.7% to 4.0%) in Tier 1 prescribing, controlling for baseline differences between intervention and control physicians and for changes over time. Based on average costs for private insurers, we estimated that full adoption of e-prescribing with FDS could result in savings of $3.91 million per 100,000 patients.

Outcomes. Baseline proportions for the control physicians were 53.2%, 36.4%, and 10.4% in tiers 1, 2, and 3, respectively. Physicians in the intervention group had slightly higher Tier 1 prescribing rate and lower Tier 2 and 3 prescribing rates in the baseline period (54.8%, 35.8%, and 9.4% respectively). After intervention physicians began e-prescribing, Tier 1 prescribing increased sharply for e-prescriptions. During the intervention period, 61.4% of e-prescriptions were in Tier 1, an increase of 6.6% (95%CI, 5.9% to 7.3%) over the baseline proportion, compared with the 2.6% (95%CI, 2.5% to 2.7%) increase in the control group. The Tier 2 prescription rate was 30.6%, a decrease of 5.2% (95%CI, -5.9% to –4.5%) compared with a 2.7% decrease (95%CI, -2.8% to –2.6%) for controls. The Tier 3 proportion was 8.0%, a decrease of

1.4% (95% CI, -1.8% to –1.0%), compared with a 0.2% ***increase*** (95%CI, 0.1% to 0.2%) in controls. None of the confidence intervals overlapped. Including the non-e-prescriptions written by intervention physicians in the analysis moderated the effect of e-prescribing.

The Figure provides a visual depiction of these trends over time relative to when physicians first began e-prescribing, showing that intervention physicians (when not e-prescribing) were more likely than controls to prescribe Tier 1 drugs both before and after the start of e-prescribing, but that when the intervention physicians actually used e-prescribing they prescribed Tier 1 medications at higher rates.



Although the descriptive analyses are highly suggestive, we performed multivariate analyses to account for variable start dates, baseline differences among prescribers, and whether e-prescribing was used or not during the intervention period. These results are summarized in Table 6, which shows the predicted probabilities of medications in each tier during the intervention period, adjusting for temporal trends. The fourth data row of Table 6 shows the baseline differences between intervention and control groups, with the intervention group prescribing 1.4% (95%CI, 0.6% to 2.0%) more Tier 1 medications, 0.3% (95%CI, –0.8% to 0.2%) fewer Tier 2 medications, and 1.0% (95%CI, –1.4% to -0.7%) fewer Tier 3 medications. The fifth data row of Table 3 shows the specific effect of e-prescribing with FDS, controlling for time, baseline differences between groups, and accounting for whether prescriptions were written electronically or non-electronically by intervention physicians. These effects correspond to an increase of 3.3% (95%CI, 2.7% to 4.0%) in Tier 1 prescriptions, a decrease of 1.9% (95%CI, –2.5% to -1.3%) in Tier 2 prescriptions, and a decrease of 1.5% (95%CI, –1.8% to -1.1%) in Tier 3 prescriptions.

Table 6. Predicted prescribing by copayment tier based on e-prescribing status (predicted probability of a prescription being in a given tier, adjusted for month)

	Tier 1 (%)	Tier 2 (%)	Tier 3 (%)
Control	55.0 (54.7, 55.2)	34.5 (34.3, 34.7)	10.5 (10.4, 10.7)
Intervention, non-electronic prescription	56.3 (55.7, 57.0)	34.1 (33.7, 34.7)	9.5 (9.2, 9.8)
Intervention, electronic prescription	59.7 (58.9, 60.5)	32.3 (31.6, 33.0)	8.0 (7.7, 8.4)
Baseline risk difference: intervention vs control	1.4 (0.6, 2.0)	-0.3 (-0.8, 0.2	-1.0 (-1.4, -0.7
Risk difference for intervention physician e-prescribing vs. not e-prescribing	3.3 (2.7, 4.0	-1.9 (-2.5, -1.3)	-1.5 (-1.8, -1.1)

Notes: Values represent the predicted probabilities of an individual prescription being in a given copayment tier, based on the model. The 95% confidence intervals are shown in parentheses and have been adjusted for clustering within prescriber and patient. The first three rows total to 100% across the row. The risk differences in the fourth row estimate the difference in the probability of a prescription being in a given tier between intervention prescribers and control prescribers for prescriptions that were not e-prescribed, representing baseline differences between groups. The risk differences in the last row estimate the difference in the probability of a prescription being in a given tier for prescriptions written electronically compared to non-electronically for prescribers in the intervention group, controlling for all other effects, thus providing an estimate of the impact of e-prescribing.

Table 7. Estimated savings with e-prescription under various cost assumptions

Tier 1 cost	Tier 2 cost	Tier 3 cost	Prescriptions per patient per month	Savings per 100,000 patients per year – Full uptake	Avg of full uptake and 2004-5 uptake	Uptake at 2004-05 level
$ 15	$ 35	$ 60	0.5	$ 619,265	$ 380,753	$ 142,242
$ 28	$ 55	$ 90	0.5	$ 846,924	$ 520,707	$ 194,490
$ 28	$ 80	$ 110	0.5	$ 1,304,422	$ 796,455	$ 288,488
$ 28	$ 115	$ 139	0.5	$ 1,953,653	$ 1,188,041	$ 422,429
$ 15	$ 35	$ 60	1.0	$ 1,238,529	$ 761,507	$ 284,484
$ 28	$ 55	$ 90	1.0	$ 1,693,847	$ 1,041,414	$ 388,981
$ 28	$ 80	$ 110	1.0	$ 2,608,844	$ 1,592,911	$ 576,977
$ 28	**$ 115**	**$ 139**	**1.0**	**$ 3,907,307**	**$ 2,376,082**	**$ 844,857**
$ 15	$ 35	$ 60	2.0	$ 2,477,058	$ 1,523,013	$ 568,968
$ 28	$ 55	$ 90	2.0	$ 3,387,695	$ 2,082,828	$ 777,961
$ 28	$ 80	$ 110	2.0	$ 5,217,689	$ 3,185,821	$ 1,153,954
$ 28	$ 115	$ 139	2.0	$ 7,814,614	$ 4,752,164	$ 1,689,714

Table 7 displays the results for a range of average costs, utilization levels, and rates of e-prescribing uptake. These calculations of the financial impact were based on the percentage changes in prescribing in each co-payment tier (Δ_{T1}, Δ_{T2}, Δ_{T3}), drawn from the results in the final row of Table 4. To calculate the impact on a population, one must incorporate the number of filled prescriptions per-patient per-month (RX_{PMPM}), and average cost for medications in each tier ($\$_{T1}$, $\$_{T2}$, $\$_{T3}$). In the actual calculation is shown in steps 1-3 below.

1. The change in spending per-patient per-month is calculated as follows:
   $(RX_{PMPM} \times \$_{T1} \times \Delta_{T1}) + (RX_{PMPM} \times \$_{T2} \times \Delta_{T2}) + (RX_{PMPM} \times \$_{T3} \times \Delta_{T3})$

2. For example this calculation becomes:
   (1 x $28 x .034) + (1 x $115 x -.019) + (1 x $139 x -.015) = -$3.26 per-patient per-month

3. To project this to larger populations for a full year, the per-month result is multiplied by 12 and by the number of patients in the population. Again, drawing on the example t: -$3.26 x 12 x 100,000 = $3.91 million

The "Savings per 100,000" column presents the main results: potential savings with full adoption of e-prescribing. The right-most column presents the results for e-prescribing at the (relatively low) uptake rate observed in our 2004-05 data, and the second column from the right presents the average of these two results. As the level of e-prescribing uptake increases, the potential savings change linearly in the range shown in the table.

Discussion. We found that physicians who used the e-prescribing system prescribed a higher proportion of Tier 1 medications. Although the size of the effect may appear modest (3.3% increase in Tier 1 medications vs. controls), the potential financial impact is substantial. The size of the financial impact depends critically on the extent to which e-prescribing is utilized. In Massachusetts, the proportion of e-prescribing may well increase over time, since health plans have recently begun offering physician incentives for increased use of e-prescribing (incentives were not in place at the time of this study).

There are several possible explanations for our findings. The modest effect for intervention physicians when not e-prescribing suggests that physicians did not learn from the FDS but required the information at the moment of prescribing. Massachusetts mandates generic substitution by pharmacists, so simple generic substitution is unlikely to explain our findings, suggesting that physicians using the system chose different agents with preferred formulary status. It is possible, though unlikely, that differences in Tier 1 prescribing among intervention physicians when not using e-prescribing resulted from deliberate choices by physicians to use paper when prescribing Tier 2 and Tier 3 medications. Our lack of information on prescriptions that were not written electronically prevents us from exploring this issue in the present analysis. Additional research on how physicians actually use e-prescribing systems will help better understand how these systems achieve the impact that we observed.

Conclusions. We found that an office-based e-prescribing system with FDS at the point of prescribing, used in a cross-section of community practices, could have a significant impact on the prescribing of less expensive medications. This impact was only observed, however, for prescriptions written with the e-prescribing system.

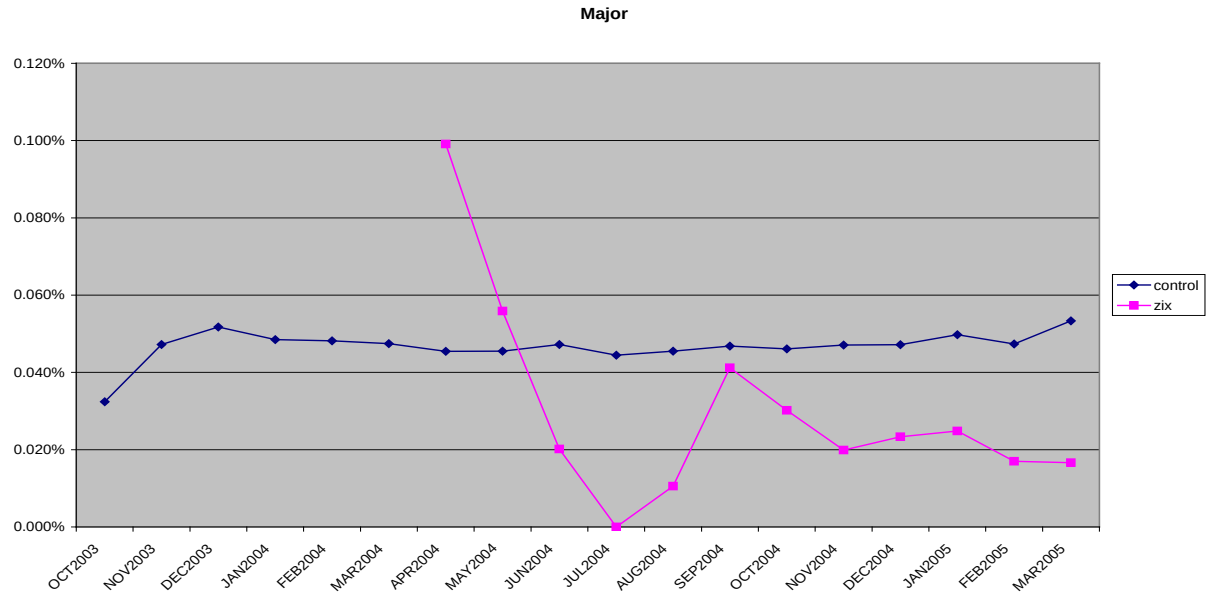
Significance. Our results suggest that there are important economic gains achievable through the broader use of e-prescribing with FDS, but that merely providing e-prescribing systems to clinicians will not necessarily achieve those savings. Rather, prescribers need to adopt the e-prescribing systems fully in order for these gains to be realized. Making those changes represents an important goal for physicians, insurers, and all those with a stake in the cost of prescription medications.

Implications. Physicians using e-prescribing with FDS were significantly more likely to prescribe Tier 1 medications; the potential financial savings were substantial. Widespread use of e-prescribing systems with FDS could result in reduced spending on medications.

Study #3: E-Prescribing Impact on Poor Prescribing Habits

Principal Findings. Current measurements of the impact of e-prescribing on potential drug-drug interactions are limited by measurement problems, but do show a tendency towards reduced frequency of the most serious potential DDIs (defined a "major") with e-prescribing.

Outcomes. The first level of analysis was at the prescription level. In the first several months of e-prescribing the rate of major potential drug-drug interactions was higher than in the control population; however, as we know from our earlier analyses the rate of e-prescribing use in these months was very low. As the number of e-prescriptions increased in later months, the level of major potential DDIs stabilized and was two or more percentage points lower in the intervention group.



Discussion. These initial results suggest a potentially beneficial effect of e-prescribing on safety, but conclusive analyses have not yet been performed. The addition of the Multum data, as described in the Methods section above, will allow for more definitive analysis.

Conclusions. Our conclusions are necessarily tentative at this stage, but the possible signal of increased safety with use of e-prescribing should stimulate further study.

Significance. The ability to measure with accuracy the safety impact of e-prescribing systems will allow for a more complete understanding of their value and allow for insights into how to improve the next generation of software.

Implications. Future research will build on the techniques that we have developed for these analyses and allow for more conclusive studies.

Study #4: E-Prescribing Impact among Persons With Chronic Conditions

Principal Findings. For each of the 4 specific condition cohorts examined (Heart conditions, hypertension, diabetes, pulmonary conditions) as well as other conditions, there were very minor differences between persons in the control and intervention groups. Among persons with pulmonary conditions, those in the intervention group tended to be somewhat older (52.2 years) in comparison to persons in the control group (48.4 years). Among persons with other chronic conditions, those in the intervention groups tended to be older and male. Specific co-morbid conditions and Charleson scores were similar for the intervention and control groups as well for all four chronic condition groups. However the mean number of filled prescriptions tended to be somewhat larger among persons in the intervention group.

Overall 25% of patients with a chronic condition had either a death or a hospitalization in the year following their first e-prescription. However we found no impact of e-prescribing on the risk of death for the four specific chronic conditions of interest or among patients with any chronic condition. Findings remained null when a proportional hazards model that controlled for calendar month was used. Both regressions used Cox hazard models that modeled the change in hazard for persons after the first e-prescription relative to before the first e-prescription. Both models also used combined mortality or hospitalization as the outcome.

Table 8. Adjusted hazard ratios for time to first hospitalization or death for e-prescribers and controls; Standard regression models and proportional hazard models, by condition

Chronic Condition	Model	Ever ERx user: Hazard ratio	Pr>Chi Sq
Diabetes	Regression model	1.010	.8853
Diabetes	Proportional Hazards model	1.071	0.5998
Heart failure	Regression model	1.091	0.5129
Heart failure	Proportional Hazards model	1.114	0.6737
Hypertension	Regression model	1.065	0.1333
Hypertension	Proportional Hazards model	0.935	0.4191
Lung	Regression model	1.117	0.1019
Lung	Proportional Hazards model	0.112	0.4061
Other Chronic condition	Regression model	1.072	0.2239
Other Chronic condition	Proportional Hazards model	1.098	0.3942

Note: Models Control for having an e-prescribing provider, gender, age (18-45, 45-64, 65+), Co-morbid condition, Charlson score. The proportional hazards model includes an additional control for calendar month.

Discussion. There was no impact of e-prescribing on death or hospitalization.

Conclusions. Because of the null findings to this initial analysis this line of inquiry was not pursued.

Significance. See above.

Implications. See above.

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1. Lesar TS, Briceland LL, Delcoure K, Parmalee JC, Masta-Gornic V, Pohl H.Medication prescribing errors in a teaching hospital *JAMA* May 2 1990; 263(17):2329-2334.

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List of Publications and Products

Manuscripts

Michael A. Fischer, Christine Vogeli, Margaret R. Stedman, Timothy G. Ferris and Joel S. Weissman . Uptake of Electronic Prescribing in Community-Based Practices. *Journal of General Internal Medicine*, Vol 23, no 4, 358-363

Fischer MA, Vogeli C, Stedman MR, Lii J, Weissman JS. Primary medication adherence in patients receiving electronic prescriptions. Abstract presentation, April 10, 2008 at Society of General Internal Medicine annual meeting. (manuscript in development)

Fischer, MA, Vogeli C, Stedman MR, Ferris TG, Brookhart AM, Weissman JS. Impact of electronic prescribing with formulary decision support on medication use and cost. *Archives of Internal Medicine*, second review

Fischer, MA, Vogeli C, Stedman MR, Ferris TG, Brookhart AM, Kaushal R, Weissman JS. Impact of electronic prescribing on potential drug-drug interactions. Manuscript in development.

Presentations

Fischer MS. Adoption of electronic prescribing in community-based medical practices. {Oral Presentation. }Annual Meeting of AcademyHealth. Seattle, WA, June 2006.

Weissman JS. Impact of electronic prescribing on use of generic and preferred medications. {Poster}Annual Meeting of AcademyHealth. Seattle, WA, June 2006.

Fischer MS. Adoption of electronic prescribing in community-based medical practices. {Oral Presentation. } 2006 Patient Safety and Health Information Technology Conference: Strengthening the Connections, June 6, 2006.

Weissman JS. "Emerging Research on Patient Safety: Issues of Measurement, Causes, and Evaluation". Kick-off guest lecturer for 2006-7 Seminar Series sponsored by the Center for Health Outcomes Policy and Evaluation Studies, Division of Health Services Management and Policy, Ohio State University. October 18, 2006.

Fischer MS. Impact of electronic prescribing on medication use and cost in community-based practices. Oral Presentation, SGIM, Toronto, April 2007

Weissman JS. "Research on Patient Safety at the Other IHP: Measurement, Causes, and Evaluation". Inst of Health Professions Research Breakfast; April 6, 2007. Boston, MA

Weissman JS. "Impact Of Electronic Prescribing On Medication Use And Cost In Community-based Practices " Roundtable on The Electronic Health Record: From Research to Policy. AcademyHealth Annual Research meeting, Orlando, June 4, 2007.

Final Invention Statement and Certification

There were no inventions conceived or put into practice during the project period.