ORIGINAL RESEARCH

Factors Associated with Ordering Laboratory Monitoring of High-Risk Medications

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BACKGROUND: Knowledge about factors associated with provider ordering of appropriate testing is limited.

OBJECTIVE: To determine physician factors associated with ordering recommended laboratory monitoring tests for high-risk medications.

METHODS: Retrospective cohort study of patients prescribed a high-risk medication requiring laboratory monitoring in a large multispecialty group practice between 1 January 2008 and 31 December 2008. Analyses are based on administrative claims and electronic medical records. The outcome is a physician order for each recommended laboratory test for each prescribed medication. Key predictor variables are physician characteristics, including age, gender, specialty training, years since completing training, and prescribing volume. Additional variables are patient characteristics such as age, gender, comorbidity burden, whether the medication requiring monitoring is new or chronic, and drug-test characteristics such as inclusion in black box warnings. We used multivariable logistic regression, accounting for clustering of drugs within patients and patients within providers.

RESULTS: Physician orders for laboratory testing varied across drug-test pairs and ranged from 9 % (Primidone-Phenobarbital level) to 97 % (Azathioprine-CBC), with half of the drug-test pairs in the 85-91 % ordered range. Test ordering was associated with higher provider prescribing volume for study drugs and specialist status (primary care providers were less likely to order tests than specialists). Patients with higher comorbidity burden and older patients were more likely to have appropriate tests ordered. Drug-test combinations with black box warnings were more likely to have tests ordered.

CONCLUSIONS: Interventions to improve laboratory monitoring should focus on areas with the greatest potential for improvement: providers with lower frequencies of prescribing medications with monitoring recommendations and those prescribing these medications for healthier and younger patients; patients with less interaction with the health care system are at particular risk of not having tests ordered. Black box warnings were associated with higher ordering rates and may be a tool to increase appropriate test ordering.

KEY WORDS: laboratory monitoring; high-risk medications; ambulatory.

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INTRODUCTION

Following the Institute of Medicine's influential report, "To Err is Human,"¹ efforts to improve patient safety and reduce the incidence of medical errors have increased. Errors in monitoring medications constitute a major portion of the medical errors that lead to actual patient harm.² However, reducing monitoring errors is difficult in the absence of evidence about factors associated with ordering recommended laboratory monitoring.

One major challenge to appropriate laboratory monitoring by health care providers is the lack of national guidelines and lack of expert agreement on appropriate monitoring standards.³ However, even when guidelines are introduced, monitoring does not meaningfully improve.⁴ The recommendations that do exist, whether from expert guidelines or product inserts, are not routinely followed.⁵

In past studies of laboratory monitoring, only test completion rates have usually been reported.⁵⁻⁸ These rates capture the combined activities of both ordering a test by a provider and completion of the test by the patient. Using electronic medical records, a distinction can be made between test ordering and test completion, and in some cases ordering rates have been reported^{9, 10}; occasionally, but rarely, both are available.^{11, 12} Capturing these two components of monitoring separately offers the potential for better quality measurement, allowing evaluation of individual provider behavior.¹³ More importantly, it can provide evidence to direct intervention efforts.

We conducted this study to identify provider characteristics associated with ordering recommended laboratory tests for high-risk medications in the ambulatory setting, as well as associated patient and drug-test factors. In past studies of laboratory monitoring, generally only test completion rates were reported, based on administrative

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claims,^{5–8} meaning that a test was either both ordered and completed, or that it was neither ordered nor completed. This study uses electronic medical record data in which the distinction can be made between test ordering rate and test completion rate. The specific aims were to identify factors associated with provider ordering of recommended laboratory monitoring, including age, gender, specialty training, and years in practice for providers and age, gender, comorbidities, and new versus chronic user status for patients, as well as to stratify by evidence level for the testing and to compare the factors associated with ordering tests in each of these subgroups.

METHODS

Study Design and Population

This study was conducted in a large multispecialty group practice that provides most of the medical care for members of a New England-based health plan. The practice uses a widely used, commercially available electronic medical record (EMR) system and provides medical care to approximately 180,000 individuals. The age and gender characteristics of the study population are similar to those of the general population of the United States and include 36 % who are aged 65 years and older.

Inclusion Criteria

We included patients if they received care from the multispecialty group, were 18 years or older, and had insurance coverage from the health plan between 1 January 2007 and 31 December 2008. Patients had to be continuously enrolled during the observation period, not residing in a long-term care facility, and prescribed one of the study medications during 2008.

Selection of Study Medications

The medications included in this study were based on a list of high-risk medications with recommended laboratory monitoring tests developed for a clinical decision support system that was subsequently embedded in the EMR. The development process included a multi-step review process by a national advisory committee as well as local review of a comprehensive list of high-risk medications as described in detail in a previous publication (Table 1).¹² Clinical rules determining test completion (180 days before to 14 days after for a new dispensing, or 365 days before or 14 days after the index dispensing for chronic medications, or 180 days before to 14 days after index dispensing if test was indicated every 6 months) were determined the same

way. Baseline serum medication level for new dispensings was measured from the date of index dispensing to up to 14 days after index dispensing.

Data Sources

Data about medication exposures were derived from the prescription drug claims of the health plan, while data about laboratory test orders were derived from the multispecialty group practice electronic medical record. In cases where a patient had more than one new start of the same drug during the study time frame (no refills or prescriptions for 180 days and then a new prescription), we included the first prescription for that drug only. Each prescription was then linked to laboratory orders for the patient in question during the relevant time period based on date of prescription and a specific time frame for each medication, as well as to demographic and medical information for both the provider and patient. Provider data were drawn from the EMR and an internal provider demographic database; patient data were drawn from the EMR.

Analysis

The outcome was ordered status for a monitoring test, dichotomized as ordered or not for each patient-drug-test combination. Predictor variables were provider characteristics, including gender, age, provider type, primary care provider versus specialist, full-time working status, years of experience, frequency of prescribing a given drug, and number of patients to whom the drug was prescribed. We also analyzed patient characteristics, including age, gender, number of study prescriptions, comorbidities, and visit frequency. Comorbidity was measured using the Charlson score derived from ICD-9 codes.^{14–16} Prescription characteristics, including drug, evidence for testing category/guidelines, whether the drug had single or multiple recommended tests, and testing frequency were also included.

Because physician clinical behavior is affected by level of evidence and guidelines,^{17, 18} and given the lack of clear standards, for this study we focused on a few categories when addressing guidelines. We identified black box warnings (BBWs) on specific medications recommending certain tests. These warnings, which can be required by the Food and Drug Administration (FDA), are the most serious warnings in prescription drug labeling. Even these are inconsistently reported,¹⁹ and adherence is poor even to these warnings,^{20, 21} but they are validated, well disseminated, and the strongest form of guideline available to a practitioner, thus most likely to drive ordering behavior. These drugs are commonly prescribed.²⁰ The BBW category was identified by individually checking whether

Table 1. Study Medications and Recommended Tests and Ordering Rates. Persons Prescribed the Following High-Risk Medications (or Classes) During 2008 Were Included in the Analysis

MEDICATION	TEST	ORDERED %	N
ACE/ARB	BMP	91.26 %	12,713
ALLOPURINOL	CREATININE	91.88 %	973
AMIODARONE	AST or ALT	69.57 %	69
	TSH	72.46 %	69
AZATHIOPRINE	AST or ALT	43.66 %	71
	CBC	97.18 %	71
AZOLE ANTIFUNGAL	AST or ALT	32.33 %	764
CARBAMAZEPINE	AST or ALT	60.22 %	186
	CARBAMAZEPINE	65.59 %	186
	CBC	81.72 %	186
COLCHICINE	CBC	75.16 %	616
	CREATININE	88.15 %	616
CYCLOSPORINE	AST or ALT	72.00 %	25
	CREATININE	72.00 %	25
	CYCLOSPORINE	88.00 %	25
DIGOXIN	CREATININE	65.56 %	906
	DIGOXIN	93.16 %	906
	POTASSIUM	93.27 %	906
DIURETIC-LOOP	BMP or K+Cr	95.62 %	3,103
DIURETIC-NOT-K-SPARING	BMP or K+Cr	75.00 %	36
DIURETIC-POTASSIUM SPARING	BMP or K+Cr	90.08 %	1,592
DIURETIC-THIAZIDE	BMP or K+Cr	90.19 %	8,480
FENOFIBRATE	AST or ALT	68.25 %	504
	CBC	86.31 %	504
GEMFIBROZIL	AST or ALT	82.20 %	955
ISONIAZID	AST or ALT	46.67 %	15
LITHIUM	CBC	41.46 %	41
	CREATININE	48.78 %	41
	LITHIUM	60.98 %	41
	TSH	75.61 %	41
METFORMIN	CREATININE	92.70 %	3,177
METHOTREXATE	AST or ALT	88.26 %	298
	CBC	88.59 %	298
	CREATININE	90.27 %	298
METHYLDOPA	AST or ALT	59.26 %	54
	CBC	62.96 %	54
NEFAZODONE	AST or ALT	55.56 %	9

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Table 1. (continued)

MEDICATION	TEST	ORDERED %	N
NIACIN	AST or ALT	80.72 %	249
PHENOBARBITAL	AST or ALT	36.14 %	83
	CBC	55.42 %	83
	PHENOBARBITAL	69.88 %	83
PHENYTOIN	AST or ALT	58.02 %	293
	PHENYTOIN	75.43 %	293
POTASSIUM	POTASSIUM	95.27 %	1,839
PRIMIDONE	CBC	9.21 %	76
	PHENOBARBITAL	11.84 %	76
	PRIMIDONE	71.05 %	76
QUINIDINE	AST or ALT	22.22 %	9
	CREATININE	77.78 %	9
	POTASSIUM	77.78 %	9
	QUINIDINE	77.78 %	9
RIFAMPIN	AST or ALT	50.00 %	20
STATIN	AST or ALT	84.94 %	16,337
TERBINAFINE	AST or ALT	57.38 %	61
THEOPHYLLINE	THEOPHYLLINE	57.14 %	91
THIAZOLIDINEDIONE	AST or ALT	81.54 %	677
THYROID REPLACEMENT	TSH	73.26 %	5,422
VALPROATE SODIUM	AST or ALT	52.47 %	162
	CBC	53.70 %	162
	VALPROIC ACID	77.78 %	162

Test completion for a new dispensing marked as occurred if there was at least one associated monitoring test ordered 180 days before to 14 days after dispensing, and for chronic dispensing as occurred if there was at least one recommended test for the medication-test pair up to 365 days before or 14 days after the index dispensing in 2008 (or 180 days before to 14 days after index dispensing if test was indicated every 6 months). Baseline serum medication level for new dispensings was measured from the date of index dispensing to up to 14 days after index dispensing

Abbreviations: ACE/ARB Angiotensin-Converting Enzyme Inhibitors/Angiotensin II Receptor Blockers; ALT alanine aminotransferase; AST aspartate aminotransferase; BMP basic metabolic panel; Cr creatinine; K potassium; TSH thyroid stimulating hormone

a given test addresses a drug warning using the online databases listed below (labeling relevant drug-test combinations as BBW). We next identified guidelines by physician practice groups or quality of care organizations with recommendations for monitoring. At the next level, we classified drugs for which there were no clear guidelines, but for which testing was recommended in standard references, specifically UpToDate,²² Micromedex,²³ Pharmacist's Letter,²⁴ and the Physician's Desk Reference.²⁵

Our analytic modeling strategy accounted for multiple prescriptions nested within a patient and multiple patients nested within a provider. The unit of analysis was a prescription-test pair. To account for the complex nature of the data set, which included patients who had

multiple providers prescribing study medications, we developed logistic regression models with a robust covariance estimator (sandwich estimator) to adjust standard errors for clustering. This approach provides conservative nonparametric estimates.^{26–29} We first calculated robust standard errors based on clustering of medications within patient and separately performed calculations based on clustering within providers. The models with patient and provider clustering produced similar parameter estimates, but the models clustered by provider yielded more conservative estimates of the standard errors and we present results for these models. Parameter estimates are reported as odds ratios (ORs) of factors associated with test ordering.

The modeling approach was focused on identifying factors that could be changed through intervention, rather than on obtaining the best predictive model.³⁰ Initial models included all factors hypothesized to be associated with test ordering a priori. Unadjusted models examined relationships between each variable and the outcome of test ordering. We tested correlation between the total number of patient visits in the system the prior year and the Charlson comorbidity score, and found correlation between these variables at the $\sigma>0.40$ level. We chose to include the number of patient visits in our models as both covariates gave similar results. Similarly, prescribing frequency and patient panel size were correlated, and we chose to include only prescribing frequency. We also decided to examine interactions of BBW status with provider specialty and number of study medications per patient, and found a significant interaction of BBW status. Further models were stratified by BBW. Final multivariable models included factors hypothesized to be associated with test ordering a priori and factors associated with test ordering at the $p<0.20$ level in unadjusted analyses. Goodness of fit for the models was examined using the c statistic and receiver operating characteristic (ROC) curve.

Analyses were conducted in SAS 9.2 (SAS Institute, Cary, NC) and StataSE (Stata Statistical Software: Release 11.1, Stata Corporation, College Station, TX, USA). This study was approved by the institutional review boards of the University of Massachusetts Medical School and the multi-specialty group practice.

RESULTS

Patient Population and Use of Medications Requiring Laboratory Monitoring

The study included 31,417 unique patients and 278 providers, for a total of 65,135 medication-test pairs. This included prescriptions for 34 high-risk medications or medication classes, some of which had multiple recommended tests, for a total of 60 medication-test combinations, described in Table 1. Rates of test ordering are also reported by medication and test in Table 1.

Provider Characteristics

Primary care caregivers accounted for about 56 % of the prescribers, including primary care nurse practitioners and physician assistants, as well as physicians. The most frequent specialty was internal medicine. The mean number of prescriptions per provider was 215, with the median being 13 prescriptions. Providers had as few as one or as many as 784 patients to whom they prescribed a study medication, with a median of 11.5 patients. The mean

number of times a study medication was prescribed by a provider was 43, though that ranged from one to 420 prescriptions of the same medication. Forty-seven percent of patients had a single prescription for a study medication and 98 % had four or fewer. Sixteen percent of prescriptions had associated BBWs. Baseline characteristics of patients and providers are described in Table 2.

Multivariable Analysis

The final model included the following variables: provider primary care status, sex, age, patient volume, working status, and experience; patient characteristics including patient age, gender, number of providers, number of study medications, and visit frequency; and prescription type (chronic or new), number of recommended tests, recommended test frequency, and BBW or other evidence level (Table 3).

Prescriptions with BBWs, those for patients who were sicker, and those written by providers who were younger were again associated with ordering. Tests that were to be ordered less frequently in a year were more likely to be ordered, and patients on more than one medication were more likely to have a test ordered, as were male patients. Older patients were more likely to have tests ordered, as were patients with more visits (by quartile) in the study year. There was also a significant interaction between the BBW status and the number of medications a patient was taking, with BBW status having a larger effect among those on more medications.

Table 2. Summary of Provider and Patient Characteristics

Providers		N, of 278 providers
Mean age (years)	48.1	235
Female	42.6 %	275
Physician vs. other kind of prescriber	86.0 %	278
Primary care physician (PCP) vs. specialist	56.3 %	247
Fulltime	74.4 %	195
Years of experience (years since graduation)	20.3	235
Mean number of prescriptions in study	215	278
Patients		31,417
Mean age (years)	66.1	
Female	56.8 %	
Study medications per patient	1.9	
Medication-test pairs		65,135
New vs. chronic use	38.6 % new	
Black box warning	15.6 %	

Table 3. Adjusted Model: Factors Associated with Ordering, Including Stratification by BBW

Variable	Unstratified Fully Adjusted Model N=60,347 OR [95 % CI]	Stratified Models	
		Non-BBW pairs N=51,132 OR [95 % CI]	BBW pairs N=9,215 OR [95 % CI]
Patient gender			
Male	1 [Reference]	1 [Reference]	1 [Reference]
Female	0.83 [0.75 – 0.92]	0.85 [0.76 – 0.94]	0.79 [0.64 – 0.98]
Patient age			
< 40 years old	1 [Reference]	1 [Reference]	1 [Reference]
40–50	1.38 [1.21 – 1.57]	1.14 [0.98 – 1.33]	1.45 [1.12 – 1.88]
50–60	1.74 [1.56 – 1.95]	1.38 [1.21 – 1.57]	1.96 [1.51 – 2.56]
60–70	2.25 [1.95 – 2.58]	1.73 [1.48 – 2.01]	3.06 [2.28 – 4.12]
70–80	2.19 [1.89 – 2.54]	1.68 [1.41 – 2.00]	3.36 [2.57 – 4.39]
≥ 80	2.04 [1.73 – 2.41]	1.59 [1.30 – 1.93]	3.06 [2.29 – 4.08]
Number of patient visits, by quartile			
0–5 visits	1 [Reference]	1 [Reference]	1 [Reference]
6–10 visits	1.65 [1.50 – 1.82]	1.64 [1.48 – 1.81]	2.00 [1.58 – 2.53]
11–18 visits	2.02 [1.78 – 2.30]	2.04 [1.78 – 2.34]	2.38 [1.91 – 2.97]
≥ 19 visits	2.63 [2.26 – 3.06]	2.56 [2.19 – 3.00]	4.54 [3.55 – 5.80]
Number of study medications patient is taking			
Single medication	1 [Reference]	1 [Reference]	1 [Reference]
Multiple medications	1.55 [1.43 – 1.68]	1.55 [1.44 – 1.68]	1.77 [1.46 – 2.14]
Number of providers per patient			
One	1 [Reference]	1 [Reference]	1 [Reference]
More than one	0.98 [0.88 – 1.10]	0.97 [0.87 – 1.09]	1.00 [0.78 – 1.27]
Provider gender			
Male	1 [Reference]	1 [Reference]	1 [Reference]
Female	0.81 [0.58 – 1.13]	0.82 [0.58 – 1.15]	0.82 [0.54 – 1.23]
Provider age			
< 40 years old	1 [Reference]	1 [Reference]	1 [Reference]
40–50 years old	0.80 [0.52 – 1.23]	0.81 [0.51 – 1.27]	0.60 [0.34 – 1.06]
50–60 years old	0.71 [0.40 – 1.28]	0.67 [0.37 – 1.20]	0.86 [0.35 – 2.10]
> 60 years old	0.30 [0.13 – 0.70]	0.30 [0.12 – 0.72]	0.48 [0.14 – 1.64]
Provider specialty			
Specialist	1 [Reference]	1 [Reference]	1 [Reference]
PCP	0.71 [0.45 – 1.10]	1.01 [0.68 – 1.52]	0.30 [0.15 – 0.62]
Patients per provider			
First quartile (1 patient)	1 [Reference]	1 [Reference]	1 [Reference]
Second quartile (2–11)	2.16 [0.93 – 5.02]	2.19 [0.69 – 6.92]	2.33 [0.86 – 6.31]
Third quartile (12–179)	2.77 [1.22 – 6.30]	2.16 [0.72 – 6.51]	4.65 [1.85 – 11.70]

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Table 3. (continued)

Variable	Unstratified Fully Adjusted Model N=60,347 OR [95 % CI]	Stratified Models	
		Non-BBW pairs N=51,132 OR [95 % CI]	BBW pairs N=9,215 OR [95 % CI]
Fourth quartile (≥ 190)	3.38 [1.49 – 7.64]	2.65 [0.87 – 8.02]	5.15 [2.12 – 12.55]
Working status			
Part-time	1 [Reference]	1 [Reference]	1 [Reference]
Full time	1.05 [0.75 – 1.48]	1.13 [0.81 – 1.59]	0.86 [0.53 – 1.39]
Years of experience, per year	1.00 [0.97 – 1.03]	1.00 [0.97 – 1.03]	1.00 [0.96 – 1.04]
Prescription type			
Chronic use	1 [Reference]	1 [Reference]	1 [Reference]
New use	0.52 [0.48 – 0.56]	0.57 [0.52 – 0.62]	0.39 [0.31 – 0.49]
Evidence for test			
Recommended test	1 [Reference]	1 [Reference]	1 [Reference]
BBW	1.78 [1.49 – 2.13]		
Guidelines	1.31 [1.10 – 1.56]		
Test frequency			
Yearly	1 [Reference]	1 [Reference]	1 [Reference]
More frequent	0.38 [0.29 – 0.49]	0.51 [0.39 – 0.65]	0.18 [0.13 – 0.24]
Number of tests recommended for this medication			
Single	1 [Reference]	1 [Reference]	1 [Reference]
Multiple	0.48 [0.40 – 0.57]	0.43 [0.37 – 0.51]	0.62 [0.38 – 0.99]

Abbreviations: BBW black box warning; CI confidence interval; OR odds ratio; PCP primary care provider

Patients with more visits were more likely to have a test ordered (which also served as a proxy for comorbidity index), as shown in Table 3 (OR of 2.6 for top quartile compared to bottom quartile, 95 % confidence interval [CI] [2.26 – 3.06]); The c statistic of the final model was 0.72.

Subanalysis—Stratification. In models stratified by BBW status of the medication-test pair, the relationships of most covariates were similar. However, PCPs were somewhat more likely than specialists to order a test for the non-BBW pairs, though this was not statistically significant. In the medication-test pairs with BBW warnings, PCPs were much less likely to order tests than specialists (OR 0.30, 95 % CI [0.15 – 0.62]).

DISCUSSION

We found associations between several factors and ordering of laboratory monitoring of high-risk medications in the ambulatory setting, most notably the provider specialty status (specialists ordering more often), frequency of patient contacts, provider volume (using either number of patients or frequency of prescribing) and both provider and patient

age (more test ordering was associated with older patients and younger providers). Provider full-time working status and years of experience were not related to ordering rates, after controlling for provider age.

There is little published evidence about physician factors associated with medication test monitoring. Prior studies have shown that barriers to monitoring identified by physicians include lack of clarity regarding which physician was responsible, uncertainty about the necessity of monitoring in the first place, a lack of automated reminders, and physician specialty, as well as patient non-adherence with their recommendations.³¹ However, physician characteristics such as experience and prescribing volume have not been examined, and physician demographics associated with monitoring are relatively understudied. One study found that younger physicians and female physicians were more likely to order potassium tests for patients on diuretics.^{6, 32}

Physician Adherence to Guidelines and Levels of Evidence

One major factor in adherence to monitoring is adherence to clinical guidelines, which is known to be low.^{12, 33, 34} In one study, guidelines in general were followed 67 % of the

time, with large variations between physicians and between guidelines.^{17, 20, 35} When interventions are introduced to target adherence specifically to BBWs, improvement in adherence is limited.²¹ BBWs as a class even among themselves have varying levels of alerts,²¹ perhaps accounting for the low overall adherence rate to monitoring recommendations (below 50 % in one study³⁶), even in this high-risk category.

The reasons for physician non-adherence in general to guidelines are complex. In addition to lack of familiarity with clinical guidelines, research suggests other barriers to guideline adherence include lack of awareness, lack of agreement/expectation of outcomes or benefits, lack of self-efficacy, inertia, concerns about patient adherence and preferences, and other external barriers.^{37, 38} Even when providers are aware of guidelines and want to follow them, the guidelines are often difficult to interpret; for an example in our topic of monitoring, more than half of the BBWs in one study required clarification from a specialist.²⁰ In some cases, providers may doubt the credibility or applicability of guidelines, particularly with proscriptive guidelines,³⁹ and perhaps with good reason, as noted above. However, even good evidence and good source credibility do not ensure adherence.⁴⁰ Furthermore, when monitoring guidelines do exist, the appropriate test frequency is often unknown, with recommendations including language like “periodically” or “routine.”²³ The implications of the lack of good guidelines is concerning and needs remedy; some have recommended increasing frequency of updating guidelines,⁴⁰ though that is sometimes difficult to do when based on large studies. Many guidelines address situations that are not well positioned for randomized trials, including, for example, frequency of testing for frequently prescribed medications, so the evidence is difficult to improve. It is for this reason that we used an expert system to determine our ultimate list of recommendations; the existing literature was too inconclusive.¹²

However, as our study showed, when there is a strong recommendation, providers’ behavior changes. While a study of black box warnings concluded that the oldest patients, healthier patients, and patients at a hospital-based clinic were prescribed medications in violation of BBW at a higher rate than others,²¹ we found the odds ratios for test ordering to be significantly higher for BBW in older patients and in those on more medications. This is further evidence for the importance of a system to evaluate and rate monitoring guidelines; like the U.S. Preventive Services Task Force levels applied to clinical guidelines, so too should monitoring parameters have ratings for the level of evidence supporting the recommendation as well as indicating the source.

Lastly, it should be noted that a significant portion of test non-completion is due to patients not completing ordered tests.⁴¹ Physician quality metrics should always take into account ordering and completion rates separately, rather than just overall test completion, to best capture physician behavior.¹³

Volume

Surgical literature has long shown an association between procedure volume and outcomes. Recent work on quality indicators also suggests an association between frequency of prescribing or treating and associated quality indicators.⁴² Volume has been shown to correlate with better outcomes in other settings, such as surgery,^{43–45} and generally, volume is associated with better adherence.⁴⁶ Our results show a relationship between number of patients or frequency of prescribing and ordering rates, suggesting familiarity with a medication increases adherence to testing guidelines, with providers with the top quartile of patient load 3.4 times as likely to order a test as those in the bottom quartile (95 % CI [1.5 – 7.6]). Whether measured by patient panel size, as shown in Table 3, or by other measures of volume such as prescription number and frequency of prescribing a specific medication, which we included in additional analytic models, the providers in the top quartile of volume were between two and four times as likely to order a recommended test ($p < 0.01$). Volume appears to be significantly associated with test ordering.

Specialists Versus Generalists

Specialty has been shown to be associated with clinical behavior in providers,^{47–49} and past research has found that specialists showed greater adherence to expert guidelines.^{47–50} In models stratified by evidence level, we found that specialists were more likely to order tests in those medication-test pairs with stronger warnings (BBW).

Limitations of our study should be noted. The group practice was an early adopter of electronic medical records and computerized physician order entry, and this is likely to have an impact on ordering of laboratory monitoring. The providers represent a range of experience and specialties, but employees of a multispecialty group practice may differ from private practitioners and hospital-based providers. We may have missed monitoring that was done outside our system,⁵¹ and we were unable to confirm patient adherence to medications. We used claims data of medication dispensing from the insurer to identify medication use, to avoid including prescriptions that patients had not filled. However, these data may not have included all medications if patients also used special discount programs. The study only included specific medications, and again only data within our system, thus perhaps leading to some of the imbalances seen between the mean and median in some of the distributions; this skewed distribution is another limitation.

A major strength of this study is its data source: the electronic nature of the records allowed us to track a medication from prescription through test ordering.^{52, 53} Furthermore, because we have information about both providers and patients in an electronic system, we have been able to study associations with test ordering that have not been previously reported, such as provider specialty, provider volume, and years of practice. We were able to directly link providers with their prescriptions and their patients along with orders and their completion.

CONCLUSION

This study had novel findings in factors associated with test ordering in ambulatory patients taking high-risk medications. Younger patients and those with fewer interactions with the health care system were less likely to have testing ordered, and ordering was higher for medication-test combinations with black box warnings. This higher rate for BBW combinations suggests that these warnings have permeated provider consciousness, and suggests a role for provider education and reminders in improving test ordering, particularly as specialists had higher ordering rates as well, and argues for a clearer system of delineating the source and strength of evidence behind monitoring guidelines.

Further research will benefit from our approach of analyzing ordering and completion separately, allowing for separate conclusions regarding factors contributing to provider behavior and patient behavior. Evidence-based interventions would focus on target areas with the lowest rates or those with the greatest potential for improvement; including providers most who have less familiarity prescribing a given medication, given the role of volume in ordering rates, and medications with the greatest risk of harm. Patients with less interaction with the health care system are also at risk of not having tests ordered, and their providers should be reminded of the need to administer monitoring tests. With more complete data and better systems in place, we can achieve the high rate of medication monitoring desired to keep patients safe.

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