Pharmacist Workload and Pharmacy Characteristics Associated With the Dispensing of Potentially Clinically Important Drug-Drug Interactions

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Background: Drug-drug interactions (DDIs) are preventable medical errors, yet exposure to DDIs continues despite systems that are designed to prevent such exposures. The purpose of this study was to examine pharmacy characteristics that may be associated with dispensed potential DDIs.

Methods: This study combined survey data from community pharmacies in 18 metropolitan statistical areas with pharmacy claims submitted to 4 pharmacy benefit managers (PBMs) over a 3-month period from January 1, 2003 to March 31, 2003. Pharmacy characteristics of interest included prescription volume, the number of full-time equivalent pharmacists and pharmacy staff, computer software programs, and the ability to modify those programs with respect to DDI alerts, the use of technologies to assist in receiving, filling and dispensing medication orders, and prescription volume. The dependent variable in this study was the rate of dispensed medications that may interact.

Results: A total of 672 pharmacies were included in the analysis. On average ($\pm$SD), the respondents filled 1375 $\pm$ 691 prescriptions per week, submitted 17,948 $\pm$ 23,889 pharmacy claims to the participating PBMs, had 1.2 $\pm$ 0.3 full-time equivalent pharmacists per hour open, and 545 (81%) were affiliated with a chain drug store organization. Factors significantly related to an increased risk of dispensing a potential DDI included pharmacist workload (odds ratio [OR] 1.03; 95% confidence interval [CI] 1.028–1.048), pharmacy staffing (OR 1.10; 95% CI: 1.09–1.11), and various technologies (eg, sophisticated telephone systems, internet receipt of orders, and refill requests) that assist with order processing, and the ability to modify DDI alert-screening sensitivity and detailed pharmacological information about DDIs.

Conclusions: This study found that there was an increase in the risk of dispensing a potential DDI with higher pharmacist and pharmacy workload, use of specific automation, and dispensing software programs providing alerts and clinical information.

Key Words: drug-drug interactions, medication safety, workload, pharmacist, medical errors

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The Institute of Medicine's reports on the quality of health care in the United States have highlighted the importance of reducing medical errors.[1-4] Drug-drug interactions (DDIs) are a subset of preventable errors; pharmacists are in a unique position to identify and intervene. Commonly, within community pharmacies, computer software programs assist pharmacists in identifying DDIs of potential clinical importance (hereafter termed potential DDIs). Software algorithms that identify potential interactions are often based on rules developed by proprietary companies such as First DataBank and Medi-Span; these algorithms may be modified by pharmacists or pharmacy software developers. In the normal process of entering prescription information into computer systems, alerts are generated when 2 medications in a patient's profile may interact. Previous studies have found that some pharmacists have become desensitized to the alerts and spend little time evaluating them.[5,6] As a result of decreasing manpower,[7] pharmacists may be required to process prescriptions at higher rates, thus reducing their ability to adequately assess potential DDIs.

Few studies have been conducted to identify pharmacy factors that might be related to higher rates of patient exposure to potential DDIs. The purpose of this study was to examine pharmacy operational characteristics and rates of dispensed potential DDIs in community pharmacies. A DDI occurs when 1 drug causes the modification of another drug, resulting in a physiological change in response to the interaction.[8] The administration of 2 medications that may interact does not always manifest as a true DDI. Some change in physiological processes or other activity must occur for a true interaction to be present. Consequently, this study refers to pharmacy claims data indicating that 2 medications obtained by the same patient could lead to an interaction. We refer to this as a "dispensed potential DDI."

METHODS

This study examines the relationship between the rate of dispensed potential DDIs and operational characteristics in community pharmacies. Pharmacy claims data submitted to 4 large pharmacy benefit managers (PBMs) were combined with survey data from community pharmacies. Participating PBMs represented approximately 120 million covered lives in the United States at the time of this study. The research was approved by the University of Arizona Human Subjects Protection Program.

Pharmacy Sample

A postal survey was used to obtain data from community pharmacies in 18 distinct metropolitan statistical areas (MSAs) or consolidated MSAs (CMSAs) in the United States (Atlanta, GA; Austin, TX; Baltimore, MD; Chicago, IL; Dallas-Ft. Worth, TX; Denver, CO; Detroit, MI; Houston, TX; Los Angeles, CA; Miami, FL; Minneapolis, MN; New York/New Jersey/Long Island; Philadelphia, PA; Phoenix, AZ; San Diego, CA; Seattle, WA; St. Louis, MO; and Washington, DC). These MSAs were selected based on the theory that pharmacies in large metropolitan areas are more likely to have a greater proportion of their prescriptions paid for by third-party payers than pharmacies located in rural areas. In addition, costs of obtaining the pharmacy sample and survey mailing expense were factors in limiting the study to these MSAs. A list of 18,596 community pharmacies with a valid National Council for Prescription Drug Programs (NCPDP) Inc. identification number in these 18 areas was obtained from American Medical Information, a proprietary medical marketing company. The NCPDP number for these community pharmacies was then sent to the participating PBMs to select pharmacies with at least 500 prescription claims submitted during June and July of 2003, which reduced the eligible sample to 9523 pharmacies. A stratified random sample of 3000 community pharmacies was selected from this list. Community pharmacies were stratified by MSA/CMSA with a minimum of 100 pharmacies selected from each area to ensure adequate representation.

Pharmacy Survey

A survey instrument specific to this study was developed, tested in a focus group, piloted, and revised based upon the comments received.[9,10] The final survey instrument contained 34 items and covered the following 4 topics: (1) workload issues, (2) use of technology in prescription processing, (3) handling of DDIs and alerts, and (4) pharmacists' attitudes toward computerized DDI alerts. In particular, 1 question asked if pharmacy personnel could customize the DDI alert levels and another asked whether the software provided detailed clinical information about DDIs (eg, mechanism of interaction and alternative therapies to suggest to prescribers). The results related to the pharmacists' attitudes toward DDI alerts are reported elsewhere.[9]

All correspondence to the community pharmacies was addressed to the pharmacy manager. The survey process included an announcement postcard, followed by the distribution of the questionnaire, a reminder postcard, and finally a second mailing of the questionnaire. Chain organizations represented in the study were contacted and asked to provide a letter of support for the study. Fifteen chain organizations provided a letter of support that was sent to 555 pharmacies.

PBM Data

For survey respondents, the pharmacy NCPDP numbers were sent to the participating PBMs to determine the number of potential DDIs dispensed at that pharmacy. Twenty-five DDIs of interest based on work previously conducted by the investigators were evaluated.[11,12] The participating PBMs ran a standard DDI algorithm developed by the research team for pharmacy claims submitted from January 1, 2003 to March 31, 2003. Results from the algorithm were provided to the research team and aggregated across the PBMs. Data were provided at the pharmacy level, including the number of dispensed potential DDIs and total prescription claim volume over the 3-month period of interest.

Data Analysis

In the data analysis we first describe the sample in terms of pharmacy personnel and operational characteristics. Data from the surveys were examined for out-of-range values and missing data. Analysis of pharmacy characteristics measured on a continuous scale was conducted using descriptive statistics. Chain pharmacies were defined as 4 or more pharmacies under the same ownership. For questions concerning the use of technology the response choices of, "Yes," "No," or "Not sure" were collapsed into 2 categories (ie, yes or no/not sure). The presence of (1) a tablet/capsule counting machine, (2) Baker cell or similar vial filling device, (3) computerized control of an automated filling device, (4) a filling device that automatically attaches a label to a vial/package, and (5) a bar code scanner for medication verification was transformed from yes/no to an ordinal scale ranging from 0 (no technology) to 5 (all 5 types of technology). Additional detail on the distribution of technologies in these pharmacies is reported elsewhere.[10]

The next step in the analysis was to create summary measures of prescription volume, adjusted for pharmacist staffing. This was done by calculating a ratio of the reported prescriptions processed per week divided by the hours the pharmacy was open per week. The product was then divided by the total number of pharmacist hours per week. A similar ratio was created by dividing prescriptions per hour by the sum of all pharmacy staffing (pharmacists, technicians, interns, and nontechnician supportive personnel) hours per week.

We then examined predictors of dispensed potential DDIs which were evaluated using a Poisson regression model, with the exposure variable being the number of prescriptions dispensed. The multivariate model adjusted for the following covariates: prescriptions per pharmacist hour; prescriptions per pharmacy staff hour; ability to customize computer generated DDI alerts; presence of software that provides detailed information about DDIs; presence of automated telephone and fax systems for new drug orders; ability to receive prescriptions via the internet; number of pharmacy terminals; affiliation to a chain pharmacy organization; and ordinal scale pertaining to the presence of technology to assist in filling prescription orders.

In addition, those pharmacies falling into the 10th and 90th percentile of dispensing potential DDIs were compared to determine if any pharmacy characteristics differed between the 2 groups. Statistical analyses were conducted using SAS 9.0 (SAS Institute; Cary, NC) and Stata 9.0 (StataCorp; College Station, TX). A type I error rate of 0.05 was chosen a priori as the level of statistical significance.

RESULTS

A total of 755 usable surveys were returned, resulting in an overall response rate of approximately 25%. Comparisons were made between respondents and nonrespondents with respect to geographical location, ownership status (chain or nonchain), and prescription claim volume to the participating PBMs. There was no difference between respondents and nonrespondents with respect to ownership status ($P = 0.92$) or prescription claim volume ($P = 0.19$). There was a statistically significant difference between the 2 groups with respect to geographical region, with respondents more likely to be located in Denver and Phoenix. Low response rates were observed from Miami, Philadelphia, and Washington DC. To determine if response rate may have been influenced by the inclusion of a letter of support for the study from management, we examined the proportion of surveys sent with such a letter and geographical location. There was no clear relationship between those regions that had a higher proportion of pharmacies with a letter of support and response rate. For example, a letter of support was included in over 20% of sampled pharmacies located in Philadelphia and Washington, whereas 19% of pharmacies located in Denver and 36% of pharmacies located in Phoenix had such letters.

From the 755 respondents, 19 failed to report information for all the variables of interest. An additional 61 pharmacies did not have any prescription claims (and by definition no dispensed potential DDIs) from the participating PBMs during the observation period. Both of these groups were excluded. Three pharmacies had more than 1000 potential DDIs reaching their patients in the 3-month study period, which was more than twice the number of any other pharmacy. Because these pharmacies had outlier rates of DDIs, they were excluded from the primary analysis, but included in a secondary analysis to determine if the results changed.

Pharmacy personnel and operational characteristics are shown in Tables 1 and 2. On average, there were more technician hours per week (113.6 ± 71.5) than pharmacist hours (97.3 ± 37.2). In terms of pharmacist workload, the mean number of prescriptions processed per pharmacist hour was 14.1 ± 4.9.

Most pharmacies in the sample (81.1%) were part of pharmacy chain organizations (Table 2). Most pharmacies reported that they could not customize DDI alerts, but a slight majority (56.1%) indicated that their software programs could provide detailed information about particular DDIs. Most pharmacies used some automation to assist in the repackaging and dispensing of prescription drugs, but few pharmacies had integrated filling and labeling devices. Descriptive statistics related to prescription volume, pharmacy claims, and rates of the 25 DDIs of interest are shown in

TABLE 1. Pharmacy Personnel (n = 672)

Item	Mean	Standard Deviation	Median	Range
Pharmacist hours per week	97.3	37.2	86	36–328
Technician hours per week	113.6	71.5	100	1–507
Pharmacy intern hours per week	10.5	21.8	0	0–220
Other support personnel hours per week	28.4	54.8	0	0–508
Prescriptions per pharmacist hour	14.1	4.9	13.8	2.9–41.5
Pharmacist FTEs per hour open	1.2	0.3	1.1	0.9–5.3
Pharmacy staff FTEs per hour open	3.2	1.5	2.9	1–14.3

TABLE 2. Pharmacy Operation Characteristics (n = 672)

Item	Yes (%)
Pharmacy belongs to a chain	545 (81.1)
Computer software allows customization of drug-drug interaction alerts	201 (29.9)
Computer software provides detailed information on drug-drug interactions	377 (56.1)
Pharmacy accepts new prescriptions via automated telephone system	417 (62.0)
Pharmacy accepts new prescriptions via fax	571 (85.0)
Pharmacy accepts new prescriptions via internet	230 (34.2)
Pharmacy has a patient operated telephone refill request system	536 (79.8)
Pharmacy has a patient operated internet refill request system	407 (60.6)
Pharmacy has a counter top tablet/capsule counting device	420 (62.5)
Pharmacy has a Baker cell or similar device	126 (18.7)
Pharmacy has computerized control of an automated filling device	71 (10.6)
Pharmacy has a device to automatically attach a prescription label to a vial/package	33 (4.9)
Pharmacy has a bar code scanner for medication identification/verification	364 (54.2)

Table 3. In general, the pharmacies in this study were fairly busy, filling an average of 1375 ± 691 prescriptions per week. In addition, the number of pharmacy claims submitted by respondents to the participating PBMs was almost 18,000 over a 3-month period, with a range of 64 to 179,233. In contrast, the average number of potential DDIs of interest dispensed to patients during this same period was lower (32.1 ± 56.3).

Results from the Poisson model examining factors related to dispensed potential DDIs are shown in Table 4. Pharmacist workload, overall pharmacy workload, and automated telephone systems for prescription orders were significant predictors of higher numbers of dispensed potential DDIs. The results indicate that the relative risk for dispensing a potential DDI increases by just over 3% (odds ratio [OR] 1.03; 95% confidence interval [CI] 1.028–1.034) for each additional prescription processed per pharmacist hour. The

TABLE 3. Prescription Volume, Pharmacy Claims, and Dispensed Potential Drug-Drug Interactions

Variable	Mean	Standard Deviation	Median	Range
Prescriptions filled/wk	1375	691	1251	230–5,040
Prescription claims to PBMs (over 3-mo period)	17,948	23,889	9649	64–179,233
Dispensed potential drug-drug interactions	32.1	56.3	12	1–548
Dispensed potential drug-drug interactions per pharmacy claim (%)	0.19	0.3	0.13	0.001–6.25

TABLE 4. Pharmacy Characteristics as Predictors of Potential Drug-Drug Interactions

Characteristic	Relative Risk	Lower 95% Confidence Interval	Upper 95% Confidence Interval
Prescriptions per pharmacist hour	1.03	1.028	1.034
Prescriptions per pharmacy staff hour	1.10	1.09	1.11
Ability to customize drug-drug interaction alerts	1.23	1.19	1.26
Pharmacy software provides detailed information about drug-drug interactions	0.89	0.86	0.96
Pharmacy has automated telephone system for new drug orders	1.46	1.41	1.50
Pharmacy has fax for new drug orders	0.97	0.93	1.01
Pharmacy can receive new drug orders via intranet	0.87	0.84	0.90
Pharmacy has patient operated refill request via telephone	1.21	1.15	1.28
Pharmacy has patient operated refill request via internet	0.83	0.80	0.86
Number of computer terminals in pharmacy	0.93	0.91	0.93
Belongs to a chain pharmacy organization	1.02	0.97	1.08
Pharmacy automation of filling/dispensing	0.98	0.96	0.99
Geographical area	0.93	0.92	0.94

LR χ^2 = 5023, $P < 0.001$, Pseudo R^2 = 0.16.

results suggest that as pharmacists become busier, they have less time to evaluate DDI warnings or to act on those warnings. Pharmacy staffing (pharmacist, pharmacy technician, and other supportive personnel) was also significantly related to dispensed potential DDIs (OR = 1.10; 95% CI 1.09–1.11). Other pharmacy characteristics related to efficient prescription order processing also were significant predictors as well, except for fax prescription order receipt and pharmacy ownership. These findings suggest that as pharmacies process more prescriptions per hour, they are more likely to dispense more potential DDIs per prescription processed. There was no significant change in the results when the 3 outlier pharmacies were included in the analysis. We also assessed the model for multicollinearity and found the variance inflation factor values did not exceed 1.85, indicating a low degree of multicollinearity.

To further investigate differences between pharmacies that had low rates of dispensed potential DDIs when compared with those with high rates, pharmacies with less than 2 (n = 67, 10.1%) dispensed potential DDIs per 1000 pharmacy claims and pharmacies with more than 50 (n = 73, 10.5%) dispensed potential DDIs per 1000 pharmacy claims were examined. Table 5 displays comparisons between pharmacies with low and high rates of dispensed potential DDIs with respect to pharmacist workload and pharmacy charac-

teristics. Significant differences exist with respect to the pharmacist workload between the 2 groups, with stores having higher prescriptions per pharmacist hour being associated with an increased likelihood of dispensing potential DDIs. There was no difference between low and high pharmacies with respect to the ability to customize DDI alerts ($P = 0.68$), but there was a significant difference between the 2 groups with respect to whether detailed DDI information was provided by their computer systems ($P = 0.008$). Pharmacies with higher rates of dispensed potential DDIs were more likely to have computer systems that provide detailed DDI information when compared with pharmacies with low rates of dispensed potential DDIs.

DISCUSSION

This study found that pharmacist workload, as determined by the number of prescriptions dispensed per pharmacist work hour, was significantly associated with rates of dispensed potential DDIs. Other pharmacy characteristics, such as total pharmacy staffing levels and automation, were also significant predictors of dispensed potential DDIs. The findings are intuitive because pharmacies attempt to become more efficient in order processing once prescription volume exceeds existing capacity. Unfortunately, implementation of

TABLE 5. Pharmacy Volume and Pharmacist Workload Among Low and High Rates of Dispensed Potential Drug-Drug Interactions

Item	10th Percentile Pharmacies		90th Percentile Pharmacies		
	Mean	Standard Deviation	Mean	Standard Deviation	*P*
Prescriptions per week	1285	614	1566	648	<0.0094
Prescriptions/pharmacist hour	13.7	4.6	17.0	5.5	0.0002
Pharmacies that can customize DDI alerts	19	28.4	23	31.5	0.68
Dispensed potential drug-drug interactions per prescription claim (%)	0.12	0.04	9.99	4.68	<0.0001

automation and other pharmacy staffing may not sufficiently compensate for the increased pharmacist workload, leading to an increased risk of dispensing a potential DDI. This finding is consistent with other reports concerning workload and medication errors.[13]

Prescription volumes in community pharmacy settings have risen at phenomenal rates since the mid-1990s, from slightly over 2 billion prescriptions in 1994 to almost 3.3 billion in 2004.[14] This is driven by a multitude of factors, including a greater number of unique medications, an increase in the overall population, an increasing number of elderly patients who take more medications per person, and increasing availability of prescription drug insurance. Meanwhile, the number of pharmacists in the United States has not kept pace with this trend; the number of prescriptions dispensed annually per community-based pharmacist increased from 16,500 in 1992 to 22,200 in 2000.[15] Numerous reasons have been cited for the pharmacist shortage, including the expansion of pharmacists' practice roles, development of alternative practice settings, limited use of automation, inefficient work flow, and increased proportion of part-time pharmacists.[15] Another complicating factor is that there are many more pharmacies opening annually and more pharmacies are staying open 24 hours a day. The shortage has reportedly resulted in 64% of the US population living in states where there was moderate difficulty in filling pharmacist positions.[7] Interestingly, recent data on pharmacist workforce indicate that overall there has been little change in hours worked by male and female pharmacists.[16] On the other hand, pharmacists' personal prescription workload has increased from 2000 to 2004 with almost half (47%) of surveyed pharmacists reporting that their workload was high or excessively high.[17] Forty-three percent of pharmacists indicated that workload had a negative impact on the opportunity to reduce potential errors. The increased workload may contribute to additional medical errors and DDIs, although the relationship between the pharmacist shortage and occurrence of medical errors is not well established.[18] Although anecdotal evidence suggests increased risk of patient harm,[19] no large scale studies in community pharmacies have been conducted.

The relationship between clinical pharmacy services in hospitals and medication errors, mortality, and costs has been evaluated in a series of articles by Bond and colleagues.[20–24] These researchers found an inverse relationship between availability of clinical pharmacy services and number of medical errors.[24] Most striking was that a comparison of the 10th to 90th percentile in terms of clinical pharmacist staffing found a difference in medication errors of 286%. Another study by the same authors found a statistically significant reduction in inpatient mortality among hospitals with provision of certain types of clinical pharmacist services.[21] Other studies have also found that inclusion of clinical pharmacists in hospital settings can reduce medication errors and adverse drug events.[25–27]

Similar to pharmacists, excessive workload is associated with higher rates of medical errors for other health professionals.[28,29] Aiken and colleagues studied the patient-to-nurse ratio in California hospitals and found that the risk of 30-day mortality or failure to rescue (defined as deaths within 30 days of admission among patients who experienced complications) during hospitalization increased by 7% for each additional patient per nurse.[28] Other studies have found similar relationships between nursing workloads and patient safety.[29] Consequently, some states now dictate minimum nurse-to-patient ratios by licensed nurse classification and by hospital unit.[30]

Other factors may contribute to higher rates of dispensed potential DDIs. Previous research has found that pharmacists and physicians have difficulty recognizing potential DDIs.[31–33] Widespread use of pharmacy computer systems to screen for DDIs seems to be a powerful mechanism to identify lapses in detection by pharmacists and prescribers. However, many pharmacy computer systems fail to recognize clinically important DDIs[34,35] and pharmacists frequently override DDI alerts.[5,6] To our knowledge, there have been no other published reports that examine the relationship between dispensed potential DDIs and pharmacy characteristics except those related to pharmacy software systems.[36]

The extent of harm induced by DDIs is largely unknown. Several studies have found the prevalence of clinically significant potential DDIs to be relatively low. A study using data obtained from a single PBM found that the rate of clinically important DDIs occurred at a frequency of 0.04% of all pharmacy claims dispensed.[37] Although the overall rate is relatively low, it is important to note that yet another study evaluating the same 25 interactions found that rates of potential DDIs varied substantially by medication pairs and by patient age.[38] For some interactions, such as warfarin and

nonsteroidal anti-inflammatory drugs, the prevalence was as high as 243 per 1000 persons using warfarin. In this study it was not possible to link dispensed potential DDIs to actual patient outcomes, however, researchers have found that DDIs contribute to significantly higher rates of hospitalizations.[39–43] In some cases, exposure to DDIs can be lethal.[44,45]

The ability of pharmacists to multitask in busy settings has not been well studied. However, it is well known among pharmacists in community settings that interruptions are the norm. The ability to complete a task without being interrupted is limited by telephone calls from physicians or patients and questions from pharmacy support personnel or in-store customers. Frequent interruptions can have a significant effect on memory[46]; interruptions may result in loss of concentration, leading to medical errors.[47] Interruptions may also lead to a reduction in the ability of a pharmacist to appropriately follow-up on DDI alerts. This study controlled for some factors that would decrease the likelihood of interruptions and affect the rate of dispensed potential DDIs (eg, automated telephone systems for new and refill orders and internet receipt of new prescription orders). However, these factors were statistically different between pharmacies with high or low numbers of potential DDIs. Additional research is needed to investigate the impact of interruptions on the ability of pharmacists to process medication orders error-free.

There are several limitations that should be kept in mind when interpreting the results of this research. This study examined dispensed potential DDIs, but the actual patient outcomes associated with exposure to DDIs were not evaluated. Therefore, the degree of harm induced by DDIs is likely to vary according to a number of factors (eg, patient characteristics, appropriate monitoring, patient education, physician knowledge, etc). Another limitation is that this study captured potential DDIs associated with billing a third-party payer (ie, a PBM), and did not capture all prescriptions dispensed by respondents; most prescriptions (83.6%) are associated with a claim to a PBM.[48] The relatively low response rate for this study is a concern. Thus, any findings may be subject to nonresponse error. Differences in response rates by geographical region were observed. The reason for these differences is not known, but may be due to pharmacies in Western states being more familiar with the investigators or the institution conducting the study. Another possible explanation is that pharmacies located in Eastern cities have a higher prescription volume and had less time to complete the survey. The Poisson regression models included numerous covariates, of which 2 were nonsignificant: (1) chain affiliation, and (2) the ability to receive new medications orders via facsimile. It is possible that the lack of significant findings may be a function of study power, leading to a type II error. The analysis included several pharmacy characteristics that are known to be related to prescription volume.[10] As such, control variables were included in the Poisson model although they were not of primary interest.

CONCLUSIONS

This study found that there was an association between dispensed potential DDIs and the number of prescriptions processed per pharmacist hour, overall pharmacy full-time equivalent staff levels, and other pharmacy characteristics that assist in the efficient dispensing of medications. This finding suggests that high workloads may lead to higher rates of exposure to potential DDIs. Future research is needed to confirm these findings and also to evaluate workflow and technological interventions that may reduce rates of dispensed potential DDIs.

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