A Prescription For Appropriate Antibiotics Usage: Physicians and Pharmacists Collaborate Within a Workplace Health Center

Sharon Frazee, PhD[1], Pamela Ryan, RN BSN MHA CPHQ CCM[2], Rochelle Broome, MD FAAFP[3], Raymond Fabius, MD[4], James Manfred, RPh[5]

[1]VP Health Informatics, CHD Meridian Healthcare, Nashville, TN
[2]SVP Medical Management, CHD Meridian Healthcare, Albany, NY
[3]VP, Corporate Medical Director, CHD Meridian Healthcare, Nashville, TN
[4]President and CMO, CHD Meridian Healthcare, Chadds Ford, PA
[5]RPh, CHD Meridian Healthcare, Nashville, TN

ABSTRACT

Objective: Rising healthcare costs, particularly in prescription drug spending, are of great concern to self-insured employers and other healthcare payers. There is much concern especially among employer purchasers that this increased spending is not associated with healthcare improvement yielding greater value. Worksite-based health facilities that integrate primary care and pharmacy provide a unique opportunity to reduce costs and improve patient outcomes. This study illustrates how antibiotic prescribing can be improved through programmatic collaboration of physicians and pharmacists at the workplace.

Methods: This retrospective cohort study tests whether workplace health center treated patients receive a higher prescription rate of first-line antibiotics than community-treated patients over a three-year period.

Results: Dramatic differences were found between workplace-treated patients and community treated patients. Workplace-treated patients had much higher rates of first-line antibiotic use than community-treated patients. First-line antibiotics were associated with an average nearly $20 less per prescription than community-treated patients.

Conclusion: Employers concerned with providing clinically optimal care while managing prescription drug costs should consider the use of collaborative workplace health centers that provide medical and pharmacy services.

KEY WORDS: Antibiotic Prescribing; Prescriptions, Drug; Outcome and Program Assessment; Employer Health Costs; Antibiotic Resistance

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INTRODUCTION

Antibiotics have dramatically changed the ability of healthcare providers to fight infection. The therapeutic value of penicillin was discovered in the 1930s and saw widespread use during World War II.[1] The development of other antibiotics quickly followed and the use of antibiotics increased dramatically over the next 60 years. Today, largely because of increased public health efforts to educate clinicians about the dangers of over-prescribing antibiotics, the total number of antimicrobial prescriptions has decreased from their peak in the mid-1990s. This trend, however, is not seen in the case of expensive, road-spectrum antimicrobials, which have been on the rise.[2] Physicians and mid-level clinicians (for brevity, mid-level clinicians are included in the term "physicians" from this point) in some regions of the country prescribe broad-spectrum antibiotics up to 76% of the time.[3,4]

While there are cases when newer drugs are more effective than older drugs and therefore are clinically superior, multiple studies have shown that older, less expensive drugs are often as or more effective as newer drugs.[5-9] In fact, in some cases, patients prescribed older drugs had fewer return physician visits than patients prescribed newer antibiotics.[10] It must also be considered that antibiotics can have adverse side effects[11-12], and in some cases may not even be clinically beneficial[13-14]. Physicians are also susceptible to the same marketing forces as consumers and in the case of new pharmaceutical products are often more susceptible.[15] This can lead to prescribing the newest and often most expensive antibiotic for an infection treatable with first-line, usually generic, antibiotics, such as penicillin.

Prescription drug spending has risen precipitously over the past few decades. According to a PriceWaterhouseCoopers

2006 report on the factors fueling rising healthcare costs, 16% of healthcare premium dollars are spent on prescription drugs, with spending on prescription drugs rising 8.6% between 2004 and 2006. Because of increased cost pressures on healthcare spending, employers, insurance plans and government health plans are increasingly utilizing benefit design methods to promote more cost-effective prescription drug choices. These include limits on the number of prescriptions per month, multi-tiered drug plans, higher co-payments,[16] and other similar programs designed to rein in utilization and costs. This study looks at another approach to help control prescription drug spending by providing optimal care to patients through the collaboration between health providers and pharmacists dedicated to serving patients at a workplace health center.

It has often been said that the best way to influence prescription patterns is to influence the prescribing physician's pen. Ambulatory care physicians in the U.S. write approximately 126 million prescriptions for antibiotics each year,[2] making antibiotics the second largest category of drugs prescribed by primary care physicians. The major reason so many antibiotic prescriptions are written is that nationally, infectious diseases account for 18% of all outpatient visits, with respiratory tract infections, otitis media, and urinary tract infections constituting the largest percentage of infectious disease visits.[17]

Pharmacists are in an ideal position to promote appropriate antibiotic use through patient education. The integral role of pharmacists in educating patients on complying with medication has been well documented.[18-21] This is particularly important with antibiotics where patient nonadherence to antimicrobial regimens often results in failure to eradicate the infecting organism and development of drug-resistant strains of bacteria.[22] Creating collaborative teams of primary care physicians and pharmacists have also been shown to improve the quality and cost-effectiveness of patient care.[18]

Employers and entities interested in improving health and productivity have a vested interest in appropriate antibiotic prescribing. Increasingly, employers understand that the health of employees affects the success of their company. Healthy employees tend to be more productive, with less absenteeism and presenteeism than unhealthy employees. There is good evidence that productivity losses can be reduced by appropriate pharmacological treatment.[23] For instance, in a randomized, double-blind, placebo-controlled trial on the effects of erythromycin to treat acute bronchitis it was found that patients treated with erythromycin missed 1.35 days less work (average 0.81 days versus 2.16 days) than patients treated with a placebo.[24]

While the specific line of antibiotic prescribed has not been linked directly to health and productivity in the literature, prescribing the most appropriate antibiotics when an employee has an infection is likely to be one way to improve health and productivity for several reasons.

First, treating with the most appropriate antibiotic results in fewer return doctor visits for the same ailment, which equates to less lost time at work.[10] Second, first-line antibiotics often have less severe side effects and more is known about the potential side effects; mild gastrointestinal distress is the most common, due to a longer history of use. Also, the incidence of adverse drug reactions (ADR) is lessened with first-line antibiotics as more is known about them. One retrospective study that randomly selected patients in ambulatory settings found that 18% of patients reported some drug complication and 3% of these patients had a verifiable adverse drug reaction.[25] Two to five percent of hospital admissions are for adverse drug reactions[26-27] and antimicrobial agents are the second most frequent drug class (second only to Central Nervous System agents) cited as a factor in emergency department visits for ADR.[26] Therefore, it follows that reducing ADRs through more appropriate use of antibiotics is one way to reduce the number of days away from work.

Inappropriate use and overuse of third-line antibiotics have also been linked to the development of drug-resistant community infections such as methicillin-resistant *Staphylococcus aureus* (MRSA) strains, which can cause not just work absence but disability and even death.[28-31] Optimal prescribing of antibiotics helps inhibit the dangerous growth of these "super bugs" and have been promoted by vigorous campaigns led by both the Centers for Disease Control and Prevention (CDC Get Smart Campaign) and World Health Organization (WHO Global Strategy for Containment of Antimicrobial Resistance). The CDC Get Smart Campaign has enlisted a large number of partners including healthcare purchasers/insurers and businesses/business associations as well as state and local health departments.[32]

Lastly, some third-line antibiotics may not be stocked in retail pharmacies, delaying therapy and creating the need to go to the pharmacy more times, possibly interfering with work attendance and presenteeism.

Costs for antibiotics vary widely, with a typical 10-day course of antibiotics for newer drugs costing up to 56 times that of older, less expensive therapeutics.[5,6,9] For instance, in a study by Berman and colleagues,[6] 10-day treatment costs for treating acute otitis media in children aged 10-13 years ranged from $4.30 for amoxicillin to $113.60 for cefuroxime. Whenever possible it makes sense both clinically and economically to use the lowest-cost, effective drug to treat infections. In addition, sick employees are not productive employees. Employers want the best clinical solution to allow their employees to not miss work and to be fully effective while at work.

In the past, interventions to affect physician prescribing behavior and adopt evidence-based practices in treating infections have proven effective.[28,29, 33-35] Worksite-based health centers that integrate primary care physicians with onsite pharmacists offer a unique environment to encourage evidence-based use of antibiotics. By bringing these two key providers of healthcare together under one roof, physicians and pharmacists can collaborate to provide the most appropriate use of medications. By providing each other with ongoing feedback they can share in the success of the achievement of prescribing goals, and leverage their expert knowledge to choose the best therapeutic regimen for their patients. Together this creates optimal prescribing and patient compliance.

Antibiotic prescribing behavior is influenced by clinician, patient, and system factors.[36] Clinician factors include physician sociodemographics, knowledge, perceived patient expectations, and physician experience and training.[4, 37-41] Examples of patient factors are patient sociodemographics, reported symptoms, illness severity and expressed expectations,[4, 37, 40-43] while examples of system factors include practice setting, pharmaceutical detailing, and health benefit structures such as co-pays, formularies and restrictions.[4, 37, 44-45]

Workplace-based health facilities provide a unique opportunity to impact many of these factors. By educating both clinicians and patients, and by leveraging the "peer to peer" clinical relationships that develop between primary care and pharmacy services working together, the goal of appropriate antibiotic prescribing can be attained. By integrating primary care and pharmacy in one location under shared management, physicians and pharmacists can share information in a way that promotes better clinical practices and capitalizes on the trusted relationship between the on-site clinician and the patient. The results presented in this article demonstrate the power of such collaboration.

METHODS

Study Objectives and Design

The objective of this study is to document how the collaboration of physicians and pharmacists at a workplace health center leads to more appropriate antibiotic utilization within a defined population. As discussed in the introduction, there are times when newer, more expensive antibiotics are appropriate. However, for the majority of community-based infections, less expensive antibiotics are just as effective.

In 2002, CHD Meridian Healthcare implemented a program designed to improve antibiotic prescribing patterns. This effort was initiated to not only maximize appropriate antibiotic prescribing but to realize cost savings afforded by the use of less expensive generic antibiotics. The results of such an effort are described in this article.

Appropriate antibiotic prescribing awareness programs reinforce the treatment delivered by workplace physicians and pharmacists. The program presented in this paper was developed by a multi-disciplinary team at CHD Meridian, which included physicians and mid-level clinicians, pharmacists, quality improvement specialists, and corporate medical leadership. Medical and pharmacy advisory boards adopted and adjusted national guidelines for antibiotic utilization in order to prevent their overuse and inappropriate use at our workplace health centers. The program was called the Antibiotic Prescription Awareness Program and consisted of four main interventions: education on evidence-based guidelines; quality audits; monthly measurement and feedback; and, inclusion of the clinician's performance in this area as part of the annual provider bonus determination.

This program focused on providing general guidelines for antibiotic prescribing practices for chronic and acute conditions. The main focus was on respiratory tract infections, particularly acute manifestations of infection that are often treated in the primary care setting. These include conditions such as otitis media, pharyngitis, sinusitis, rhinitis and community-acquired pneumonia. Specific guidelines for genito-urinary tract infections were also provided and measured. The selection of these two general categories of infectious diseases was based on the large number of patients seen in a primary care setting with those conditions.[17]

The program stressed the collaboration of physicians and pharmacists to meet quality goals for antibiotic prescribing. Pharmacy and therapeutic committees were created for each health center that provided feedback, reinforced the benefits of appropriate antibiotic prescribing and addressed issues around physician and patient resistance. This provided a forum to regularly discuss prescribing practices where physicians and pharmacists worked together toward the goal of clinical excellence. In addition to the formal work done by the pharmacy and therapeutics committee, pharmacists were empowered with the ability to challenge every prescription for second- and third-line antibiotics. Through this pharmacy intervention portion of the program, physicians provided the pharmacist with a clinical reason for prescribing a non-first-line antibiotic or could revise the prescription if appropriate.

Pharmacists and physicians also collaborated to ensure that pharmaceutical detailing is in alignment with meeting pharmacy goals and providing optimal care for patients. Pharmacists scheduled all pharmaceutical representative visits with the physician, which allowed the content of the discussion to be focused and controlled as well as being more convenient for the physician and their patients than unscheduled visits would be. Following the pharmaceutical detailing, physicians met with the pharmacist for a "counter-detailing" meeting.

In this meeting, the pharmacist provided a review of the drug class of the products presented by the pharmaceutical representative. This provided an opportunity for the physician to tap into the expertise of the pharmacist to better process the information presented by the pharmaceutical representative.

Under this program, antibiotics are categorized into three levels according to spectrum of activity and cost. First-line antibiotics are older, somewhat more narrow-spectrum drugs that can be used for the vast majority of infections. These include penicillins, such as ampicillin and amoxicillin, and first-generation cephalosporins, such as cephalexin, tetracycline and macrolides, such as erythromycin.

Second- and third-line drugs are newer, typically more expensive, broad-spectrum antibiotics that are more appropriately reserved for resistant bacteria, complicated infections or first-line failure. Second-line antibiotics include second-generation cephalosporins, such as cefaclor and loracarbef, amoxicillin/clavlanate, and macrolides, such as azithromycin and dirithromycin.

Third-line antibiotics include third-generation cephalosporins and fluoroquinolones, such as ciprofloxin and levofloxacin. Utilization goals for first-line antibiotics were set at 65-75% of antibiotics prescribed. Goals for second-line and third-line antibiotics were set at 15-25% and 5-10%, respectively. This is in line with the CDC report published in 2003 which states that, "While most efforts to date promoting appropriate antibiotic use have focused on reducing the use of antimicrobial agents for viral infections, future efforts should be directed towards ensuring that when antimicrobial agents are indicated, first-line or targeted therapy is employed."[2, p. 435]

Antibiotic goals for respiratory infections are shown in Figure 1. Similar goals were also developed for genito-urinary antibiotic prescribing but consideration was given to complicated versus uncomplicated infections unique to conditions of this type. Describing the differences between complicated and uncomplicated UTI is beyond the scope of this article but is well documented in the literature.[46]

While the program's prescribing goals focused on meeting utilization percentages, the program also included education on determining when an antibiotic is even necessary. Many times respiratory infections are viral and will not be helped by the use of antibiotics. To counter patient expectations to receive a prescription when they go to the doctor for respiratory symptoms,[47] physicians were armed with Antibiotic Awareness kits. These kits contained supportive therapies, including OTC antihistamines, decongestants, cough lozenges, tissues and patient educational materials and were designed as an alternative to an antibiotic prescription for patients for whom antibiotics were deemed inappropriate. In addition, physicians could write a prescription for OTC medications to treat respiratory symptoms which the patient could "fill" at the pharmacy. This helped achieve a secondary goal of maintaining a high patient satisfaction level while decreasing inappropriate prescribing.

An important aspect of this program was the ongoing feedback to the clinicians regarding their prescribing habits. During the study period, physicians and pharmacists received reports with verbal feedback on a monthly basis. Workplace health centers with third-line antibiotic prescription fill rates greater than 15% had their medical charts reviewed by clinical staff utilizing an internally developed audit tool to determine medical appropriateness of third-line antibiotic use. Those who did not meet quality criteria standards based on the chart review were required to develop an action plan.

Having the entire health center involved in both meeting the goals and working together to remedy any shortfalls further encouraged collaboration.

As stated earlier in the section, the objective of this study is to document how the collaboration of physicians and pharmacists at a workplace health center leads to more appropriate antibiotic utilization within a defined population. We test this through the hypothesis that patients who are cared for at workplace health centers that combine primary care and pharmacy will have a higher rate of first-line antibiotic utilization than patients who use non-workplace physicians in the same community.

First-line antibiotics are defined as those shown in Figure 1. The principal metrics are percentage of prescriptions filled for first-, second- and third-line antibiotics. This study design was a retrospective cohort study using data collected in the course of normal medical center and pharmacy operations.

STUDY POPULATION

The population from four locations of a large, self-insured employer's active and retiree population along with their eligible dependents was selected for this study. The employees, retirees and dependents in this population had access to a worksite primary care health center and full-service pharmacy. These workplace health centers were located in four different geographic regions in the Midwestern, Western and Southeastern portions of the U.S.

Pharmacy data for patients who used any of the workplace pharmacies were collected for calendar years 2003-2005. Antibiotics were identified by using the National Drug Code (NDC) codes designated by the drug class prefix 03 ("antimicrobials"). We excluded polymyxins, aminoglycosides, antimycobacterial, and antifungal agents as they are either not typically used in an ambulatory setting or are topical antibiotics. First- through third-line antibiotics were then defined

Figure 1: Antibiotic Prescription Awareness Program Goals

	Respiratory Antibiotics	Utilization Goals
First-Line Antibiotics	Penicillin ampicillin amoxicillin First-Generation Cephalosporins cephalexin (Keflex) Tetracyclines doxycycline (Vibramycin) Macrolides erythromycin Misc. trimethoprim/sulfamethoxazole (Bactrim)	65-70%
Second-Line Antibiotics	Second-Generation Cephalosporins cefaclor cefprozil (Cefzil) cefuroxime axetil (Ceftin) loracarbef (Lorabid) Penicillin amoxicillin/clavlanate (Augmentum) Macrolides azithromycin (Zithromax) clarithromycin (Biaxin) dirithromycin (Dynabac) Ketolides telithromycin (Ketek)	15-25%
Third-Line Antibiotics	Third-Generation Cephalosporins cefdinir (Omnicef) cefuxune (Suprax) cefpodoxime (Vantin) Fluoroquinolones ciprofloxin (Cipro) gatifloxacin (Tequin) levofloxacin (Levaquin) moxafloxacin (Avelox) ofloxacin (Floxin)	10-15%

according to predefined criteria developed for the program (see Figure 1). The excluded population included all employees, retirees or eligible dependents who did not fill a prescription for an antibiotic at any of the workplace pharmacies during the three-year study period.

Selection of Patient Population

To test the main research hypothesis, all patients who had filled a prescription for an antibiotic at any one of the four locations described above were included in this study. These patients were divided into two groups: those who had their prescription written by a workplace-based physician and filled at one of the workplace pharmacies (from this point on called the "workplace treated" group) and those who had their antibiotic prescription written by a community physician and filled at one of the workplace pharmacies (from this point on called the "community treated" group).

The full employee, retiree and dependent population that used an onsite pharmacy to fill prescriptions for antibiotics consisted of 23,501 unique members with an average age of 49 (std. dev. 23.29). Slightly over half (50.96%) of this group were female. Workplace treated patients (n=4,645) were younger with an average age of 46 (std. dev. 21.51) versus 50 (std. dev. 23.63) and more likely to be female (51.03% versus 48.97%) than the community treated group (n=18,856). Because the differences in age and gender were statistically significant at the p<.01 level, we controlled for them in the analysis. This group of patients filled 84,088 prescriptions for antibiotics during the three-year study period.

Analyses conducted

The x^2 and Student t tests were used for simple comparisons of differences between the groups for categorical and continuous variables respectively. Logistic regression was used to assess categorical differences (antibiotic line) between the workplace treated and community treated groups while adjusting for age and gender. Linear regression was used for continuous variables (cost, quantity, and days supply), also controlling for age and gender. For all statistical tests, a two-tailed p value of <.05 was considered statistically significant. All analyses were conducted using SAS Version 9.1 software (SAS Institute Inc., Cary, NC).

We made several assumptions in structuring the model. First, it is assumed that all patients who used the worksite-based medical center or pharmacy were part of the eligible population. This is a closed-door worksite-based center and only employees, retirees and dependents of the employer being studied are eligible to use the health center. Second, we assumed that prescriptions filled within four days following the date of the office visit to the clinician (doctor, physician's assistant or nurse practitioner) were prescribed at the time of the office visit.

RESULTS

The main hypothesis tested in this article is that patients who have their prescriptions written by workplace-based physicians and filled at collaborating workplace pharmacies (the "workplace treated" group) will have a higher rate of first-line antibiotic utilization than patients who receive primary medical care from community physicians and have their antibiotic prescription filled at one of the workplace pharmacies (the "community treated" group).

Linear regression models were constructed that compared first-, second- and third-line antibiotic prescriptions by group. We also tested differences in cost, quantity and days supply of antibiotics, controlling for age and gender.

The workplace treated group had 15,739 antibiotic prescriptions, or an average of 3.39 prescriptions per patient over the three-year period (1.13/year). The community treated group had 68,349 antibiotic prescriptions filled during the three-year period with an average of 3.62 prescriptions per patient for the study period (1.21/year). The differences in the number of prescriptions were statistically significant at the p<.01 level.

As shown in Table 1 and Figure 2, nearly 66% of antibiotic prescriptions for the workplace treated group were for first-line antibiotics compared to 45% for the community treated group. Similarly, second-line and third-line antibiotics rates were lower for the workplace treated group: 26% versus 33% for second-line

Table 1: Antibiotic Line, Cost, Days Supply and Quantity: Workplace Treated v. Community Treated, Controlling for Age and Gender

Variable	Workplace (n=15739) n	%	Community (n=68349) n	%	Difference	*p*-value	Adjusted *p*-value*
Antibiotic Line							
First Line	10356	65.8	30818	45.09	20.71	<.0001	<.0001
Second Line	4082	25.94	22736	33.26	-7.32	<.0001	<.0001
Third Line	1301	8.27	14795	21.65	-13.38	<.0001	<.0001
	M	SD	M	SD			
Cost	26.87	29.77	46.82	46.09	-19.95	<.0001	<.0001
Quantity	32.01	42.19	27.93	43.96	4.08	<.0001	<.1302
Days supply	9.91	8.01	9.29	9.20	0.62	0.3733	0.6262

* Controlling for age and gender

and 8% versus 22% for third-line, respectively. All differences in level of antibiotics are statistically significant at the $p<.0001$ level.

Of the other factors considered, cost, quantity and days supply, only cost was significantly different for the workplace treated versus community treated groups. Average drug acquisition costs were almost $20 dollars less per prescription for the workplace treated group. With this population receiving more than 84,000 antibiotic prescriptions over the study period, the savings potential exceeded $1.5 million.

Differences among days supply and quantity, while not statistically significant, were explored further as the potential for drug sampling to play a role was considered. However, even under fairly intense scrutiny, looking at drug for drug differences, no statistically significant variation was seen between the workplace treated and community treated groups.

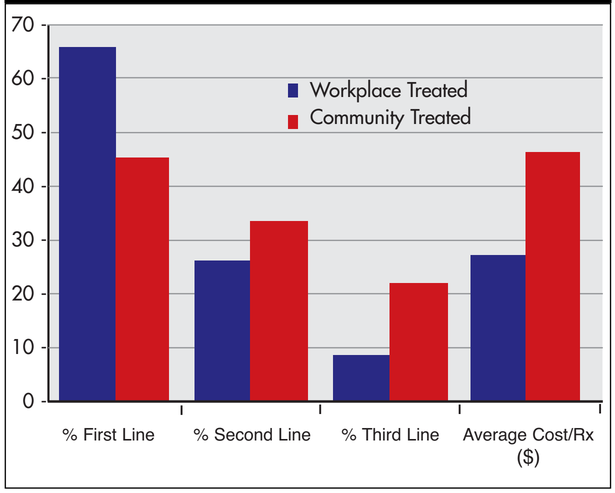
The overall difference in days supply was accounted for by the larger percentage of second- and third-line antibiotics prescribed by community physicians. These medications tend to have shorter therapy duration due to their differing pharmacology. For instance, the second-line antibiotic Zithromax only requires five days of therapy and only six tablets while the first-line antibiotic erythromycin generally is taken four times a day for 10 days of therapy. Our detailed analysis found no ascertainable differences between like drugs due to drug sampling when the same drug was prescribed by both community and workplace physicians, although it is presumed that differences in what drug was actually prescribed could have been influenced by the presence of antibiotic samples as seen in the much higher levels of second- and third-line prescribing by community physicians. First-line antibiotics are typically not sampled as these are established, low-cost and usually generic prescribing options.

Differences in prescribing patterns between the four locations were also explored, the results of which are shown in Table 2. Physician practices both at the workplace health centers and in the community vary by location as does the patient population to some extent but the trend remains that workplace treated patients have significantly higher rates of first-line antibiotics and lower average costs per antibiotic prescription than community treated patients at all locations.

Because prescribing patterns can change over time we explored the rates of first-line antibiotics for each of the three years studied. As shown in Figure 3, the rates for workplace treated patients and community treated patients persisted throughout the study period. From 2003 to 2005, first-line antibiotics for workplace treated patients were 66.59%, 64.39%, and 66.27%. Similarly for community treated patients, first-line antibiotics were 45.36% in 2003, 46.58% in 2004 and 43.07% in 2005. Similar patterns were found when looking at each location individually.

Since second- and third-line antibiotics may be clinically necessary if first-line antibiotics fail, we explored potential differences between the workplace and community treated groups on drug switching. To do this we looked at any patient who was initially prescribed a first-line antibiotic and then had a prescription for a second- or third-line antibiotic filled after the prescription is exhausted was considered a "drug switch." We also looked at prescriptions switched within the limits of days supply for the first-line antibiotics to see if either side effects or early failure on the first-line antibiotic would differ (second- or third-line prescription filled between first-line fill date and limits of days supply). No statistically significant differences were found between the workplace treated group and the community treated group for either scenario. The results of this analysis are shown in Table 3.

Figure 2: Antibiotic Line and Average Cost: Workplace Treated v. Community Treated



DISCUSSION AND CONCLUSIONS

Markedly escalating prescription drug costs have caused the healthcare industry to strongly consider the use of effective, low-cost options. Pharmacy and Therapeutics Committees have dedicated themselves to promote the use of effective and efficient medicines through the implementation of formularies. Most large U.S. companies have a vested interest in the topic. Large employers are usually self-insured, meaning that every unnecessary dollar spent on healthcare reduces company profits. While employers want to provide good health benefits for their employees and their dependents, they also need to constantly strive to control healthcare dollars spent just as they control waste in their production processes.

The topic of appropriate antibiotic use has many facets, including proper prescribing, patient satisfaction and perceptions of the need for antibiotics, therapeutic adherence by patients, drug-resistant pathogen development, and the effects that marketing tactics used by pharmaceutical companies have on prescribing practices. This paper focused on prescribing patterns in worksite-based health centers compared to community-based physician offices for relatively common conditions: respiratory tract infections and urinary tract infections. The results of this study indicate that physicians working in collaboration with pharmacists at worksite health centers pre-

Table 2: Antibiotic Line and Cost: Workplace Treated v. Community Treated by Location, Controlling for Age and Gender

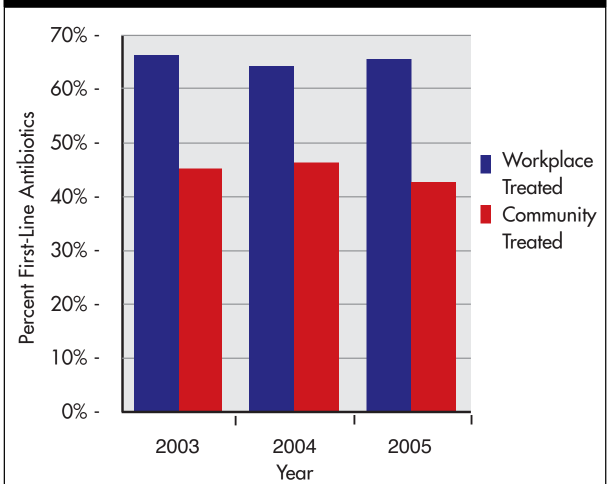
Variable	Workplace	Community	Difference	Adjusted *p*-value*
Antibiotic Line				
First Line - Location 1	59.76%	46.57%	13.19%	<.0001
First Line - Location 2	65.17%	43.91%	21.26%	<.0001
First Line - Location 3	68.30%	38.02%	30.28%	<.0001
First Line - Location 4	72.82%	61.73%	11.09%	<.0001
Second Line - Location 1	28.15%	29.64%	-1.49%	<.0001
Second Line - Location 2	22.85%	23.38%	-0.53%	<.0001
Second Line - Location 3	26.89%	47.06%	-20.17%	<.0001
Second Line - Location 4	20.82%	22.88%	-2.06%	<.0001
Third Line - Location 1	12.01%	23.78%	-11.77%	<.0001
Third Line - Location 2	11.98%	27.71%	-15.73%	<.0001
Third Line - Location 3	4.81%	14.92%	-10.11%	<.0001
Third Line - Location 4	6.37%	15.40%	-9.03%	<.0001
Cost - Location 1	$29.92	$42.46	-$12.54	<.0001
Cost - Location 2	$24.49	$40.44	-$15.95	<.0001
Cost - Location 3	$22.96	$41.03	-$18.07	<.0001
Cost - Location 4	$22.59	$31.20	-$8.61	<.0001

* Controlling for age and gender

scribe a greater percentage of first-line antibiotics than physicians in their communities, reducing costs while providing appropriate levels of second- and third-line antibiotics needed for more difficult to treat infections. There are situations where using second- and third-line antibiotics are appropriate. For instance, when the patient is infected with a strain of bacteria that is resistant to first-line antibiotics or when they are allergic to first-line antibiotics.

The American Academy of Pediatrics (AAP), the CDC, and the Infectious Diseases Society of America (IDSA) recommend the use of first-line antibiotics for the treatment of most common, uncomplicated infections.[8, 48-50] The recommendations of such highly respected organizations combined with evidence that appropriate use of pharmaceuticals improves both health and productivity[23-24] provide a strong argument to continue to find ways to improve prescribing behavior.

Figure 3: Percent First-Line Antibiotics by Year: Workplace Treated v. Community Treated



It is important to note that antibiotics are often clinically unnecessary. The first step toward appropriate prescribing is knowing when to prescribe an antibiotic and when not to.[51-53] While this was a secondary goal, the study results did demonstrate that workplace treated patients who were treated for an infection had fewer antibiotic prescriptions than community treated patients. This goal is well documented in the literature and supported by campaigns such the CDC Get Smart Campaign and Tuft's Alliance for Prudent Use of Antibiotics (APUA). The growing issue of antibiotic resistance around the world has created a flurry of recommendations and continues to be a viable area of active research.[30,31, 54-55] Patients often lack knowledge about the dangers of antibiotic misuse[56-57] so it is up to the healthcare community to be proactive in educating their patients and decreasing patient risk through more responsible antibiotic prescribing behavior.

Drug advertising and academic detailing by pharmaceutical companies influence physicians' prescribing behavior, specifically favoring the use of more expensive third-line antibiotics.[58-59] We believe the reduced use of second- and third-line antibiotics in the workplace treated group was at least in part due to controlled and counter-pharmaceutical detailing. This is illustrated in that patients treated by community physicians had a third-line prescription rate more than 2.5 times that of workplace treated patients. Drug samples provided by pharmaceutical companies also influence prescribing patterns. Prior research has found that physicians are more likely to dispense and subsequently prescribe drugs that differ from their preferred drug choice because of the availability of samples.[60]

While this study showed that workplace treated patients are

Table 3: Antibiotic Switching from First-line to Second-/Third-Line Workplace Treated v. Community Treated

Switching Scenario	Workplace	Community	Difference	Adjusted *p*-value*
First-line to second-/third-line within five days supply of first-line therapy duration	2.39%	2.46%	-0.07%	<.3641
First-line to second-/third-line within five days supply of first-line therapy duration	2.07%	2.03%	0.04%	<.6216

* Controlling for age and gender

much more likely to be prescribed first-line antibiotics, it should be remembered that choosing the best treatment for infectious diseases is more complicated than it may initially appear. The least expensive antimicrobial agent may not be the most effective. Cost must be weighed against the drug's efficacy against resistant organisms, the acuity level of the patient at clinical presentation and the cost associated with treatment failure. This requires knowledge of local resistance patterns, an area where information is often incomplete or missing altogether[35] as well as some knowledge of what type of treatment regimen a patient is likely to actually complete. In some cases a more expensive drug with a simpler treatment regimen (shorter course of therapy and minimizing doses per day) is the best choice for the patient.[61] The more complex nature of providing effective, cost-efficient healthcare is supported by the collaborative expertise of the primary care provider and the pharmacist, working together to best meet the needs of the individual patient.

The importance of providing regular feedback to the physicians and pharmacists should be stressed. This allows for a special collaborative relationship to develop between these clinicians in the medical center and the pharmacy. Their joint efforts encourage problem-solving and the sharing of information that help both medical and pharmaceutical staff to be more effective and efficient than they would be separately. Together they achieve the goals of providing clinical excellence, patient satisfaction, and provide value for the healthcare dollars spent by both employers and employees.

While the results of this study are quite promising, there are several limitations. Because of the nature of the study, patients were not randomized and this could result in confounding. While we took steps to ensure that the populations were similar, characteristics that we were unable to measure might have had an effect. For instance, disease severity might have differed between the groups but this is difficult to ascertain using claims data.

Next, while the same pharmacy-prescribing goals are implemented across all CHD Meridian health centers in a consistent fashion, only one self-insured employer was studied. However, this employer has a large employee population and the results obtained statistical significance. There were two primary reasons for selecting a single client with multiple sites versus multiple employers. First, the types of employees, distribution of age, job types, race/ethnicity and health benefit penetration and design are more similar for a single employer than for multiple employers, particularly if they are from different industries. There are differences in healthcare utilization and expectations between patients of different socioeconomic statuses, races/ethnicities and with different benefit plans. Second, obtaining complete medical and pharmacy claims from multiple clients would have dramatically increased the costs associated with the study.

While not directly related to the results of this study, it should be noted that worksite primary care and pharmacy centers are most commonly established by self-insured employers that have a geographically concentrated workforce. The need for a critical mass of employees at a given location (typically around 1,500 employees) achieves a certain level of utilization necessary to justify the investment required to implement and operate a worksite health center.

We also could only assess prescribing behavior based on those prescriptions actually filled. Nationally, 14-21% of original prescriptions written are never filled[62] and claims data only reflect those services that were actually rendered. The nature of administrative claims data lends itself to some limitations beyond prescribing behavior. Claims data are collected primarily for billing purposes. Thus, using coding algorithms to determine the existence of disease may be incorrect insofar as the data may not include all clinically relevant information.

Lastly, this research is based on the use of a closed-door, worksite-based health center that includes both primary care and pharmacy and may not be applicable to other types of healthcare benefit design and delivery system.

Using evidence-based guidelines to improve prescribing behavior has shown promise in recent studies.[28,29, 33-35] Future research should extend this study to multiple employers in order to improve the generalizability of the results. In addition, adding measures of employee absenteeism and presenteeism in order to determine if there is a direct relationship between which antibiotic is prescribed and productivity should be explored.

This study suggests that by coordinating the "trusted clinicians at the workplace™": primary care physicians and pharmacists, aligning caregivers into a single, integrated delivery model will bring us closer to realizing the potential value of population health management which includes healthier employees, reduced healthcare costs, increased productivity, and reduced absenteeism. These additional benefits further justify employer support.

A recent issue of the magazine *Health and Productivity Management*[63] stressed the importance of employers and physicians developing partnerships if they want to improve the health and productivity of the workforce. Worksite-based healthcare centers and implementation of programs that foster collaboration between physicians and pharmacists promote the practice of evidence-based, cost-effective medicine and can keep the workforce healthy and productive. JHP