

# Resistance to In-Office Dispensing of Generic Antibiotic Samples

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In this issue of *JMCP*, Conklin, Culley, and O'Donnell describe the results of an initiative to foster greater use of generic antimicrobial medications through the use of an in-office automated generic medication samples kiosk.<sup>1</sup> A similar report describing the result of this initiative on overall rates of generic product use and cost was previously published in the June 2007 issue of *JMCP*.<sup>2</sup> In the current study examining the impact of the kiosk program on prescribing of antimicrobial drugs specifically, the authors found that rates of "first-line" (generic) antimicrobial use, measured as a proportion of all antimicrobial prescriptions, were similar among network prescribers with versus without access to the medication kiosks (42.0% vs. 41.4%, respectively;  $P=0.028$ ) in 2006, the most recent year measured. For the same year, the authors report a lower average cost per antimicrobial claim among prescribers with kiosk access (\$28.44) than among those without access (\$32.40;  $P<0.001$ ).

The authors also compared mean cost per antibiotic claim and rates of use of "first-line" (generic) antibiotics between the 2 groups using a difference-in-difference analysis that measured change from the pre-intervention year (2003) to the post-intervention year (2005). They found that rates of use of "first-line" (generic) antibiotics declined among both groups during this 2-year period, from 49.1% to 47.0% (-2.1%) among prescribers having access to the samples kiosks and from 46.0% to 42.6% among the other network providers (-3.4%). The between-group difference in the magnitude of this reduction was not found to be statistically significant. Average cost per claim was also less in 2005 as compared with 2003 for both groups (changes from \$33.56 to \$29.42 for the kiosk users versus \$38.26 to \$34.91 for the other network providers), yet the between-group difference in magnitude of the reduction in antibiotic drug cost was also found to be statistically insignificant.

The premise of this intervention is a logical one. In many instances, lower-cost generic medications are a cost-effective substitute for higher-priced brand name products, particularly in generic substitution, and also when it is within the boundaries of evidence-based care to utilize a generic drug from a different therapeutic class in place of a branded product that does not have a generic substitute (i.e., therapeutic selection). Increasing access to generic antimicrobials via the use of in-office medication kiosks represents a novel approach in attempting to reduce the over-prescribing of broad spectrum higher-cost antibiotics. Yet this method of facilitating access to generic antibiotics raises a range of important issues, including what constitutes appropriate antimicrobial drug use from the perspective of the health plan, the implications of drug dispensing in the absence of pharmacist involvement, and overall, the role of drug sampling programs within our health care system. Moreover, this study provides

another example of the drug product being parsed from the service, with technology having a fundamental role in reshaping the order fulfillment process. Specifically, pharmacists are increasingly providing patient education and counseling without having a direct role in the order-fulfillment function because newer dispensing technologies are enabling order fulfillment with diminishing pharmacist involvement. Yet, order fulfillment in the absence of pharmacist counseling raises substantial concerns with respect to patient safety and promoting appropriate medication use. Thus, we believe that it is imperative that the health professions, regulators and health plans consider the broader implications of newer technologies, such as the medication sampling kiosk initiative described in this study.

## Does Facilitating Access to Generic Antibiotics Affect Providers' Selection of Therapy?

The purported aim of the study was to increase the prescribing of agents described by the authors as first line. However, the apparent aim of this initiative was to increase the rate of utilization of lower-cost generic medications, of which many but not all are first-line anti-infective therapies in every circumstance. For example, for the treatment of community acquired pneumonia in adult outpatients who have received a beta-lactam or macrolide within the previous 3 months, a respiratory fluoroquinolone is recommended,<sup>3</sup> and no product from this category is currently available in a generic form. Thus, we believe the authors would have been more accurate in stating that the study's aim was to increase the use of lower-cost antibiotics. Alternatively, the analysis could have been restricted only to infection types and clinical circumstances where first-line antibiotics are available in generic form, for example in the treatment of uncomplicated urinary tract infections.<sup>4,5</sup>

We also note that while Conklin et al.'s study included analyses to determine the statistical significance of between-group differences in prescribing rates and per-claim cost, the study employed a non-randomized design that did not control for potentially important covariates. While randomization was likely impractical, the researchers could have assessed potential differences in group composition such as prescriber specialty, size of practice, or a provider's past prescribing patterns (other than volume). The authors note that the program targeted high-volume prescribers and those having below average generic use rates.<sup>1,2</sup> Yet no data are provided to present these characteristics in comparison with those of network prescribers without access to the samples kiosks. Stratification according to these and other characteristics would have likely yielded interesting findings. Furthermore, we wonder if the kiosks were more likely to be installed within group practices that used payment incentives to prescribe

generic products. Or perhaps the kiosks were more likely to be used by physicians receptive to newer technologies or who hold more contemporary viewpoints regarding the efficacy of generic medications. Differences in location, population demographics, and office policies towards pharmaceutical representatives and sampling are also potentially important covariates.

The sole substantial between-group difference noted in the paper is a lower cost per claim among kiosk prescribers (\$28.44) as compared with non-kiosk prescribers (\$32.40) in 2006. Yet because rates of prescribing of first-line antibiotics were nearly identical during this period, this difference in cost likely reflects a different mix of first-line antibiotics; the dispensing kiosks contained only a subset of the first-line antibiotics that were included in the claims analysis. This issue could have been explored more thoroughly by presenting dispensing rates for each first-line antibiotic product for the 2 study groups. Additionally, while the authors state that cost calculations included administrative costs associated with the sampling program, detail is lacking regarding the nature and breakdown of such costs. Relevant costs may include, for example, the costs of licensing and maintaining the kiosks, provider training and service, patient education materials, and restocking the machines. It is not clear if these or other costs were included in the cost calculations. Nevertheless, the authors do not overemphasize the statistically significant difference in per-claim costs for 2006, but instead highlight the results of the difference-in-difference analysis, which revealed that the sampling initiative did not appear to improve rates of use of first-line antibiotics beyond that measured for network providers overall. The authors should be given credit for reporting this nonsignificant finding.

### The Role of Academic Detailing

Another aspect of the study that warrants discussion is the academic detailing service, which was apparently an additional and cross-cutting intervention. The authors indicate that an employee of the managed care organization, specifically a clinical pharmacist, provided academic detailing and education on a number of topics, including appropriate antibiotic prescribing. Conklin et al. acknowledge that many infections, including acute upper respiratory tract infections, do not require initiation of any antibiotic therapy, and that the convenient presence of the kiosks could potentially have promoted the overuse of antibiotics for clinically inappropriate indications. It is well known that antibiotic therapy for numerous infections in adults, including acute sinusitis, bronchitis, and pharyngitis, as well as acute otitis media in children, is generally not beneficial.<sup>6-9</sup> Additionally, a recent analysis of data from the United Kingdom General Practice Research Database demonstrated that the number of cases of upper respiratory infection, sore throat, or otitis media needed to treat with antibiotics in order to prevent 1 serious complication (e.g., mastoiditis, pneumonia) is more than 4,000.<sup>10</sup>

Additionally, one must question whether the prescribers received education regarding current evidence-based recommendations for treating lower respiratory tract infections, including

community-acquired pneumonia, which may require utilization of “more expensive, second-line”<sup>1</sup> antibiotics in patients with underlying comorbidities or recent antibiotic use.<sup>3</sup> It is critical that prescribers be made aware of the differentiating factors (e.g.: adverse effects, dosing frequency, drug interactions) when selecting narrower spectrum, less expensive agents as opposed to broader spectrum, branded antibiotics in order to optimize outcomes and prevent treatment failures. One may wonder if further facilitating access to antibiotics via these kiosks will contribute to the ever-rising incidence of antibiotic resistance among community-acquired pathogens.

It would have been interesting for the authors to reveal more detail regarding the scope of messages and role of the academic detailing pharmacist. Nevertheless, because the academic detailing service was provided to all prescribers having access to the generic samples kiosk, and also to many other prescribers not having access to the generic samples, it is not possible to determine the effect of the academic detailing service on generic antimicrobial prescribing rates.

### Drug Sampling and the Role of the Pharmacist

At a broader level, we have concerns about the practice of in-office dispensing and specifically the exclusion of pharmacist involvement from the dispensing process. The use of the in-office dispensing kiosks provides an avenue for order fulfillment that does not include a drug utilization review (DUR) as performed by a pharmacist prior to dispensing. In the process of conducting the DUR, drug-drug interactions are often discovered and appropriateness of antibiotic choice and dosing regimen are reviewed. Through this process, errors are often identified and avoided through consultation and recommendations made to the prescriber. This process is especially critical for antibiotics, which have the potential to result in clinically significant interactions with a multitude of chronic maintenance medications. For example, numerous generic antibiotics, including several of those included in the kiosk in this study (amoxicillin, cephalexin, doxycycline, sulfamethoxazole/trimethoprim) interact with warfarin, and may cause significantly elevated prothrombin times and increased risk of bleeding.<sup>11,12</sup> If interactions such as these are not recognized, patient harm may result, and the risk is more than theoretical. Results of a large nationally representative survey revealed that warfarin is second only to insulin use as a leading cause of drug-related adverse events treated in emergency departments.<sup>13</sup> The lack of a pharmacist DUR component could also have medicolegal ramifications, as antibiotics are one of the most frequently associated medication categories associated with malpractice claims.<sup>14</sup>

Another implication of the lack of pharmacist involvement in the dispensing process is the absence of the medication counseling typically provided by the pharmacist to the patient at the time of dispensing. Important counseling points for proper antibiotic use include the management and prevention of common antibiotic-related adverse effects. A recent study published by Shehab and colleagues in *Clinical Infectious Diseases* noted that antibiotics

caused 19.3% of all adverse drug reaction-related visits to the emergency department from 2004 through 2006.<sup>15</sup> The authors estimated that more than 142,000 emergency department visits every year were a direct result of antibiotic-related adverse events, with an overall rate of 10.5 emergency department visits per 10,000 outpatient office visits at which an antibiotic was prescribed. This research highlights the value of independent DUR performed by the pharmacist in dispensing the medication to the patient, confirming that prescribed therapies are appropriate given a particular patient's clinical circumstances and concomitantly prescribed therapies, and ensuring that patients have an accessible resource for receiving drug information and counseling throughout the course of therapy. Such patient education includes instruction regarding the importance of completing the entire course of antibiotic therapy, rather than discontinuing the medication once symptoms resolve, and reinforcing the importance of proper storage of the antibiotics. The pharmacist can also explain why antibiotics should never be shared with others, including family members and friends. There are a number of key points that should be impressed upon the patient when an antibiotic is dispensed, and we wonder if the patient education provided in the office setting measures up against the level of educational services provided by community pharmacists. Lastly, we note that the pharmacist serves as a double check for identifying drug allergies.

### Do Standards for Drug Utilization Review Apply to Sampling?

It is beyond the scope of this commentary to detail the myriad benefits of pharmacy care services and the pharmacist's role in medication management. We note that Congress recognized the importance of medication therapy management (MTM) in the Medicare Prescription Drug Improvement and Modernization Act of 2003, and MTM is recognized as an eventual "cornerstone" of the Part D benefit.<sup>16</sup> MTM notwithstanding, the DUR function as provided by pharmacists has been established as a standard of practice, as described in the Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy,<sup>17</sup> and including the state of Pennsylvania where this study was conducted.<sup>18</sup> Specifically, the rules and regulations of the Pennsylvania Board of Pharmacy require pharmacists to perform a prospective drug review (PDR) in attempting to "identify potential drug therapy problems that might result from therapeutic duplication, drug-drug interactions, incorrect dosage, incorrect duration of drug treatment, drug-allergy interactions, and clinical abuse or misuse."<sup>18</sup> We wonder if this standard of care is met by dispensing physicians distributing antibiotic samples using the medication kiosks. We recognize that the requirement for a pharmacist PDR apparently does not extend to physicians dispensing in the office setting. Yet we posit that the PDR requirements for pharmacy exist for good reason, and thus should be considered a standard of care to be applied across all settings. In the institutional setting, Joint Commission standards for safe medication use apply to sample medication distribution. For example, actual or potential adverse drug events and errors

must be addressed, education is provided where appropriate, and patient-specific medication information must be made available.<sup>19</sup> It is our understanding that these standards apply to outpatient functions existing within medical centers accredited by the Joint Commission. We argue that these standards of care are no less valid as applied to the prescribers studied here.

One may argue that a pharmacist-conducted DUR is not typically a facet of the office-based dispensing of brand-name drug samples either, and this practice has been commonplace for years. Yet just because the practice has been in existence for years does not mean that it should continue. Increasingly, institutions are eliminating brand-name drug sampling for reasons relating to patient safety and equity, and because of the influence on prescribing decisions (e.g., starting patients on relatively expensive drug therapy). Examples of such institutions are provided in a report by the Prescription Project, created with support from the Pew Charitable Trusts; the effort "promotes evidence-based prescribing and works to eliminate conflicts of interest in medicine due to pharmaceutical marketing to physicians."<sup>20</sup> The group's April 2008 report *Pharmaceutical Samples* highlights several example policies excerpted from high-profile institutions.<sup>17</sup> These include the use of vouchers supplied by the institution which can be used by the patient to acquire prescription drugs at reduced or no cost, and the establishment of funds for directing charitable donations to purchase medications for those in need. Many of these programs are directed through and overseen by the medical center's pharmacy services. Additionally, the American Society of Health-System Pharmacists has expressed strong opposition to the practice of drug sampling, urging that "the use of drug samples within the institution be eliminated to the extent possible."<sup>21</sup> The American Medical Association has also called for academic medical centers to eliminate the use of drug samples.<sup>22</sup> These positions appear to be founded primarily upon concerns regarding manufacturer influence, whereas issues pertaining to safe medication use have seemed to receive lesser emphasis.

The impact of drug sampling programs on quality of care is difficult to evaluate. Whereas brand drug sampling has been utilized as a marketing tactic for many years, there exists a paucity of research describing the impact of drug sampling on patient safety, despite potential concerns about the lack of involvement of the pharmacist in the dispensing process. However, the published literature contains at least 1 review of studies examining the consequences of drug sampling.<sup>23</sup> Of the 23 articles identified in a review conducted by Groves et al., most studies addressed the impact of drug sampling on prescribing and program costs, while little was found regarding the impact of drug sampling on patient safety specifically, and with no reports addressing safety published in recent years.

In conclusion, Conklin et al.'s study brings to the forefront numerous issues with respect to medication sampling programs and antibiotic utilization. The greatest concern we have is the potential for compromised patient care and safety. While new technologies hold great promise for improving the effectiveness, safety, and efficiency of medication use, they must be assessed by

considering their impacts on each of these outcomes. We wonder if the health plan considered adequately the potential threats to desirable clinical outcomes in its implementation of physician dispensing of generic antibiotics from medical office-based kiosks. This research by Conklin et al. informs about some drug cost outcomes and highlights how much we don't know about the subject, including clinical and service outcomes.

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### DISCLOSURES

The authors report no financial or other conflicts of interest regarding the subject of this commentary. Stephen Kogut is a former member of the Rhode Island Board of Pharmacy (2003-2008).

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