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Original Article

The Impact of Drug Samples on Prescribing to the Uninsured

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Kp **Objective:** To determine whether drug samples are associated with physicians prescribing fewer generic, less-costly medications.

Methods: We conducted a retrospective study at a large university-affiliated internal medicine practice containing over 70 physicians. Using a pharmacy database, we identified all prescriptions written to uninsured or Medicaid patients that belonged to one of four classes of chronic medications. For the 9 months before and after the clinic closed its drug sample closet, we calculated the percentage of medications prescribed as generics and the mean cost of a 30-day supply of a prescription.

Results: Of 8911 prescriptions, 1973 met inclusion criteria. For uninsured patients, the percentage of medications prescribed as generics rose from 12% to 30% after the clinic closed its drug sample closet ($P = 0.004$). By consecutive three month periods, the percentage of prescribed generic medications rose steadily to a maximum of 40.0% ($P < 0.001$). For Medicaid patients, there was no significant change in generic prescribing (63% generic with samples versus 65% generic without samples, $P = 0.42$). Two factors were associated with generic prescribing in logistic regression: the absence of drug samples (OR 4.54, 95% CI 1.37–15.0) and the prescriber being an attending physician (OR 5.26, 95% CI 2.24–12.4). There was no statistically significant change in cost for either group.

Conclusions: Physicians were three times more likely to prescribe generic medications to uninsured patients after drug samples were removed from the office. Drug samples may paradoxically lead to higher costs if physicians with access to samples prescribe more brand-name only drugs.

Key Words: drug samples, drug utilization, generic drugs, pharmaceutical marketing, physicians' practice patterns

Drug samples are ubiquitous. Pharmaceutical companies distribute over 15 billion dollars worth of medication samples to office-based physicians in the United States yearly.[1] Over 90% of physicians receive free drug samples, and over 50% of elderly patients report receiving at least one drug sample in a given year.[2,3]

Much controversy surrounds the distribution of drug samples. Prior studies suggest that the availability of samples influences medical decision making. Physicians with access to drug samples have been found to more frequently prescribe heavily advertised drugs and less frequently prescribe first-line antihypertensives.[4,5] Some have called for healthcare systems to ban all free samples.[6] Others regard drug samples as an important source of free medications for the uninsured.[7–9]

Because only the newest, brand-name medications are distributed as samples, the use of samples may paradoxically increase the out-of-pocket costs of the uninsured if physicians who use samples prescribe fewer generic drugs. The effect of drug sample availability on the prescription of generic drugs has been mixed, and no studies have examined the effect of

Key Points

- Free drug samples are frequently used in medical practice.
- Physicians were over three times more likely to prescribe generic medications to uninsured patients after drug samples were removed from the clinic.
- The proportion of generic prescriptions given to Medicaid patients was not affected by the presence of free drug samples.
- Free drug samples may lead to higher costs for uninsured patients by encouraging physicians to write prescriptions for brand-name only drugs.

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drug sample availability on prescriptions given to uninsured patients.[10] Therefore, it is not known whether drug samples lead to lower or higher medication costs for the uninsured.

We hypothesized that the presence of samples would be associated with physicians prescribing fewer generic, and therefore more costly, medications. To test this hypothesis, we conducted a retrospective study examining the prescriptions written by a large internal medicine ambulatory practice in the months preceding and following the closure of its drug sample closet.

Methods

Study-Site Characteristics

The Wake Forest University Institutional Review Board approved the study protocol. We studied a large community-based, ambulatory internal medicine practice comprised of 10 attending physicians, 63 internal medicine residents, and 5 mid-level providers, all affiliated with the Wake Forest University School of Medicine. The majority of the practice's patients are black (63% black, 27% white, 9% Hispanic), and fewer than 8% have commercial insurance (35% uninsured, 31% Medicare, 26% Medicaid). A large on-site pharmacy fills approximately 50% of all prescriptions written by the practice, and it tracks all prescriptions in an electronic database. The on-site pharmacy's extensive inventory is similar to that of a typical large retail pharmacy, and any prescribed drug that is not stocked is ordered for next day pick up.

The practice had a heavily utilized drug sample closet until December 2000 when the practice moved to a new building located three blocks away. Because the new facility lacked a locked storage area for samples, the drug sample closet was discontinued. All samples were discarded, and pharmaceutical representatives delivered no new samples.

Database Query

We queried the on-site pharmacy's electronic database (CRx, QS/1 Data Systems, Inc., Spartanburg, SC) to identify all prescriptions written by the clinic's internal medicine providers and filled at the on-site pharmacy during the nine months before and after the drug sample closet was discontinued (March–November 2000 and January–September 2001, respectively). To focus on two distinct patient populations for whom we expected physicians would be maximally and minimally cost-sensitive, we included only prescriptions written to patients who either had no prescription drug coverage (uninsured patients) or comprehensive drug coverage (Medicaid patients). In addition, we limited our analysis to four classes of chronic medications which were chosen before any data was collected (Table 1). Medication classifications were assigned by a consensus agreement among four of the investigators. We excluded any prescription written for less than seven days' duration and any prescription distributed free of charge. Because the practice's mid-level providers are responsible for the clinic's refill requests, we excluded any prescription written by a nonphysician.

Table 1. Classification of included study medications

Antihypertensives
Alpha 1 receptor blockers
Angiotensin-converting enzyme inhibitors
Angiotensin receptor blockers
Beta blockers
Calcium channel blockers
Central alpha 2 receptor agonists
Combination products
Diuretics
Rauwolfia alkaloids
Vasodilators
Oral diabetic agents
Alpha glucosidase inhibitors
Biguanides
Combination products
Sulfonylureas
Thiazolidinediones
Peptic ulcer and gastroesophageal reflux medications
H2 receptor blockers
Mucosal protectants
Promotility agents
Proton pump inhibitors
Nonnarcotic analgesics
Combination products
COX-2 inhibitors
Nonsteroidal anti-inflammatory drugs

Definitions of Outcomes

The two outcomes of interest were the percentage of medications prescribed as generics and the mean cost of a 30-day supply of a prescription. We defined a prescription as generic if it had received approval for generic manufacture from the Food and Drug Administration (FDA) as listed in the FDA's Electronic Orange Book.[11] We defined the cost of each prescription as the price the on-site pharmacy paid for a 30-day supply of the medication.

Statistical Analyses

Descriptive data were available for patient age, gender, and the number of prescriptions received for the uninsured and Medicaid populations. Univariate comparisons were assessed with chi-square values for proportions and Student t-test for means. To examine physicians' prescribing patterns, we compared the proportion of prescriptions that were generic before and after the drug sample closet was discontinued and by three month intervals, stratified by insurance status. We assessed the differences in prescribing frequencies by

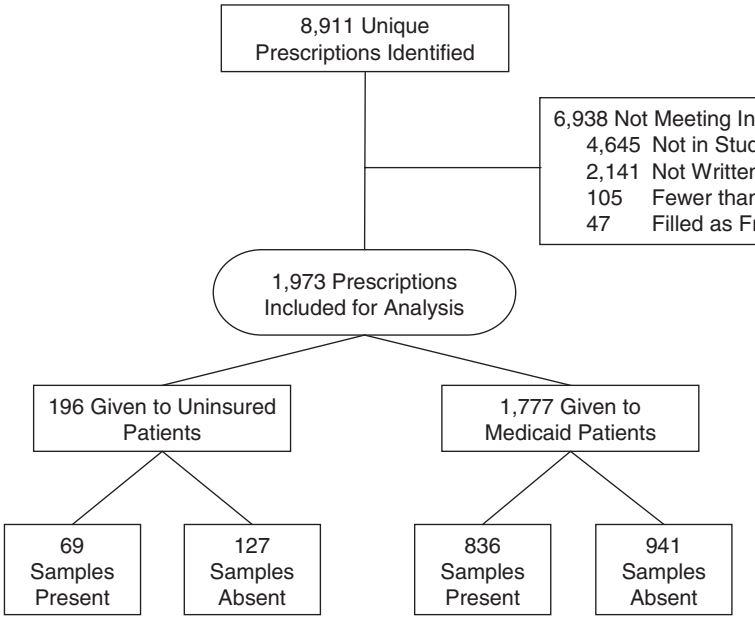

Fig. 1 ●●●.

the chi-square test for the before-after comparison and by the Cochrane-Armitage test for trends over three month intervals.

To account for possible physician cluster effect, we employed logistic regression models using generalized estimating equations to assess the relationship between the presence of samples and the frequency of prescriptions for generically available drugs. Covariates in the model were patient age, patient gender, total number of prescriptions received, and physician training level (attending vs. resident).

We then compared the mean 30-day cost of all prescriptions when drug samples were present versus absent, stratified by payer status. Because the distribution of the cost data was highly skewed, statistically significant differences were assessed parametrically with the Student t-test after log transformation of the data.

SAS software (SAS Institutes, Inc., Cary, NC) was used for all statistical calculations. Statistical tests were two-sided, using a P value of 0.05 or less to determine significance.

Results

We identified 8911 prescriptions written by the clinic's providers to uninsured and Medicaid patients during the study period. Of these prescriptions, 1973 met inclusion criteria (Fig. 1). Sixty-three medical residents wrote 59% (1166/1973) of the prescriptions and 10 attending physicians wrote the remaining 41% (807/1973). Approximately 90% (1777/1973) of the prescriptions were given to 438 Medicaid patients, and 10% (196/1973) went to 119 uninsured patients. Compared to uninsured patients, Medicaid patients were more often female and received a larger number of prescriptions per person (Table 2).

Uninsured patients received fewer prescriptions for generic drugs when the drug sample closet was present. When samples were present, 12% (8 of 69, 95% CI 5.1–21.6%) of prescriptions to uninsured patients were generic compared to 30% (38 of 127, 95% CI 22.1–38.7%) when samples were absent ($P = 0.004$). The percentage of generic prescriptions written to uninsured patients more than doubled after the closure of the sample closet, whether the prescriber was a resident or attending physician (Fig. 2).

When examined by consecutive three month periods, the percentage of generic prescriptions to uninsured patients rose from less than 15% when samples were present to a maximum of 40.0% (95% CI 26.4–54.8%) during the last three months of the study (Fig. 3). Logistic regression using generalized estimating equations showed that two factors were associated with uninsured patients receiving a generic prescription: the absence of the sample closet (OR 4.54, 95% CI 1.37–15.0) and the prescriber being an attending (OR 5.26, 95% CI 2.24–12.4) (Table 3). To remove any potential bias caused by some medications converting to generic status dur-

Table 2. Baseline characteristics of Medicaid versus uninsured patients

Patient characteristic	Medicaid patients (n = 438)	Uninsured patients (n = 119)	*P*
Age (mean, 95% CI)	56.3 (54.9–57.7)	54.2 (51.5–56.8)	0.17[a]
% female (95% CI)	66.0 (61.3–70.4)	50.4 (41.1–59.7)	<0.001[b]
No. prescriptions per patient (mean, 95% CI)	4.11 (3.78–4.44)	1.55 (1.36–1.75)	<0.0001[a]

[a] t test.
[b] χ^2.

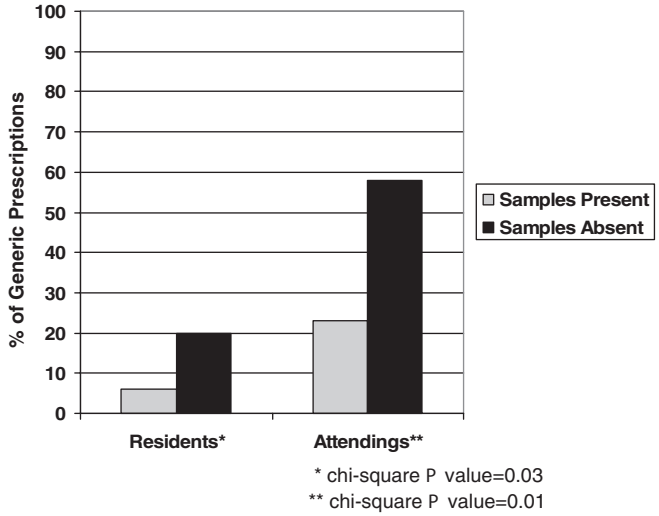

Fig. 2 ●●●.

ing the study period, we re-ran all analyses excluding all prescriptions for these medications (excluded 10 of 196 prescriptions). Excluding these prescriptions did not signicantly affect our results (data not shown).

The percentage of generic prescriptions written to Medicaid patients was similar whether drug samples were present or absent (63.4% generic with samples versus 65.3% generic without samples, $P = 0.42$). The mean cost per prescription did not change significantly after the clinic closed its sample closet (mean cost fell 1.2% for uninsured patients, $P = 0.95$; mean cost rose 16% for Medicaid patients, $P = 0.15$). However, because the frequency of generic prescribing increased over time, by the last three months of the study period there was a trend toward lower cost for uninsured patients ($17.49 versus $15.71, $P = 0.16$).

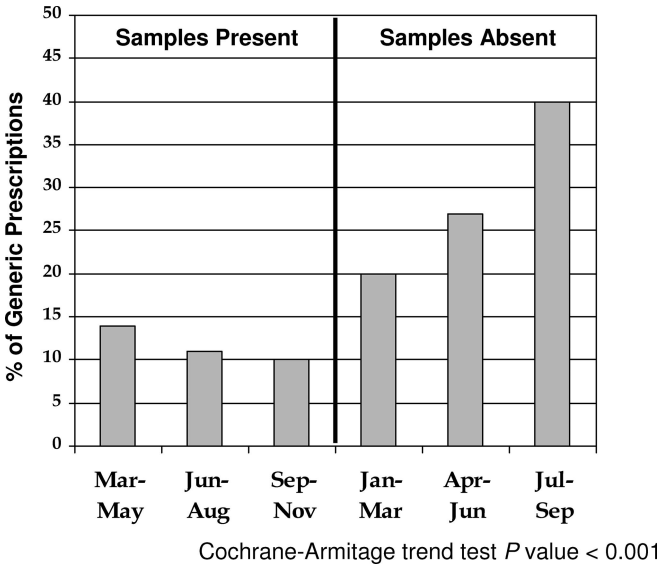

Fig. 3 ●●●.

Table 3. Association between clinical characteristics and uninsured patients receiving a generic prescription[a]

Characteristic	Odds ratio (95% CI) for receiving generic prescription	*P*
Samples absent (versus present)	4.54 (1.37–15.0)	0.01
Attending physician (versus resident)	5.26 (2.24–12.4)	0.0001
Patient gender = male (versus female)	1.65 (0.93–2.90)	0.08
Patient age	1.00 (0.98–1.02)	0.70
Number of prescriptions per patient	1.07 (0.91–1.26)	0.41

[a]*Data presented are derived from logistic regression using generalized estimating equations.*

Discussion

We found that physicians are over three times more likely to prescribe generic medications to uninsured patients when drug samples are not available; however, patients with comprehensive drug coverage (Medicaid) received a high proportion of generic prescriptions regardless of sample availability.

To our knowledge, ours is the first study examining the impact of drug samples on physicians' actual prescribing to uninsured patients. The presence of an electronic pharmacy database allowed us to abstract accurate data for a wide assortment of medications prescribed by a variety of physicians. The retrospective data collection also precluded any unintended influence on prescribing behavior. In addition, it is important to note that the clinic disbanded its drug sample closet for lack of a secure storage area, not because of a sentiment that samples were undesirable, minimizing the possibility of physician selection bias in our results.

Our finding that drug samples influence prescribing complements prior published studies. In a survey study, Chew and colleagues asked physicians to select the best drug treatment for various clinical scenarios. The physicians were then offered the choice of writing a prescription or dispensing a sample from a typical sample closet inventory. Greater than 90% of physicians who chose to dispense samples selected medications that differed from their initial drug choices.[12] Others have found that physicians with access to samples are less likely to prescribe generic nonsteroidal anti-inflammatory agents, less likely to prescribe guideline-recommended antihypertensives, and more likely to prescribe heavily advertised drugs.[4,5,10]

Studies examining the impact of samples on medication costs have been mixed. One study found that the presence of drug samples did not affect average prescription cost, and a second study found that patients' out-of-pocket expenditures increased when drug samples were unavailable.[10,13] A third study found that patients who received samples had higher out-of-pocket costs than those patients not receiving samples.[14] However, these studies were limited by either their

focus on a single class of medications or the presence of a prescription drug benefit in the study population. We are aware of no studies examining the impact of samples specifically on drug costs for the uninsured.

Our finding that uninsured patients receive fewer prescriptions for generic drugs when samples are available suggests that samples will lead to higher out-of-pocket costs. We did observe a decline in prescription cost after drug samples were removed from the study clinic, but the difference did not reach statistical significance. Of note, the study pharmacy qualifies for the Public Health Service Pricing Program which allows it to purchase many medications at deep discounts. This discounted price structure may have hampered our ability to detect a significant cost decrease after samples were removed.

Our finding that Medicaid patients consistently received a large percentage of generic prescriptions was unexpected. During the study time period, the North Carolina Medicaid program had no formulary, and patients paid a nominal one dollar fee for each prescription which we assumed would make physicians less cost-sensitive toward these patients. However, Medicaid's comprehensive drug coverage may explain the high rate of generic prescribing which was seen. Others have found that Medicaid patients are less likely to receive samples than the uninsured,[14] perhaps because physicians know that all prescription medications are easily obtainable. Therefore, the high rate of generic prescribing for Medicaid patients may indicate how prescribing would look in the absence of samples. In contrast, the low rate of generic prescribing to uninsured patients when samples are present likely reflects samples' impact on physicians' decisions. Alternatively, Medicaid patients may have a greater burden of disease for which there is more generic drug availability.

There are several ways samples may influence prescribing decisions. First, when physicians dispense samples, they may subsequently prescribe the same medication. One study found that 38% of samples dispensed in a family medicine practice were accompanied by a prescription for the same drug.[15] In Chew et al's[12] survey of physicians, 69% of physicians choosing to dispense an antihypertensive sample to an uninsured patient stated they would later prescribe the sampled agent if the patient gained insurance.

A second explanation is the unpredictable supply of drug samples. While many physicians consider samples to be good sources of medications for their uninsured patients,[7–9,12] they also report that the availability of drug samples is frequently erratic.[12] When patients return to the office for a "refill" of a sampled agent that is no longer in the closet, physicians may write a prescription for the missing medication rather than switching to a different drug.

Finally, when a practice discontinues its drug sample closet, providers may be motivated to learn which agents are generic and more affordable for patients who lack insurance. The continuous increase in the rate of generic prescribing seen in our study suggests that physicians progressed along such a learning curve.

It is possible that changes in pharmaceutical representative visits accounted for some of the increase in generic prescribing seen in our study. Contact with pharmaceutical representatives influences physicians' medical decisions.[16–20] When the study practice stopped accepting drug samples, pharmaceutical representative visits to the practice also ceased. Nonetheless, the resident physicians continued to have regular contact with pharmaceutical representatives at the program's university-affiliated teaching hospital.

Our study does have limitations. Our study site was a large resident-faculty practice, and the results may not apply to other practice structures. In addition, as with all retrospective studies, it is possible that unaccounted for factors contributed to the outcome we observed. However, the dramatic and continuous rise in generic prescribing to uninsured patients correlating with the time the drug sample closet was discontinued argues against this possibility. We also re-ran all analyses excluding drugs which became generically available during our study period, and our results were unchanged.

We could only abstract data on prescriptions filled at the on-site pharmacy. If the pharmacy's inventory significantly changed over time, then our results could be biased. This bias is unlikely as the on-site pharmacy maintained a diverse inventory of brand-name and generic drugs, and it had access to overnight ordering if needed.

Another limitation is that our dataset does not include prescriptions that patients chose to not get filled. If patients systematically chose to fill only their generic prescriptions, then we would overestimate the rate of generic prescribing. However, we would expect the frequency of unfilled prescriptions to be distributed evenly over our study time period, and therefore, it should not affect the temporal differences we observed. One could hypothesize that patients would be more likely to fill only generic prescriptions in the pharmacy when they were able to obtain their brand-name prescriptions as samples. This selective purchasing behavior would cause us to underestimate the true increase in generic prescribing associated with the removal of drug samples.

In conclusion, we found physicians are over three times more likely to prescribe generic medications to uninsured patients when drug samples are not available. Although many physicians believe drug samples benefit their uninsured patients by serving as a source of free medications, samples are likely to lead to higher costs for the uninsured as physicians tend to prescribe more nongeneric, expensive products. Future studies are needed to confirm these findings, as the results will have important policy implications for physicians, insurers, and governments struggling to control rising health care costs.

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