Estimating Generic Drug Use with Electronic Health Records Data from a Health Care Delivery System: Implications for Quality Improvement and Research

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ABSTRACT

BACKGROUND: Generic drug use in the outpatient setting is typically measured with adjudicated pharmacy claims; however, not all delivery systems have access to these data for their clinical populations.

OBJECTIVE: To develop an algorithm to estimate generic drug use in an outpatient setting using electronic health records (EHR) data.

METHODS: Twenty-five therapeutic classes were chosen with the potential for low generic use that were prescribed to managed care beneficiaries in a health care system in Northern California. An algorithm was developed to estimate generic drug use based on medication names and dispense-as-written requests from electronic prescriptions, as well as information on generic availability at the time the prescriptions were written. The algorithm was used to quantify a generic utilization rate (GUR) across therapeutic classes and was validated by comparing the estimated GUR to the true GUR, using pharmacy claims corresponding to prescriptions in the same patient cohort.

RESULTS: Among managed care beneficiaries, 104,859 prescriptions were identified for drugs in the therapeutic classes of interest with corresponding pharmacy claims. The algorithm estimated a GUR of 73.7% across 25 unique classes. The actual GUR based on pharmacy claims was 73.1%. Sensitivity (97%) and specificity (89%) of the algorithm were high, and total percentage of agreement was 95%.

CONCLUSIONS: An algorithm that estimates generic drug use performed well in a population of managed care beneficiaries. Health care delivery systems may apply methods described in this article to quantify generic drug use in their ambulatory populations for quality improvement and research initiatives, particularly when pharmacy claims are unavailable.

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What this study adds

- An algorithm that combines electronic health record data with information on generic drug availability accurately estimated generic drug use.
- Given a generic utilization rate of approximately 73% for managing care beneficiaries prescribed drugs within the select therapeutic classes of interest, opportunities exist for improved generic drug use.

Generic drug use helps to contain health care costs. Between 2005 and 2014, the use of generic drugs saved the U.S. health care system \$1.68 trillion.¹ Health care delivery systems, with the exception of managed care organizations, have traditionally not had to bear financial risk for outpatient pharmacy costs. Yet, as many fee-for-service or mixed-payer health care systems become accountable care organizations (ACOs) or adopt shared savings programs, the promotion of outpatient generic drug use may progressively become an important strategy to control health care spending and serve as a metric for health care value.^{2,3} Generic drug use in the outpatient setting is typically measured using adjudicated pharmacy claims; however, not all delivery systems have access to these data for their clinical populations.

Drug-prescribing data can be retrospectively extracted from electronic health records (EHR), but it is not always evident whether a drug was ultimately dispensed as a brand or a generic product. A drug may be prescribed by its generic name yet may not be available generically because of patent exclusivity so was dispensed in the community pharmacy as a branded product. Conversely, a drug may be prescribed by its brand name, based on preference or familiarity, but was dispensed in the pharmacy as a generic product, if available and permissible by law.⁴

In this study, we sought to develop an algorithm that estimates whether a prescribed drug was dispensed as a brand or a generic product. This algorithm was used to quantify a generic utilization rate (GUR) for prescriptions written to a cohort of managed care beneficiaries in an outpatient setting using EHR data. The algorithm was then validated by comparing the estimated GUR from EHR data with the true GUR,

What is already known about this subject

- Generic drug use helps to reduce health care costs, but usage is low for drugs within some therapeutic classes.
- Adjudicated pharmacy claims are typically used to measure generic drug use in an outpatient setting, but these data are not universally available.

TABLE 1 Relative Frequency Distribution of Prescriptions Across Therapeutic Classes

	Prescriptions N = 104,859 n (%)
1. Adrenals and combinations	5,893 (5.6)
2. Androgens and combinations	526 (0.5)
3. Anticonvulsants, hydantoin derivative	206 (0.2)
4. Anticonvulsants, succinimides	3 (0.0)
5. Anticonvulsants, miscellaneous	6,189 (5.9)
6. Antiemetics	478 (0.5)
7. Antigout agents	2,507 (2.4)
8. Antimanic agents	90 (0.1)
9. Antiplatelet agents	2,435 (2.3)
10. Anxiolytic/sedative/hypnotic	19,462 (18.6)
11. Cardiac drugs	7,560 (7.2)
12. Cardiac, antiarrhythmic agents	942 (0.9)
13. Anticoagulants	2,561 (2.4)
14. Estrogens and combinations	4,953 (4.7)
15. Eye/ear/nose/throat, miscellaneous	1,949 (1.9)
16. Immunosuppressants	148 (0.1)
17. Muscle relaxants, smooth-genitourinary	48 (0.1)
18. Parathyroid hormones	121 (0.1)
19. Psychotherapy, antidepressants	22,142 (21.1)
20. Psychotherapy, tranquilizers/antipsychotic	996 (1.0)
21. Stimulant, amphetamine type	834 (0.8)
22. Sympathomimetic agents	9,899 (9.4)
23. Thyroid agents	10,564 (10.1)
24. Vascular 5HT1 agonist (antimigraine)	2,599 (2.5)
25. Vasodilating agents	1,754 (1.7)

5HT1 = 5-hydroxytryptamine-1.

using pharmacy claims from corresponding prescriptions in the same patient cohort.

Methods

Study Setting

This study was conducted using data from a mixed-payer health care delivery system in Northern California. The system provides ambulatory care services to approximately 3 million patients annually. Approximately 20% of patients are commercial managed care beneficiaries (health maintenance organization/point of service, including Medicare Advantage), and 80% of patients are fee-for-service beneficiaries (55% commercial preferred provider organization [PPO] beneficiaries, and 23% and 2% are Medicare and Medicaid beneficiaries, respectively). The EpicCare EHR is integrated across all ambulatory clinics. Outpatient pharmacy claims data are available for managed care beneficiaries and are linked to prescribing data in the research database. Generic prescribing is the default option in the system. The patient population is generally representative of the underlying geographic area. This study was approved by the organization's institutional review board. Data were

de-identified according to Health Insurance Portability and Accountability Act standards.

Study Design

In this analysis, we focused on 25 American Hospital Formulary System therapeutic classes that were characterized as having the potential for low generic use, including drugs with narrow therapeutic indices (e.g., thyroid agents and antiepileptics; Table 1).⁵⁻⁸ Some products within these therapeutic classes may have been only available in branded form. We did not exclude these proprietary branded products because our intent was to develop an algorithm that could estimate generic drug use regardless of generic availability. The 25 therapeutic classes comprised 189 active product ingredients and 660 unique products based on dosage form and strength.

In the EHR, managed care beneficiaries were identified who had an active prescription for a drug in at least 1 of the therapeutic classes of interest in 2013. The prescription may have been written before 2013 (365-day prescription maximum). For patients with multiple drugs within a therapeutic class, the first active prescription in 2013 was used for analysis. Patients were permitted to have drugs in other therapeutic classes.

Electronic prescriptions were matched to corresponding pharmacy claims using (a) a unique patient identification key; (b) simple generic name of the product; (c) dosage form and strength (indicated by Generic Product Identifier); (d) date of electronic prescription; and (e) date medication was dispensed as determined from the adjudicated pharmacy claim. To be considered a match, we required that medication was dispensed on or up to 180 days after the date of the prescription. In previous analyses, we found that 99% of patients fill prescriptions within 6 months.

Estimating Generic Drug Use

An algorithm was developed to estimate whether a prescribed drug was dispensed as a brand or a generic product. The algorithm used (a) name of medication prescribed, as written in the EHR; (b) request for dispense-as written (DAW) in the EHR ("yes" or "not specified"); and (c) availability of the product in generic form on the date that prescription was written, as documented in the U.S. Food and Drug Administration's "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the Orange Book (<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/UCM071436.pdf>). We took into consideration the documented date of a product's approval, or date of discontinuation if applicable, in relation to the date that the drug was prescribed. We performed sensitivity analyses that included a lag of 3-6 months from the generic drug's first approval date to account for delays in availability.

According to the logic of the algorithm, when a prescribed medication's trade name matched the simple generic name (i.e., active ingredients), and the drug was available as a generic

product, the medication was classified as a generic drug. When a prescribed medication's trade name matched the simple generic name, but the drug was a proprietary-branded product, the medication was classified as a branded drug. When the trade name did not match the simple generic name and DAW was requested, the product was classified as a branded drug. When the trade name did not match the simple generic name and DAW was not requested, the product was classified as a generic drug, unless it was not available in generic form, in which case it was classified as a branded drug. With this algorithm, branded generics were treated as branded drugs. It was assumed that generic substitutions were made whenever possible in community-based pharmacies, as permissible by California state law.

Data Analysis

We applied the algorithm to EHR prescribing data from a population of managed care beneficiaries in order to estimate a GUR. Then, the true GUR was calculated based on the corresponding pharmacy claims for these prescriptions. The GUR is defined as the proportion of drugs prescribed/dispensed as generic products among the total number of drugs prescribed/dispensed regardless of generic product availability. The performance of the algorithm was assessed by comparing the estimated GUR to the true GUR (i.e., the "gold standard"). Sensitivity, specificity, positive predictive value, negative predictive value, and total percentage of agreement of the algorithm were calculated for the algorithm in a stepwise manner: (1) medication name; (2) medication name+DAW indicator; and (3) medication name+DAW indicator+generic availability (complete algorithm). In addition, Cohen's kappa statistic and 95% confidence intervals were reported to evaluate algorithm performance, accounting for any agreement expected from chance alone.⁹

Results

Description of Study Cohort

We identified 153,506 active electronic prescriptions in 2013 for products within the 25 therapeutic classes of interest among managed care beneficiaries. Of these, 104,859 prescriptions (68.3%) were matched to pharmacy claims. The majority of patients were female (67.9%), aged 40 years or older (88.0%), and non-Hispanic white (69.3%).

Performance of the Algorithm

When using medication name alone or medication name with the DAW indicator, the algorithm estimated a GUR of 92.6% and 95.7%, respectively (Table 2). When using the 3 components of the algorithm (complete algorithm), the estimated GUR was 73.7%. When calculated with corresponding pharmacy claims data (gold standard), the GUR was 73.1%. The algorithm performed optimally when we employed the

TABLE 2 Estimated Generic Utilization Rates and Algorithm Diagnostics

	1	2	3
	Medication Name	+DAW	+Generic Availability
Estimated generic utilization rate	92.6	95.7	73.7
Sensitivity	0.978	0.984	0.969
Specificity	0.216	0.117	0.892
Positive predictive value	0.772	0.752	0.961
Negative predictive value	0.785	0.725	0.913
Total percentage of agreement	0.773	0.751	0.948
Kappa (95% CI)	0.252 (0.246-0.258)	0.137 (0.132-0.142)	0.868 (0.864-0.871)

CI = confidence interval; DAW = dispense as written.

complete algorithm; sensitivity was 97%; specificity was 89%; and total agreement was 95%. Misclassification of a branded drug (i.e., when the algorithm predicted a generic would be dispensed) occurred for 2.9% of all prescriptions. Misclassification of a generic drug (i.e., when the algorithm predicted a brand would be dispensed) occurred for 2.1% of all prescriptions. The kappa statistic was 0.868 (0.864, 0.971). The algorithm performed similarly using a 3- or 6-month delay for the date of generic availability (data not shown).

Discussion

We developed and validated an algorithm that estimated whether a prescribed drug was dispensed as a brand or generic product in an outpatient setting. We found that EHR data alone (i.e., medication name with or without the DAW indicator) was not sufficient to accurately determine whether a prescribed medication was dispensed as a brand or generic product. Alone, this information grossly overestimated generic drug use, since generic prescribing is the default option in this health care delivery system's EHR. However, when EHR data were used in combination with information on generic drug availability, the algorithm performed well. Total agreement was 95% and Cohen's kappa was 0.87. Cohen originally described a kappa statistic between 0.81 and 1.00 as "almost perfect agreement"¹⁰; however, others have taken a more conservative approach, describing values in this range as "minimally acceptable agreement."⁹

Across the select therapeutic classes of interest, the estimated GUR was 73% in 2013. This rate is below the reported rate across all prescriptions (88%) in the United States.¹¹ This rate was expected, since we intentionally focused this analysis on therapeutic classes thought to have low generic use, such as drugs that have narrow therapeutic indices. Thus, areas of opportunity exist for improved generic use among products in these select classes.

Current evidence shows that mandatory versus permissive substitution laws do not materially affect generic drug use in the United States. At least 2 independent studies have shown that patient consent policy, at least in the short term, was a more important driver of generic drug use.^{12,13} For example, in the 6-12 months after patent expiration of the lipid-lowering drug Zocor (simvastatin), uptake of generic simvastatin lagged among Medicaid beneficiaries in states with an active patient consent policy relative to those with a presumptive consent policy, regardless of whether the drugs were dispensed in states with permissive or mandatory substitution laws.¹³ However, even this effect was not sustained long term. In future studies, we plan to further evaluate disagreement between the generic utilization algorithm and pharmacy claims data to understand for which products pharmacists may be less likely to substitute a generic, including when a patient refuses the substitution.

Limitations

There are several limitations to this analysis that should be considered when interpreting the findings. We developed and validated the algorithm using prescriptions from a cohort of managed care beneficiaries, who represent approximately one fifth of the total clinical population of the organization. This is the only population with prescribing data and pharmacy claims data. We were able to match 68% of medication orders to corresponding pharmacy claims, which was not unexpected given that approximately 30% of medications are reportedly never filled (i.e., primary nonadherence).¹⁴ Furthermore, medications that were filled under a \$4 generic program may not have generated a pharmacy claim and thus would not have matched. The analysis was also restricted to claims that were filled within 180 days from the date the prescription was written; however, extending this period did not affect outcomes (data not shown), since the vast majority of patients who filled their prescriptions did so within 6 months.

While we expect that the algorithm can be similarly applied to beneficiaries not in managed care plans, we cannot know this for certain based on the current analysis. Cost sharing for outpatient prescriptions potentially differs for most fee-for-service or PPO health plans relative to managed care plans, which may influence whether a patient chooses a brand over a generic if the cost difference is minimal. Nevertheless, these cost differences should not affect the validity of the algorithm. We cannot know if the GUR estimated in this study is generalizable to health systems in other parts of the United States or to other therapeutic classes. Again, this should not affect the validity of the algorithm, since its theoretical framework would still apply.

Finally, the algorithm itself is simple to apply; in practice, however, the electronic Orange Book file must be linked to electronic prescribing information to determine the date of a product's availability or discontinuation. Coding differences between EHR prescribing information and the Orange Book may necessitate more upfront labor costs to ensure data har-

monization, especially when a large number of products are evaluated. The algorithm, in part, relies on the premise that community pharmacists dispense a generic product whenever possible in states with permissive substitution laws, such as California. Our findings support this notion, since misclassifications associated with lack of a generic substitution (i.e., algorithm predicts a generic is dispensed and pharmacy claims show that a brand was dispensed) occurred for only 2.9% of all prescriptions. Pharmacist training and relatively higher profit margins on high volume generic drugs relative to branded drugs typically serve to incentivize generic drug dispensing.

Implications

As health care costs continue to rise in the United States, new models of health care delivery are gaining traction, such as ACOs and shared savings programs, which serve to contain spending while preserving or even improving the quality of patient care.¹⁵ With financial incentives better aligned between payers and health care delivery systems, outpatient generic drug use may become an important metric for assessing health care value.^{6,7} In a survey of 46 ACO representatives in the United States, 50% of the representatives reported a high degree of readiness to encourage generic medication use through formulary management.⁷ Indeed, some ACOs are already promoting generic drug use to contain costs, such as encouraging use of clopidogrel rather than Plavix for acute coronary syndrome and warfarin rather than Coumadin for atrial fibrillation.¹⁶ In 2014, the Centers for Medicare & Medicaid Services issued a request for information about how ACOs might improve care integration and financial accountability, with specific mention of better integration of Medicare Part D expenditures in cost calculations.¹⁷ Generic drug use is a key pharmacy-based cost-saving measure. In this regard, health care delivery systems will benefit from timely methods to accurately measure generic drug prescribing and use in the outpatient setting, particularly in the absence of adjudicated pharmacy claims data. Such information may be equally important for quality improvement initiatives and research to promote the use of the most cost-effective medicines.

Conclusions

In a cohort of managed care beneficiaries, an algorithm that estimates how many EHR prescriptions are dispensed as brand or generic products performed well in approximating a GUR in an outpatient setting, when combined with information on generic drug availability. As use of generic drugs continues to be an important strategy to contain health care costs, health care delivery systems may apply the methods described here to quantify generic prescribing and use for their clinical populations. Such methods can be used to inform the design of quality improvement and research initiatives to promote use of the most cost-efficient medicines.

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Romanelli and Segal contributed the study concept and design. Nimbal took the lead in data collection, assisted by Romanelli. All authors were involved with data interpretation and revision of the manuscript. The manuscript was written by Romanelli and Nimbal.

REFERENCES

1. Generic Pharmaceutical Association. Generic drug savings in the U.S. Seventh annual edition: 2015. Available at: http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf. Accessed August 22, 2016.
2. Colla CH, Lewis VA, Beaulieu-Jones BR, Morden NE. Role of pharmacy services in accountable care organizations. *J Manag Care Spec Pharm*. 2015;21(4):338-44. Available at: <http://www.jmcp.org/doi/10.18553/jmcp.2015.21.4.338>.
3. Dubois RW, Feldman M, Lustiq A, et al. Are ACOs ready to be accountable for medication use? *J Manag Care Pharm*. 2014;20(1):17-21. Available at: <http://www.jmcp.org/doi/10.18553/jmcp.2014.20.1.17>.
4. U.S. Department of Health & Human Services. Expanding the use of generic drugs. ASPE Issue Brief. December 1, 2010. Available at: <http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib.shtml>. Accessed August 22, 2016.
5. Briesacher BA, Andrade SE, Fouayzi S, Chan KA. Medication adherence and the use of generic drug therapies. *Am J Manag Care*. 2009;15(7):450-56.
6. Meyer J, Fardo D, Fleming ST, Hopenhayn C, Gokun Y, Ryan M. Generic antiepileptic drug prescribing: a cross-sectional study. *Epilepsy Behav*. 2013;26(1):1-6.
7. Bolton JM, Dahl M, Sareen J, et al. A population-based study of the use of selective serotonin reuptake inhibitors before and after introduction of generic equivalents. *Can J Psychiatry*. 2012;57(4):223-29.
8. Segal JB, Daubresse M, Lee CY, et al. Therapeutic class differences in generic usage. *Pharmacoeconom Drug Saf*. 2015;24(Suppl 1):abstract 245.
9. McHugh ML. Interrater reliability: the kappa statistic. *Biochemia Medica*. 2012;22(3):276-82.
10. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas*. 1960;20:37-46.
11. IMS Institute for Healthcare Informatics. Generic drug savings in the U.S. Seventh annual edition: 2015. Available at: http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf. Accessed September 1, 2016.
12. Song Y, Barthold D. The power of not asking: how generic drug substitution laws affect patient's demand for generic drugs. Social Science Research Network. January 27, 2015. Available at: http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2727943. Accessed August 22, 2016.
13. Shrank WH, Chordhry NK, Agnew-Blais J, et al. State generic substitution laws can lower drug outlays under Medicaid. *Health Aff (Millwood)*. 2010;29(7):1383-90.
14. Tamblyn R, Egual T, Huang A, Winslade N, Doran P. The incidence and determinants of primary nonadherence with prescribed medications in primary care: a cohort study. *Ann Intern Med*. 2014;160(7):441-50.
15. Pizzo JJ, Grude ME. Getting to there from here: evolving to ACOs through clinical integration programs. Kaufman, Hall & Associates. 2011. Available at: http://www.advocatehealth.com/documents/app/ci_to_aco.pdf. Accessed August 22, 2016.
16. Lewis C. The impact of ACOs on prescribing for acute coronary syndrome and atrial fibrillation: actionable insights from U.S. payers and prescribers. U.S. Physician and Payer Forum. May 9, 2014. Available at: <https://decisionresourcesgroup.com/report/437/>. Accessed August 22, 2016.
17. Shrank W, Sussman A, Gilligan P, Brennan T. Correcting the blind spot in accountability: the role of pharmacy care. June 25, 2014. Health Affairs Blog. Available at: <http://healthaffairs.org/blog/2014/06/25/correcting-the-blind-spot-in-accountability-the-role-of-pharmacy-care/>. Accessed August 22, 2016.