

Pharmacy Dispensing of Electronically Discontinued Medications

Adrienne S. Allen, MD, MPH, and Thomas D. Sequist, MD, MPH

Background: Most physician offices do not transmit orders for medication discontinuation to the pharmacy, creating the potential for errors in dispensing of previously prescribed medications. Electronic health records offer the potential to assess this patient safety concern.

Objective: To assess the frequency of and potential patient harm associated with pharmacy dispensing of discontinued medications in the ambulatory setting.

Design: Retrospective cohort study.

Setting: Multispecialty group practice in eastern Massachusetts using an electronic health record.

Patients: 30 406 adult patients with an electronic discontinuation order for antihypertensive, antiplatelet, anticoagulant, oral hypoglycemic, and statin medications between November 2008 and October 2009.

Measurements: Dispensing of discontinued medications within 12 months and associated potential patient harm.

Results: Among 83 902 targeted medications that were electronically discontinued, 1218 (1.5% [95% CI, 1.4% to 1.5%]) were

subsequently dispensed by the pharmacy a mean of 1.0 (SD, 0.3) time during the 12-month follow-up. Among the top 10 most frequently electronically discontinued medications, the rate of subsequent dispensing by a pharmacy ranged from 0.9% for metformin to 2.5% for metoprolol. Manual chart review of 416 medication-dispensing events that were predefined as high risk according to an automated algorithm identified potential harm in 50 (12%) cases, including clinical reactions ($n = 18$), laboratory abnormalities ($n = 17$), duplicated medication classes dispensed ($n = 8$), and potential allergic reactions ($n = 7$).

Limitation: Information on pharmacy dispensing was available for only 52% of medication orders.

Conclusion: The dispensing of discontinued medications represents an important ambulatory patient safety concern. Electronic health records should be used to facilitate better communication between providers and pharmacies and improve medication safety.

Primary Funding Source: National Institutes of Health.

Ann Intern Med. 2012;157:700-705.
For author affiliations, see end of text.

www.annals.org

Medication errors represent an important ambulatory patient safety concern. These errors result in patient harm, ranging from mild intolerances to life-threatening allergic reactions (1–3). Electronic health records can reduce such patient safety concerns by coupling electronic medication prescribing with real-time decision support to avoid errors related to medication dosing, medication allergies, or drug–drug interactions (4, 5). These electronic orders can also be transmitted electronically to the pharmacy to provide seamless communication, an approach required by the newly developed meaningful-use criteria for electronic health records (6).

Although the process of initiating medication prescriptions has been improved to ensure both patient safety and efficiency, less attention has been paid to the process of discontinuing medications. Physician offices do not routinely communicate medication discontinuation orders to retail pharmacies. Patient harm is possible if pharmacies dispense medications to patients after the physician has discontinued them for a clinically important reason. This phenomenon has been difficult to assess by using handwritten prescriptions and paper medical records. However, electronic health records allow providers to electronically discontinue a medication within the patient chart and therefore create the opportunity to measure the phenomenon of errors in pharmacy dispensing of such medications.

The goal of our study was to identify the prevalence of dispensing of medications after an electronic discontinua-

tion order by a provider in the ambulatory setting. We further sought to assess the associated patient harm from such events.

METHODS

Study Setting

The study was conducted at Harvard Vanguard Medical Associates (HVMA), a large multispecialty group practice consisting of 15 ambulatory health centers in eastern Massachusetts. These clinical practices use a common electronic health record (Epic, Verona, Wisconsin) that captures clinical notes and electronic diagnosis codes, medication prescriptions, and laboratory test results. The electronic health record facilitates electronic transmission of new medication prescription orders to pharmacies. It does not electronically transmit information on medication discontinuation orders and does not transmit updates on current medications that might facilitate medication reconciliation.

Patient Eligibility

We included all adult patients aged 18 years or older who had a targeted medication discontinued between 1 November 2008 and 31 October 2009 and did not have this medication reordered within 48 hours of the original discontinuation order. To facilitate measurement of medication dispensing, we further restricted this group to patients who had previously filled their medication prescription at an HVMA pharmacy. Finally, we limited the study

sample to patients actively receiving care at HVMA by including only patients with an outpatient office visit at HVMA from 1 November 2006 to 1 November 2008. In our study sample, 48% of prescriptions were not filled at HVMA pharmacies and were excluded from further analyses. We targeted long-term-use medications with the potential for significant harm when used inappropriately (2), including antihypertensive agents, antiplatelet agents, oral antiplatelet or anticoagulant agents, diabetic hypoglycemic agents, and lipid-lowering agents (statins).

Patient Variables

We collected data on patient age, sex, race, and insurance type from the electronic health record. We also used electronic health record data to identify the presence of diabetes, cardiovascular disease, and hypertension; number of medications on the active electronic medication list at the time of medication discontinuation; and relevant laboratory results, including serum creatinine, liver function test results, and hemoglobin. Chronic conditions were identified on the basis of their presence on the electronic problem list or outpatient encounter diagnosis codes. Data from this electronic health record system have been used in several previous studies of quality of care and patient safety (7–10).

Outcomes Measures

Our primary study outcome was the frequency of potentially unsafe medication dispensing after electronic discontinuation by a physician. We defined a potentially unsafe medication-dispensing event as a documented pharmacy dispensing within 12 months of the provider order to discontinue the medication in the electronic health record, and no active medication order at the time of dispensing. All medication-dispensing events within HVMA pharmacies are electronically tracked by a commercial system (RxEXPRESS, SXC Health Solutions, Lisle, Illinois) and linked to the original medication order within the HVMA electronic health record.

Our secondary outcome was potential harm associated with the dispensing of discontinued medications, identified by manual physician review of a targeted subset of medication-dispensing events at higher risk for producing adverse outcomes. High-risk medication-dispensing events were identified through an electronic chart review during the period of 1 month before to 6 months after the date of medication discontinuation. The search identified cases with a newly documented medication allergy (for all medications); systolic blood pressure less than 100 mm Hg or diastolic blood pressure less than 60 mm Hg (for antihypertensive medications); or laboratory abnormalities, including potassium level greater than 5.6 mmol/L (for angiotensin-converting inhibitors, angiotensin-receptor blockers, and β -blockers), increase in creatinine level greater than 30%, or decrease in estimated glomerular filtration rate of more than 15% (for angiotensin-converting

Context

Electronic health records make it possible to measure how often a pharmacist dispenses medication after a physician tells a patient to stop taking it but does not notify the pharmacist.

Contribution

In this study of the most frequently prescribed medications for ambulatory patients, researchers found that pharmacists dispensed discontinued medication for 1.5% of prescriptions.

Caution

Information was available for only half the prescriptions.

Implication

Dispensing discontinued medication is a safety concern.

—The Editors

enzyme inhibitors or angiotensin-receptor blockers); sodium level less than 133 mmol/L, potassium level less than 3.3 mmol/L, calcium level greater than 2.60 mmol/L, uric acid level greater than 446.14 μ mol/L, magnesium level less than 0.75 mmol/L (for hydrochlorothiazide); creatine kinase level greater than 348 IU/L, aspartate aminotransferase level greater than 35 IU/L, alanine aminotransferase level greater than 40 IU/L (for statins); and international normalized ratio greater than 4.0 (for warfarin).

Reasons for medication discontinuation were classified by a physician chart reviewer as clinical intolerance, dose adjustment, change to alternative medication, laboratory abnormality, patient preference, no further clinical indication for the medication, or electronic medication list reconciliation. Medication list reconciliation was characterized by providers removing duplicate prescriptions from the electronic medication list that may have resulted from previous medication refill orders or other historical medication entries. Potential harm was identified as the presence of a new laboratory abnormality potentially related to the medication, a clinical reaction potentially related to the medication, a duplicate medication dispensing of a similar class (for example, 2 β -blockers dispensed concurrently), or dispensing of a medication in the presence of a documented allergy.

Statistical Analysis

We compared sociodemographic and clinical characteristics among patients who were and were not dispensed a medication after its discontinuation using the chi-square test for categorical variables and the *t* test for continuous variables. We analyzed predictors for the dispensing of discontinued medications by fitting a single multivariable logistic regression model with medication dispensing as the binary dependent variable. The primary independent variables included patient age, sex, race, and insurance type;

Table 1. Patient Characteristics According to Whether a Medication Was Dispensed After Discontinuation

Characteristic	Discontinued Medication Dispensed	Discontinued Medication Not Dispensed	P Value
Patients, n	1128	29 278	
Mean age (SD), y	67 (14)	63 (14)	<0.001
Female, n (%)	581 (51)	15 812 (54)	0.098
Race, n (%)			<0.001
White	710 (64)	21 062 (74)	
Black	239 (22)	4462 (16)	
Other	155 (14)	3127 (11)	
Insurance, n (%)			<0.001
Medicaid	58 (5)	1354 (5)	
Medicare	579 (55)	10 798 (40)	
Commercial	397 (38)	14 602 (54)	
Self-pay	22 (2)	464 (2)	
Comorbid conditions, n (%)			<0.001
Coronary artery disease	260 (23)	4327 (15)	
Hypertension	806 (71)	18 794 (64)	
Diabetes	446 (40)	6969 (24)	
Active medications, n (%)			<0.001
0–5	113 (11)	6896 (24)	
6–10	381 (36)	11 994 (42)	
11–15	291 (28)	6022 (21)	
>15	273 (26)	3485 (12)	
Mean dispensing events over 12 mo (SD), n	1.0 (0.3)	–	–

presence of comorbid conditions; number of active medications; and medication class (statin, antihypertensive agent, oral hypoglycemic agent, and oral antiplatelet or anticoagulant agent). We found no relationship between provider and frequency of medications dispensed without an order and thus did not account for potential confounding by provider in the multivariable models. All analyses were conducted by using SAS software, version 9.2 (SAS Institute, Cary, North Carolina). The study was approved by the Brigham and Women's Hospital Human Research Committee. The institutional review board waived the need for patient informed consent.

Role of the Funding Source

Dr. Allen was funded by a National Institutes of Health training award. The funding source played no role in the study design, data collection, interpretation of results, or decision to publish the manuscript.

RESULTS

Patient and Medication Characteristics

We identified 83 902 unique targeted medication discontinuations by 1045 providers among a population of 30 406 adult patients during the 12-month study period. We further identified 1218 (1.5% [95% CI, 1.4% to 1.5%]) medication-dispensing events to 1128 (3.7% [CI,

3.5% to 3.9%]) patients after discontinuation of the medication in the electronic health record. The number of medication-dispensing events per provider ranged from 0 to 16, with an interquartile range of 0 to 1 and a mean of 1.2 events per provider.

Compared with patients not receiving a medication, patients dispensed a medication after its discontinuation were more likely to be older, black, and insured by Medicare (Table 1). Although lisinopril, simvastatin, and hydrochlorothiazide were the most commonly discontinued medications, metoprolol and amlodipine were associated with the highest rates of dispensing after their discontinuation (Table 2).

Correlates of Dispensing a Discontinued Medication

Black race (odds ratio, 1.5 [CI, 1.3 to 1.8]), Medicaid insurance (odds ratio, 1.4 [CI, 1.1 to 1.9]), Medicare insurance (odds ratio, 1.7 [CI, 1.4 to 2.1]), and an increasing number of current medications on the electronic medication list were all significantly associated with dispensing a discontinued medication (for full model details, see the Appendix Table, available at www.annals.org).

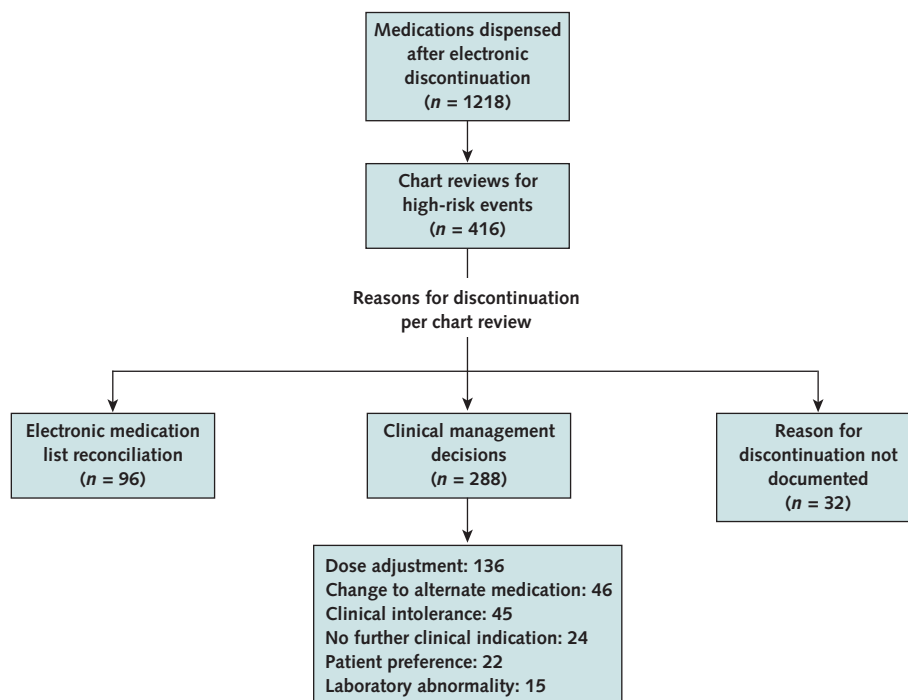
Potential Harm

Among 1218 medications dispensed, 416 (34%) met criteria for higher risk for potential adverse events on the basis of the electronic screening algorithm (Figure). The reasons for discontinuation identified by chart review for these 416 cases included clinical management decisions (69%), electronic medication list reconciliation (23%), and no documented reason (8%). The most common clinical management decisions included dose adjustments ($n = 136$), change to alternate medication ($n = 46$), and clinical intolerance ($n = 45$).

Among the 416 cases that met screening criteria for higher risk for adverse events, potential harm was identified in 50 (12%) cases. These included a documented clinical reaction ($n = 18$), laboratory abnormality ($n = 17$), duplicate medication dispensing ($n = 8$), and medication dispensing in the presence of a documented allergy ($n = 7$) (Table 3).

Table 2. Dispensing Rates Among Top 10 Electronically Discontinued Medications

Medication	Discontinued, n	Dispensed, n (%)
Lisinopril	11 358	155 (1.4)
Simvastatin	10 740	153 (1.4)
Hydrochlorothiazide	9484	110 (1.2)
Atenolol	9449	93 (1.0)
Amlodipine	4410	91 (2.1)
Metoprolol	4117	104 (2.5)
Metformin	4063	37 (0.9)
Enalapril	2996	32 (1.1)
Irbesartan	2304	35 (1.5)
Warfarin	2245	37 (1.6)

Figure. Identification of reasons for electronic discontinuation of medications detected by using manual chart review.

DISCUSSION

Electronic health records hold great promise to improve the quality and safety of health care delivery in the ambulatory setting (11–13). There are many opportunities to consider where the potential benefits of electronic health records are not being fully realized, including the area of electronic order entry and medication safety (14). We studied a mature electronic health record system with established electronic links to a pharmacy dispensing system and found that discontinued medications are dispensed and that these events do result in potential harm in many cases.

We identified several patient-level factors that were associated with dispensing of discontinued medications, such as patient race, insurance status, and increasing number of active medications. These markers may be helpful to physicians' offices and retail pharmacies to flag higher-risk patients for more robust medication reconciliation procedures.

However, despite these patient-level findings, it is most important to recognize that the potential and realized harm that resulted from the dispensing of discontinued medications affected many patients. These events were noted across all medication classes studied, with effects ranging from relatively minor laboratory abnormalities to clinically significant hypotension. The diverse nature of these events suggests that a more systematic intervention is needed to ensure that patients receive the correct medication regimens.

Table 3. Cases of Potential Harm Resulting From Dispensing of Electronically Discontinued Medications*

Adverse Event	Cases, n
Clinical reaction	
Hypotension	6
Bradycardia	3
Cough	3
Lightheadedness	3
Atrial flutter (from hypokalemia)	1
Gastrointestinal upset	1
Myalgia	1
Total	18
Laboratory abnormality	
Hyponatremia	4
Elevated liver function test results	5
Hypokalemia	4
Hyperkalemia	2
Increased creatinine level	1
Elevated uric acid level	1
Total	17
Duplicate medication	
2 statins dispensed	3
ACE inhibitor/ARBs dispensed	2
2 ACE inhibitors dispensed	1
2 ARBs dispensed	1
2 sulfonylureas dispensed	1
Total	8
Documented allergy	
Cough	5
Rash	1
Elevated creatine phosphokinase level	1
Total	7

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker.

* High-risk medication dispensing events defined as cases with a newly documented medication allergy, hypotension, or pertinent laboratory abnormalities.

Our results build on earlier work suggesting that adverse drug events do occur in the ambulatory setting (1). Prescriptions can now be easily transmitted to pharmacies with the click of a mouse, and medications can be discontinued and removed from the medication list with a similar click. However, there is little tangible feedback to physicians in this process to validate that a patient is following the map laid out by this electronic trail. In fact, many clinicians may incorrectly assume that the act of electronically discontinuing a medication is automatically transmitted to the pharmacy, in the same way that a new prescription is transmitted.

Our work suggests several potential avenues for future efforts to improve medication safety. Electronic health records offer a clear opportunity to track when a clinician discontinues a medication, and these discontinuation orders should be transmitted electronically to the retail pharmacy. Even more broadly, electronic health records should be used to facilitate ongoing bidirectional communication between physician offices and retail pharmacies, ensuring that new prescription orders are transmitted, current medications are verified, and discontinued medications are removed from the pharmacy list. This process will need to account for physician use of electronic discontinuation orders to facilitate reconciliation of the electronic medication list, as we identified in our analysis. Although such comprehensive programs are not widely in place among either vendor or “home-grown” electronic health records, we can build on existing policies and technology that require and enable the transmission of new prescription information from physician offices to pharmacies.

There are also non-technology-based solutions to address this important patient safety concern. New programs that increase patient engagement in their care management plan should include efforts to increase patient awareness of their medication list and empower patients as advocates to identify incorrect dispensing of medications. In addition, reconciling medications via manual review of electronic problem lists and verbal confirmation with patients during every office visit is also likely to identify the use of previously discontinued medications (15).

Our study is strengthened by availability of accurate information on both discontinuation orders and pharmacy dispensing information. However, our conclusions should be interpreted in the context of important limitations. First, we could analyze care for only 52% of patients who filled their medication prescriptions at HVMA pharmacies. We do not know the rates of medication dispensing after electronic discontinuation among less integrated systems that use many commercial pharmacies. Second, we conducted chart reviews for only a subset of medication-dispensing events that were at higher risk for adverse events. The prevalence of adverse events may be lower among the charts not subjected to medical record review. We also may have underestimated harm because harm and

potential harm are difficult to assess in the outpatient setting (6). Finally, we did not have detailed information on the characteristics of the prescribing clinicians and therefore cannot comment on the role of clinician features in the dispensing of medications that have been previously discontinued.

In conclusion, it is clear that pharmacy dispensing of medications after their discontinuation by physicians is a real phenomenon with important clinical consequences in the ambulatory setting. Further work should focus on evaluating methods of improving communication between providers and pharmacies to better reconcile medication lists, as well as explore strategies to improve patients' knowledge and awareness of their medication regimen.

From North Shore Physicians Group, Danvers, and Brigham and Women's Hospital, Harvard Medical School, and Harvard Vanguard Medical Associates, Boston, Massachusetts.

Grant Support: Dr. Allen was funded by a National Institutes of Health Institutional National Research Service Award (T32HP10251-02).

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-1182.

Reproducible Research Statement: Study protocol and statistical code: Available from Dr. Allen (e-mail, aallen0@partners.org). Data set: Not available.

Requests for Single Reprints: Adrienne S. Allen, MD, MPH, North Shore Physicians Group, 104 Endicott Street, Suite 104, Danvers, MA 01923; e-mail, aallen0@partners.org.

Current author addresses and author contributions are available at www.annals.org.

References

1. Gandhi TK, Weingart SN, Borus J, Seger AC, Peterson J, Burdick E, et al. Adverse drug events in ambulatory care. *N Engl J Med*. 2003;348:1556-64. [PMID: 12700376]
2. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med*. 2011;365:2002-12. [PMID: 22111719]
3. Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA*. 2003;289:1107-16. [PMID: 12622580]
4. Ammenwerth E, Schnell-Inderst P, Machan C, Siebert U. The effect of electronic prescribing on medication errors and adverse drug events: a systematic review. *J Am Med Inform Assoc*. 2008;15:585-600. [PMID: 18579832]
5. Kaushal R, Kern LM, Barrón Y, Quaresimo J, Abramson EL. Electronic prescribing improves medication safety in community-based office practices. *J Gen Intern Med*. 2010;25:530-6. [PMID: 20186499]
6. Blumenthal D, Tavenner M. The “meaningful use” regulation for electronic health records. *N Engl J Med*. 2010;363:501-4. [PMID: 20647183]
7. Sequist TD, Fitzmaurice GM, Marshall R, Shaykevich S, Marston A, Safran DG, et al. Cultural competency training and performance reports to improve

diabetes care for black patients: a cluster randomized, controlled trial. *Ann Intern Med.* 2010;152:40-6. [PMID: 20048271]

8. **Sequist TD, Schneider EC, Li A, Rogers WH, Safran DG.** Reliability of medical group and physician performance measurement in the primary care setting. *Med Care.* 2011;49:126-31. [PMID: 20421826]

9. **Sequist TD, Marshall R, Lampert S, Buechler EJ, Lee TH.** Missed opportunities in the primary care management of early acute ischemic heart disease. *Arch Intern Med.* 2006;166:2237-43. [PMID: 17101942]

10. **Allen AS, Orav EJ, Lee TH, Sequist TD.** Clinician personality and the evaluation of higher-risk patient symptoms. *J Patient Saf.* 2011;7:122-6. [PMID: 21738072]

11. **Chaudhry B, Wang J, Wu S, Maglione M, Mojica W, Roth E, et al.** Systematic review: impact of health information technology on quality, efficiency,

and costs of medical care. *Ann Intern Med.* 2006;144:742-52. [PMID: 16702590]

12. **Bates DW, Gawande AA.** Improving safety with information technology. *N Engl J Med.* 2003;348:2526-34. [PMID: 12815139]

13. **Buntin MB, Burke MF, Hoaglin MC, Blumenthal D.** The benefits of health information technology: a review of the recent literature shows predominantly positive results. *Health Aff (Millwood).* 2011;30:464-71. [PMID: 21383365]

14. **Metzger J, Welebob E, Bates DW, Lipsitz S, Classen DC.** Mixed results in the safety performance of computerized physician order entry. *Health Aff (Millwood).* 2010;29:655-63. [PMID: 20368595]

15. **Nemeth LS, Wessell AM.** Improving medication safety in primary care using electronic health records. *J Patient Saf.* 2010;6:238-43. [PMID: 21500611]

ANNALS OF INTERNAL MEDICINE JUNIOR INVESTIGATOR AWARDS

Annals of Internal Medicine and the American College of Physicians recognize excellence among internal medicine trainees and junior investigators with annual awards for original research and scholarly review articles published in *Annals* in each of the following categories:

- Most outstanding article with a first author in an internal medicine residency program or general medicine or internal medicine subspecialty fellowship program
- Most outstanding article with a first author within 3 years following completion of training in internal medicine or one of its subspecialties

Selection of award winners will consider the article's novelty; methodological rigor; clarity of presentation; and potential to influence practice, policy, or future research. Judges will include *Annals* Editors and representatives from *Annals'* Editorial Board and the American College of Physicians' Education/Publication Committee.

Papers published in the year following submission are eligible for the award in the year of publication. First author status at the time of manuscript submission will determine eligibility. Authors should indicate that they wish to have their papers considered for an award when they submit the manuscript, and they must be able to provide satisfactory documentation of their eligibility if selected for an award. Announcement of awards for a calendar year will occur in January of the subsequent year. We will provide award winners with a framed certificate, a letter documenting the award, and complimentary registration for the American College of Physicians' annual meeting.

Please refer questions to Mary Beth Schaeffer at mschaeffer@acponline.org or visit www.annals.org/public/juniorinvestigatoraward.aspx.

Current Author Addresses: Dr. Allen: North Shore Physicians Group, 104 Endicott Street, Suite 104, Danvers, MA 01923.
Dr. Sequist: Division of General Medicine, Brigham and Women’s Hospital, 1620 Tremont Street, Boston, MA 02120.

Author Contributions: Conception and design: A.S. Allen, T.D. Sequist.
Analysis and interpretation of the data: A.S. Allen, T.D. Sequist.
Drafting of the article: A.S. Allen, T.D. Sequist.
Critical revision of the article for important intellectual content: A.S. Allen, T.D. Sequist.
Final approval of the article: T.D. Sequist.
Statistical expertise: T.D. Sequist.
Collection and assembly of data: A.S. Allen, T.D. Sequist.

Appendix Table. Predictors of Dispensing Medications After Electronic Discontinuation

Variable	Odds Ratio for Receiving Discontinued Medication (95% CI)
Age	
<65 y	Reference
≥65 y	0.9 (0.7–1.1)
Sex	
Male	Reference
Female	0.9 (0.8–1.0)
Race	
White	Reference
Black	1.5 (1.3–1.8)
Other	1.6 (1.3–1.9)
Insurance	
Commercial	Reference
Medicaid	1.4 (1.1–1.9)
Medicare	1.7 (1.4–2.1)
Self-pay	1.7 (0.9–2.6)
Active medications	
0–5	Reference
6–10	1.4 (1.1–1.8)
11–15	1.6 (1.3–2.1)
>15	2.3 (1.6–2.9)
Medication class	
Statin	Reference
Antihypertensive agent	1.2 (1.0–1.4)
Oral hypoglycemic agent	0.9 (0.7–1.2)
Oral antiplatelet or anticoagulant agent	1.1 (0.8–1.6)
Comorbid conditions	
None	Reference
Diabetes	1.0 (0.9–1.2)
Hypertension	1.0 (0.9–1.2)
Cardiovascular disease	1.0 (0.9–1.2)