CLINICAL RESEARCH STUDY

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The Consequences of Requesting "Dispense as Written"

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ABSTRACT

BACKGROUND: All US states have adopted generic substitution laws to reduce medication costs. However, physicians may override these regulations by prescribing branded drugs and requesting that they are dispensed as written. Patients also can make these requests. Little is known about the frequency and correlates of dispense as written requests or their association with medication filling.

METHODS: We identified beneficiaries of a large pharmacy benefits manager who submitted a prescription claim from any pharmacy in January 2009. We categorized claims as a physician-assigned dispense as written, patient-assigned dispense as written, or no dispense as written. We described rates of these requests and used generalized estimating equations to evaluate physician, patient, treatment, and pharmacy characteristics associated with dispense as written requests. We also used generalized estimating equations to assess the relationship between dispense as written designation and rates prescriptions are not filled by patients.

RESULTS: Our sample included 5.6 million prescriptions for more than 2 million patients. More than 2.7% were designated as dispense as written by physicians, and 2.0% were designated as dispense as written by patients. Substantial variation in dispense as written requests were seen by medication class, patient and physician age, and geographic region. The odds of requesting dispense as written was 78.5% greater for specialists than generalists ($P < .001$). When chronic prescriptions were initiated, physician dispense as written (odds ratio 1.50, $P < .001$) and patient dispense as written (odds ratio 1.60, $P < .001$) were associated with greater odds that patients did not fill the prescription.

CONCLUSION: Dispense as written requests were common and associated with decreased rates of prescription filling. Options to reduce rates of dispense as written requests may reduce costs and improve medication adherence.

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KEYWORDS: Dispense as written; Generic; Medication; Prescription

With the recent expansion of health insurance coverage to millions of Americans, there is increasing pressure to control health care costs. Greater use of generic medications has been identified as one approach to reduce medication costs without compromising quality.[1] Studies do not suggest meaningful differences in clinical efficacy between brand-name and generic products.[2] Yet generic medications remain underused when appropriate, and efforts to encourage their use can reduce both patient and health system costs.[3,4]

Every state has enacted generic substitution laws to promote generic drug use.[5] However, both physicians and patients express concern about the safety and efficacy of generics.[6,7] Physicians can ensure that a brand-name medication is delivered, even when a generic equivalent is available, by indicating "dispense as written" on their prescription.[8] Similarly, patients can request that a brand be delivered rather than the generic equivalent at the point of purchase.

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Dispense as written requests may have important implications for patient adherence. Patients are more adherent when they are initiated on generic or lower-cost medications.[9] Although dispense as written requests would seem to reflect a conscious decision by patients or their physicians to use a specific agent, the increased cost-sharing that results from a dispense as written designation may decrease the likelihood that patients actually fill their prescriptions.

Little is known about how frequently physicians or patients request dispense as written, the medications for which dispense as written is most commonly used, and the physician and patient characteristics associated with dispense as written requests. Previous descriptive analyses of this practice were conducted when generic use was far less common and have limited applicability to current practice.[10-12] No prior studies have investigated the effect of dispense as written requests on patients' likelihood to fill their prescriptions or on overall health system costs. By using transactional data from a large national pharmacy benefits manager, we assessed rates and correlates of dispense as written requests and the relationship between these requests and rates of filled prescriptions.

CLINICAL SIGNIFICANCE

- Approximately 5% of all prescriptions are designated as dispense as written by either a patient or prescriber, requesting a brand name preparation.
- Doctor, patient, and medication characteristics are associated with the frequency of dispense as written requests.
- When chronic prescriptions are initiated, physician dispense as written requests and patient dispense as written requests are associated with 50% and 60% greater odds that patients did not fill the prescription, respectively.

MATERIALS AND METHODS

Sample

We identified all patients enrolled in employer-sponsored health plans who received pharmacy benefits from CVS Caremark in calendar years 2008 and 2009. From this sampling frame, we selected all members with a) continuous eligibility for pharmacy benefits between July 1, 2008, and January 31, 2009, and b) a valid entry for gender and date of birth in the administrative record. We limited our sample to patients who submitted a prescription claim from any retail or mail-order pharmacy for adjudication between January 1 and 31, 2009, the identification period. We excluded all clients who were enrolled in a plan that imposed penalties for dispense as written requests, because dispense as written requests in these settings may not reflect those in the general population.

For patients who submitted multiple eligible prescriptions within a class, we selected the prescription with the latest date during the identification period, which likely eliminates accidental or erroneous prescriptions that were delivered. If a member submitted prescriptions in multiple therapeutic classes, each was deemed eligible and included in the analysis. We included all therapeutic categories defined by MediSpan's Generic Product Identifier (GPI-2).

Dispense as Written Designation and Prescription Filling Outcomes

We identified the dispense as written assignment and the brand status from the submitted claim record. We categorized claim records into 1 of 3 mutually exclusive categories: a physician-assigned dispense as written (Physician Dispense as Written); a member-assigned dispense as written (Patient Dispense as Written); or no Dispense as Written. Brands were listed as either single-source brand, indicating no generic equivalent was available at the time of the study, or multi-source brands, which are branded medications with a generic equivalent. For every eligible prescription, we also determined whether the prescription was purchased ("filled") or reversed. Reversed prescriptions are those that the patient chose not to purchase, and therefore were not filled.

Independent Variables

For each eligible prescription submitted, we constructed explanatory variables to assess the relationship between physician, patient, treatment, and pharmacy characteristics and dispense as written use and prescription filling. Physician variables included primary specialty, practice type (primary care, specialist, non-physician prescriber), and prescriber age. Patient characteristics included age (in years), gender, and US census region of residence. Treatment variables included the dispense as written assignment, GPI4/GPI2-designated therapeutic class, brand/generic status, and patient out-of-pocket cost (in dollars per 30-day equivalent prescription). Pharmacy characteristics included the type of dispensing pharmacy (retail or mail). Prescriptions were categorized as either acute or maintenance (chronic) using the First Data Bank designation.[13] Maintenance medications were further categorized as either an "initiation" or "continuation" of therapy. Initiation prescriptions were defined on the basis of no paid pharmacy claims for a drug in the same therapeutic class in the 6 months before the index prescription claim. Maintenance continuation prescriptions were preceded by 1 or more paid claims in the previous 6 months, indicating recent use.

Analysis Plan

We used descriptive statistics to evaluate patient, physician, pharmacy, and prescription characteristics. We de-

scribed rates of dispense as written for both single-source brands and multi-source brands, despite the fact that dispense as written for single-source brands may not have any effect on prescription delivery. We also present rates of prescription reversals, prescription claims approved by a payer and then reversed by the pharmacy because they were not purchased by the patient and went unfilled, stratified by dispense as written designation and prescription type.

To assess the relationship between physician, patient, prescription, and pharmacy characteristics with physician and patient dispense as written requests, we used generalized estimating equations to adjust for clustering at the patient level. Our outcomes, at the submitted prescription level, were the presence or absence of physician dispense as written in one model and the presence or absence of patient dispense as written for the other. We studied whether physician, member, treatment, and pharmacy characteristics were associated with the submission of prescriptions with a dispense as written designation. When comparing rates of dispense as written requests by drug class, we selected oral diabetes medications as our referent category because they are essential medications, commonly prescribed, and include both generic and brand-name options.

Multivariate generalized estimating equation models were used to estimate the relationship between patient and physician dispense as written selection and whether the claim was reversed, indicating the medication was not purchased by the patient and went unfilled. In these models, we were interested in the relationship between dispense as written designation and rates of multi-source brand medication filling, because these are the medications for which dispense as written designations most clearly affect the medication received. Thus, in our primary model, we included only multi-source brand and generic medications. We ran a distinct model with single-source brands as a neutral control because we did not expect that dispense as written designation would have any effect on the medication that was delivered and, as a result, the likelihood of actual purchasing. In these models, we controlled for patient, physician, and pharmacy covariates and adjusted for clustering within patients. We included interactions between physician and patient dispense as written designations and prescription characteristics (initiation of a chronic medication, maintenance medication continuation, or acute medication), because we hypothesized that dispense as written designation may have the greatest effect on purchasing rates in new prescriptions or acute prescriptions, when patients first learn about the medication costs. Statistical evaluations were performed using SAS Version 9.1 with SAS/STAT(r) (SAS Institute Inc, Cary, NC) and Stata SE 9.1 for Windows (StataCorp LP, College Station, Tex).

RESULTS

We evaluated approximately 5.6 million prescriptions that were delivered to retail or mail-order pharmacies and adjudicated through Caremark during the 1-month period (Table 1). These prescriptions were written for 2,047,124 patients by 315,379 specialist physicians, 126,430 generalists, and 39,128 non-physician prescribers (eg, nurse practitioners). Patients and their insurance plans, respectively, paid an average of $17.90 and $26.67 for generic medications, $49.50 and $158.25 for single-source brands, and $44.50 and $135.26 for multi-source brands.

Of the prescriptions we evaluated, 151,670 (2.7%) were designated as dispense as written by physicians and 112,243 (2.0%) were designated as dispense as written by patients (Table 1). A majority of prescriptions designated as dispense as written by physicians were single-source brand products for which no generic alternatives were available. Most patient-assigned dispense as written prescriptions were for multi-source brands, which could have otherwise been substituted at the pharmacy without contacting the physician. Patient requests for dispense as written took place almost exclusively at retail pharmacies, whereas approximately one third of physician requests were filled at mail-order pharmacies.

Among multi-source brands used to treat chronic conditions (maintenance medications), patients failed to fill prescriptions more frequently when either patients or physicians requested dispense as written, compared with prescriptions with no dispense as written designation (Figure 1).

In multivariate analyses, older physicians were more likely to request dispense as written than younger ones, and patients age 55 to 74 years were most likely to receive physician dispense as written prescriptions (Table 2). The odds of requesting dispense as written was 78.5% greater for specialists than generalists ($P < .001$). Compared with rates of dispense as written request for oral antidiabetics (the referent class), a dispense as written was more likely to be written for anticonvulsants (odds ratio [OR] 2.2), estrogens (OR 2.2), migraine treatments (OR 2.4), thyroid medications (OR 9.8), and anticoagulants (OR 3.9) ($P < .001$ for all; Table 2). Physician dispense as written was more common in the northeast section of the country (OR 1.76 vs west, $P < .001$) and when submitted to mail-order pharmacies (Table 2).

The likelihood of patient dispense as written requests also varied by therapeutic class and region. Compared with oral antidiabetics, patient dispense as written requests were more common for ulcer agents (OR 6.1), hypnotics (OR 4.3), migraine medications (OR 14.4), contraceptives (OR 3.7), thyroid medications (OR 16.5), estrogens (OR 3.6), anticonvulsants (OR 4.8), anticoagulants (OR 4.5), and analgesics (OR 4.5) ($P < .001$ for all, Table 3). Patient dispense as written was requested most frequently in the west; there were 32.4% greater odds for having a patient-assigned dispense as written in the west than in the northeast ($P < .001$) (Table 3). Dispense as written was most commonly requested by patients who were 55 to 74 years of age, for maintenance medications, and at retail pharmacies (Table 3).

Table 1 Study Sample

Variables	Total (N = 5,586,700) Submitted Rx N (%)	Physician Dispense as Written (N = 151,670) Submitted Rx N (%)	Patient Dispense as Written (N = 112,243) Submitted Rx N (%)
Patient characteristics for included prescriptions			
Age, y			
<19	495,080 (8.9%)	8,544 (5.6%)	5,743 (5.1%)
19-34	610,185 (10.9%)	14,165 (9.3%)	12,333 (11.0%)
35-44	695,617 (12.5%)	18,458 (12.2%)	15,733 (14.0%)
45-54	1,134,464 (20.3%)	30,221 (19.9%)	25,136 (22.4%)
55-64	1,286,976 (23.0%)	37,261 (24.6%)	27,240 (24.3%)
65-74	684,800 (12.3%)	22,216 (14.6%)	13,026 (11.6%)
>75	679,578 (12.2%)	20,805 (13.7%)	13,032 (11.6%)
Sex			
Female	3,260,595 (58.4%)	97,266 (64.1%)	74,106 (66.0%)
Male	2,325,463 (41.6%)	54,386 (35.9%)	38,127 (34.0%)
Region			
Midwest	1,719,957 (30.8%)	45,175 (29.8%)	31,029 (27.6%)
Northeast	1,224,549 (21.9%)	51,533 (34.0%)	18,761 (16.7%)
South Central	852,124 (15.3%)	17,500 (11.5%)	15,455 (13.8%)
Southeast	1,164,521 (20.8%)	23,627 (15.6%)	25,808 (23.0%)
West	540,938 (9.7%)	12,555 (8.3%)	16,640 (14.8%)
Unavailable	84,611 (1.5%)	1,280 (0.8%)	4,550 (4.0%)
Provider characteristics for included prescriptions			
Specialty (top 20 listed here)			
Family practice	1,281,840 (22.9%)	23,547 (15.5%)	24,144 (21.5%)
Internal medicine	981,216 (17.6%)	25,994 (17.1%)	21,316 (19.0%)
Obstetrics and gynecology	275,977 (4.9%)	10,640 (7.0%)	8,593 (7.7%)
Cardiovascular	253,634 (4.5%)	10,189 (6.7%)	6,223 (5.5%)
Emergency medicine	215,946 (3.9%)	3,001 (2.0%)	3,320 (3.0%)
Pediatrics	184,634 (3.3%)	2,038 (1.3%)	2,027 (1.8%)
Nurse practitioner	181,098 (3.2%)	4,081 (2.7%)	3,023 (2.7%)
Geriatrics	144,860 (2.6%)	3,491 (2.3%)	2,727 (2.4%)
Psychiatry	139,152 (2.5%)	5,344 (3.5%)	3,821 (3.4%)
Physician assistant	118,080 (2.1%)	2,030 (1.3%)	1,990 (1.8%)
Dentistry	89,407 (1.6%)	633 (0.4%)	793 (0.7%)
Dermatology	89,003 (1.6%)	3,612 (2.4%)	1,368 (1.2%)
Gastroenterology	79,545 (1.4%)	3,074 (2.0%)	2,690 (2.4%)
General surgery	70,290 (1.3%)	1,404 (0.9%)	1,129 (1.0%)
Neurology	67,390 (1.2%)	3,990 (2.6%)	2,363 (2.1%)
Pulmonary disease	63,827 (1.1%)	2,326 (1.5%)	1,035 (0.9%)
Endocrinology, diabetes, and metabolism	62,321 (1.1%)	9,113 (6.0%)	2,071 (1.8%)
	59,877 (1.1%)	1,114 (0.7%)	955 (0.9%)
Rheumatology	51,245 (0.9%)	3,258 (2.1%)	889 (0.8%)
Ophthalmology	51,038 (0.9%)	506 (0.3%)	668 (0.6%)
Orthopedic surgery			
Age, y			
<29	5,031 (0.1%)	66 (0.0%)	73 (0.1%)
29-34	142,278 (2.5%)	2,709 (1.8%)	2,271 (2.0%)
35-44	1,165,024 (20.9%)	26,846 (17.7%)	22,942 (20.4%)
45-54	1,589,411 (28.4%)	43,502 (28.7%)	33,227 (29.6%)
55-64	1,167,810 (20.9%)	37,635 (24.8%)	24,606 (21.9%)
<65	297,576 (5.3%)	12,101 (8.0%)	6,388 (5.7%)
Unavailable	424,659 (7.6%)	9,693 (6.4%)	8,111 (7.2%)
Practice			
Physician-Extender	300,217 (5.4%)	6,128 (4.0%)	5,039 (4.5%)
PCP	2,484,785 (44.5%)	52,237 (34.4%)	48,704 (43.4%)
Specialist	2,801,698 (50.1%)	93,305 (61.5%)	58,500 (52.1%)

Table 1 Continued

Variables	Total (N = 5,586,700) Submitted Rx N (%)	Physician Dispense as Written (N = 151,670) Submitted Rx N (%)	Patient Dispense as Written (N = 112,243) Submitted Rx N (%)
Drug characteristics			
Eligible Rx received			
Generic	3,591,096 (64.3%)	19,238 (12.7%)	13,410 (11.9%)
SSBs	1,879,199 (33.6%)	95,005 (62.6%)	38,033 (33.9%)
MSBs	116,405 (2.1%)	37,427 (24.7%)	60,800 (54.2%)
Pharmacy			
Mail	848,146 (15.2%)	50,745 (33.5%)	3,590 (3.2%)
Retail	4,738,554 (84.8%)	100,925 (66.5%)	108,653 (96.8%)
Therapeutic			
Acute	1,800,591 (32.2%)	23,875 (15.7%)	24,308 (21.6%)
Maintenance-continued therapy	3,103,086 (55.6%)	112,318 (74.1%)	78,413 (69.9%)
Maintenance-initiate therapy	682,017 (12.2%)	15,416 (10.2%)	9,517 (8.5%)
Class (Top 10)			
Antihypertensives	420,195 (7.5%)	8,745 (5.8%)	5,132 (4.6%)
Antihyperlipidemics	399,562 (7.2%)	10,459 (6.9%)	2,915 (2.6%)
Antidepressants	335,568 (6.0%)	7,532 (5.0%)	5,836 (5.2%)
Analgesics, opioid	272,953 (4.9%)	2,426 (1.6%)	4,862 (4.3%)
Ulcer drugs	234,192 (4.2%)	7,092 (4.7%)	12,366 (11.0%)
Antidiabetics	229,222 (4.1%)	5,527 (3.6%)	2,394 (2.1%)
Beta-blockers	211,764 (3.8%)	4,873 (3.2%)	6,491 (5.8%)
Antiasthmatic and bronchodilator Agents	205,499 (3.7%)	5,366 (3.5%)	1,802 (1.6%)
Contraceptives	176,046 (3.2%)	6,323 (4.2%)	6,214 (5.5%)
Thyroid agents	159,018 (2.8%)	30,465 (20.1%)	18,830 (16.8%)

Rx = prescription; PCP = primary care provider; SSB = single-source brand; MSB = multi-source brand.

Among multi-source brands, physician dispense as written requests were associated with increased rates of prescription reversals (OR 1.16, $P<.001$), indicating that patients did not fill these prescriptions. New prescriptions (ie, the first maintenance prescriptions filled in a chronic medication class) had greater odds of reversal than subsequent maintenance prescriptions (OR 2.07, $P<.001$). Rates of reversal also were higher for acute medications compared with maintenance medications (OR 1.37 $P<.001$). Strong relationships were seen when we tested the interactions of dispense as written requests and initial maintenance or acute prescriptions. Among initial maintenance prescriptions, physician dispense as written (OR 1.50, $P<.001$) and patient dispense as written (OR 1.60, $P<.001$) were associated with greater odds of reversal. Similar trends were seen for acute medications; physician dispense as written was associated with 1.42 greater odds and patient dispense as written was associated with 1.61 greater odds of reversal compared with those filling subsequent maintenance medications, indicating higher rates of patient failure to fill these prescriptions ($P<.001$ for both, Table 4).

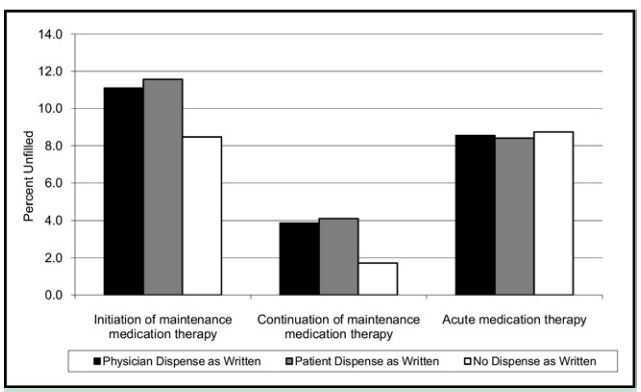

Figure 1 Unadjusted rates of prescription reversals (non-filling of prescribed medications) for multi-source medications, by medication type and dispense as written designation.

Among single-source brand medications, the neutral control where dispense as written designations should have no effect on which medication is actually filled, we found little effect of dispense as written designation on reversal rates. Overall, physician dispense as written was associated with a small reduction in reversal rates (OR 0.89, $P<.001$). Acute medications and new prescriptions for maintenance medications were more likely to be reversed (OR 2.2 and 2.9, respectively; $P<.001$ for both), although the odds of reversal was not influenced by dispense as written status (Table 4).

DISCUSSION

In this national sample of prescriptions written for patients receiving drug coverage administered by a large pharmacy benefits manager, approximately 5% of all prescriptions included a dispense as written designation requesting dis-

Table 2 Adjusted Odds of Prescribing with a Physician-Assigned Dispense as Written*

Variables	OR	95% CI	*P* Value
Patient Characteristics			
Female (ref. Male)	1.11	1.09-1.12	<.0001
Therapeutic status (ref. Acute Rx)			
Maintenance, cont. therapy	1.57	1.51-1.63	<.0001
Maintenance, initiation therapy	1.15	1.10-1.20	<.0001
Retail (ref. Mail)	0.41	0.41-0.42	<.0001
Age, y (ref. 65-74)			
<19	1.00	0.96-1.03	.8096
19-34	0.99	0.96-1.01	.3158
35-44	1.07	1.04-1.09	<.0001
45-44	0.98	0.96-1.00	.0690
55-64	0.97	0.95-0.99	.0026
75+	0.87	0.85-0.89	<.0001
Region (ref. West)			
Midwest	1.24	1.21-1.27	<.0001
Northeast	1.77	1.73-1.81	<.0001
South Central	0.96	0.93-0.98	.0013
Southeast	0.95	0.93-0.98	<.0001
Provider characteristics			
Age, y (ref. >65)			
<29	0.70	0.55-0.89	.0031
29-34	0.64	0.61-0.66	<.0001
35-44	0.68	0.66-0.69	<.0001
45-54	0.73	0.72-0.75	<.0001
55-64	0.82	0.80-0.84	<.0001
Practice (ref. PCP)			
Physician extender	1.04	1.01-1.08	.0165
Specialist	1.79	1.76-1.81	<.0001
Drug characteristics			
Drug class (ref. anti-diabetics)			
ADHD/anti-obesity	1.70	1.58-1.82	<.0001
Analgesics, non-narcotic	1.33	1.14-1.56	.0004
Analgesics, opioid	0.66	0.62-0.71	<.0001
Antianginal agents	0.66	0.59-0.74	<.0001
Antianxiety agents	0.84	0.78-0.90	<.0001
Antiarrhythmics	0.79	0.67-0.93	.0042
Antiasthmatic/ bronchodilator agents	1.20	1.15-1.26	<.0001
Anticoagulants	3.88	3.70-4.07	<.0001
Anticonvulsants	2.12	2.03-2.21	<.0001
Antidepressants	0.98	0.94-1.02	.2269
Antiemetics	0.66	0.56-0.79	<.0001
Antihyperlipidemics	1.03	0.99-1.07	.1385
Antihypertensives	0.88	0.85-0.91	<.0001
Antiparkinson agents	0.96	0.87-1.07	.4650
Antipsychotics/antimanic agents	1.03	0.95-1.11	.5300
Antivirals	1.00	0.93-1.09	.9286
Beta-blockers	0.92	0.89-0.96	.0002
Calcium channel blockers	0.81	0.77-0.85	<.0001
Contraceptives	1.40	1.34-1.46	<.0001
Estrogens	2.18	2.07-2.29	<.0001
Gastrointestinal agents, misc.	0.91	0.82-1.01	.0661
Gout agents	0.37	0.32-0.42	<.0001
Hypnotics	1.54	1.44-1.65	<.0001
Migraine products	2.44	2.24-2.66	<.0001
Ophthalmic agents	2.56	2.44-2.68	<.0001
Penicillins	0.25	0.22-0.28	<.0001
Progestins	1.32	1.17-1.49	<.0001
Thyroid agents	9.68	9.37-10.00	<.0001
Ulcer drugs	1.32	1.27-1.37	<.0001
Urinary anti-infectives	0.52	0.42-0.65	<.0001

OR = odds ratio; CI = confidence interval; PCP = primary care provider; ADHD = attention deficit hyperactivity disorder.

*Using generalized estimating equations to adjust for clustering within patients.

pensing of a brand product. Dispense as written requests were made by prescribers (2.7% of prescriptions) and patients (2.0% of prescriptions). Prescriptions written with dispense as written designations were more likely to be reversed, indicating that they were less likely to be purchased by patients and went unfilled. In particular, when chronic therapy was initiated, physician and patient dispense as written requests led to more than 50% greater odds of non-filling.

By substituting the generic alternative for each multisource brand that was filled after both physician and patient dispense as written designation, the patient population in this sample could have reduced their charges by more than $1.7 million and the health plans could have experienced more than a $10.6 million reduction in costs in the 1-month study period. By assuming a similar rate of dispense as written requests in uninsured patients, patients covered by state or federal governments, and other commercially insured beneficiaries, we can estimate the savings potential of a policy that eliminates the dispense as written option. With more than 3.6 billion prescriptions filled in the United States annually,[14] patient charges could be reduced by as much as $1.2 billion annually and health system costs could be reduced by as much as $7.7 billion by eliminating dispense as written opportunities. We are unable to estimate the implications of specifying dispense as written for single-source brands because these designations likely have minimal effect on the actual prescriptions delivered.

Physicians and patients should be aware that dispense as written designations not only increase costs to the patient but also adversely affect rates that patients purchase those prescriptions. Educational efforts to encourage generic acceptability should target those most likely to express concern about generics.[6,15,16] Our findings indicate that specialists, older physicians, and patients aged 55 to 74 years are more likely to request dispense as written and may represent targets for educational outreach. These efforts should focus on initiation of chronic medications, because patients disproportionately fail to purchase these prescriptions when either physicians or patients request dispense as written.

Table 3 Adjusted Odds of a Patient-Assigned Dispense as Written*

Variables	OR	95% CI	*P* Value
Patient Characteristics			
Female (ref. Male)	1.10	1.08-1.11	<.0001
Therapeutic status (ref. Acute Rx)			
Maintenance, cont. therapy	2.20	2.09-2.31	<.0001
Maintenance, initiation therapy	1.20	1.14-1.27	<.0001
Retail (ref. Mail)	6.53	6.30-6.76	<.0001
Age, y (ref. 65-74)			
<19	0.74	0.71-0.77	<.0001
19-34	0.81	0.79-0.84	<.0001
35-44	0.94	0.91-0.96	<.0001
45-44	0.96	0.94-0.99	.0014
55-64	1.01	0.99-1.03	.4148
75+	0.89	0.87-0.92	<.0001
Region (ref. West)			
Midwest	0.59	0.58-0.60	<.0001
Northeast	0.57	0.55-0.58	<.0001
South Central	0.60	0.59-0.62	<.0001
Southeast	0.75	0.73-0.76	<.0001
Provider characteristics			
Age, y (ref. >65)			
<29	0.83	0.66-1.06	.1337
29-34	0.77	0.73-0.81	<.0001
35-44	0.88	0.85-0.90	<.0001
45-54	0.94	0.92-0.97	<.0001
55-64	0.96	0.93-0.99	.0061
Practice (ref. PCP)			
Physician Extender	0.86	0.84-0.89	<.0001
Specialist	1.11	1.10-1.13	<.0001
Drug characteristics			
Drug class (ref. antidiabetics)			
ADHD/anti-obesity	1.37	1.23-1.54	<.0001
Analgesics, non-narcotic	4.47	3.88-5.16	<.0001
Analgesics, opioid	3.11	2.89-3.35	<.0001
Antianginal agents	1.51	1.32-1.72	<.0001
Antianxiety agents	2.95	2.72-3.19	<.0001
Antiarrhythmics	1.22	0.99-1.51	.0679
Antiasthmatic/ bronchodilator agents	0.92	0.86-0.99	.0213
Anticoagulants	5.31	4.97-5.67	<.0001
Anticonvulsants	4.82	4.57-5.09	<.0001
Antidepressants	1.66	1.58-1.75	<.0001
Antiemetics	3.20	2.79-3.67	<.0001
Antihyperlipidemics	0.80	0.75-0.84	<.0001
Antihypertensives	1.21	1.15-1.28	<.0001
Antiparkinson agents	2.53	2.28-2.81	<.0001
Antipsychotics/antimanic agents	1.09	0.97-1.22	.1559
Antivirals	0.63	0.54-0.72	<.0001
Beta-blockers	3.16	3.00-3.32	<.0001
Calcium channel blockers	2.54	2.40-2.70	<.0001
Contraceptives	3.67	3.48-3.88	<.0001
Estrogens	3.61	3.38-3.85	<.0001
Gastrointestinal agents, misc.	1.59	1.40-1.82	<.0001
Gout agents	0.58	0.49-0.70	<.0001
Hypnotics	4.29	3.96-4.66	<.0001
Migraine products	14.42	13.29-15.65	<.0001
Ophthalmic agents	2.03	1.88-2.20	<.0001
Penicillins	0.69	0.62-0.77	<.0001
Progestins	0.87	0.69-1.09	.2134
Thyroid agents	16.50	15.73-17.30	<.0001
Ulcer drugs	6.10	5.82-6.41	<.0001
Urinary anti-infectives	1.84	1.52-2.22	<.0001

OR = odds ratio; CI = confidence interval; Rx = prescription; ADHD = attention deficit hyperactivity disorder.

*Using generalized estimating equations to adjust for clustering within patients.

Prescriptions for certain classes of medications were far more likely to be accompanied by a dispense as written request. In particular, classes with narrow therapeutic indices, such as thyroid medications, anticoagulants, and anticonvulsants, were commonly delivered with a dispense as written request. There has been substantial debate in the scientific literature as to the equivalency of these products; although the literature may not corroborate these clinical concerns,[2,17] it is likely that patients and physicians have a clinical rationale for these requests. The high rates of dispense as written requests for migraine products, ulcer agents, and hypnotics are more surprising, and may be related to effective marketing campaigns to patients and physicians.

It is interesting to observe that physicians request dispense as written frequently for single-source branded products, medications for which no generics could be automatically substituted. Physicians with a strong preference for branded medications may not be aware of whether a generic is available and may request the branded agent as a preventive measure. Alternatively, physicians may request the branded medication to ensure that pharmacists do not substitute a different medication in the class for the prescribed medication (eg, substitution of simvastatin for atorvastatin [Lipitor, Pfizer Inc, New York, NY]); this so-called therapeutic substitution is generally not permitted without first contacting the physician. It is unclear whether these requests ultimately exert any influence on the medication that is delivered to the patient.

Substantial geographic variation in dispense as written requests was seen. This variation may reflect patterns of marketing or the culture of medical education and prescribing that pervade different regions. These also may reflect habit, reflex, or consequences of automatically checked boxes in electronic prescribing systems or on standardized prescription pads. In addition, these variations may be related to geographic differences in pharmacy practice that influence communication with patients and physicians.

Table 4 Adjusted Odds of a Claim Reversal (a Prescription That Went Unfilled) for Multi-Source Branded Medications and Single-Source Branded Medications (Interacting Dispense as Written Assignment and Therapeutic Status)*

	MSBs and Generics			SSBs		
Variables	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Dispense as written assignment						
Physician	1.16	1.09-1.24	<.0001	0.89	0.83-0.95	<.0001
Member	1.01	0.96-1.06	.675	1.08	1.00-1.17	.049
Therapeutic status						
Acute	1.37	1.32-1.43	<.0001	2.16	2.07-2.25	<.0001
Initiation	2.07	2.03-2.11	<.0001	2.90	2.85-2.96	<.0001
Dispense as written assignment and therapeutic class†						
Physician dispense as written by acute	1.42	1.28-1.58	<.0001	0.96	0.87-1.06	.443
Physician dispense as written by initiation	1.50	1.33-1.71	<.0001	1.00	0.90-1.12	.975
Member dispense as written by acute	1.61	1.49-1.75	<.0001	1.10	0.98-1.24	.094
Member dispense as written by initiation	1.60	1.43-1.78	<.0001	0.87	0.76-1.01	.058

MSB = multi-source brand; SSB = single-source brand; CI = confidence interval; OR = odds ratio.

Other covariates included in the regression models, suppressed from the table, include geographic region, provider and member age, therapeutic class, provider specialty, member gender, and pharmacy channel.

*Using generalized estimating equations to adjust for clustering within patients.

†Reference is maintenance (chronic) medications, after they were initiated.

STUDY LIMITATIONS

Our study has limitations. We evaluated a commercially insured population; rates of dispense as written requests and prescription reversals may differ for uninsured patients. Our measure of reversal was linked to the specific prescription that was adjudicated by the pharmacy. Some of the unfilled prescriptions may not represent clinically significant medication non-adherence, because patients may have requested new prescriptions for different medications to treat the same condition. However, previous studies indicate that patients who are initially prescribed branded medications are less likely to subsequently adhere to any medication in the class when compared with patients prescribed generics.[9] We recruited during a 1-month period in the winter. We did not account for seasonality; patient medication use and prescription requests may vary by season. We also are unsure of the extent of misclassification in this data set, because pharmacies may not accurately capture all patient dispense as written requests in administrative data sets, which may have led to conservative estimates of dispense as written rates.

CONCLUSIONS

Overall, we found that both patients and physicians commonly make dispense as written requests, totaling approximately 5% of all prescriptions. Advocates of dispense as written may argue that providing physicians and patients with greater discretion offers greater choice, opportunities for communication, and adherence to therapy. However, our results indicate that dispense as written requests are associated with excess costs, and that patients are less likely to fill prescriptions with dispense as written designations. Some private health plans have implemented financial penalties to reduce the rates of dispense as written designation. The cost savings and clinical effects of these policies should be studied to better understand what policies best encourage cost-effective medication use and adherence to chronic therapy.

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