Can Improved Prescription Medication Labeling Influence Adherence to Chronic Medications? An Evaluation of the Target Pharmacy Label

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BACKGROUND: Prescription medication labels contain valuable health information, and better labels may enhance patient adherence to chronic medications. A new prescription medication labeling system was implemented by Target pharmacies in May 2005 and aimed to improve readability and understanding.

OBJECTIVE: We evaluated whether the new Target label influenced patient medication adherence.

DESIGN AND PATIENTS: Using claims from two large health plans, we identified patients with one of nine chronic diseases who filled prescriptions at Target pharmacies and a matched sample who filled prescriptions at other community pharmacies.

MEASUREMENTS: We stratified our cohort into new and prevalent medication users and evaluated the impact of the Target label on medication adherence. We used linear regression and segmented linear regression to evaluate the new-user and prevalent-user analyses, respectively.

RESULTS: Our sample included 23,745 Target users and 162,368 matched non-Target pharmacy users. We found no significant change in adherence between new users of medications at Target or other community pharmacies (p=0.644) after implementing the new label. In prevalent users, we found a 0.0069 percent reduction in level of adherence (95% CI −0.0138-0.0; p< 0.001) and a 0.0007 percent increase in the slope in Target users (the monthly rate of change of adherence) after implementation of the new label (95% CI 0.0001–0.0013; p=0.001).

CONCLUSIONS: We found no changes in adherence of chronic medication in new users, and small and likely clinically unimportant changes in prevalent users after implementation of the new label. While adherence may not be improved with better labeling, evaluation of the effect of labeling on safety and adverse effects is needed.

KEY WORDS: label; prescription medication; adherence.
J Gen Intern Med (24)5:570–8
DOI: 10.1007/s11606-009-0924-x

BACKGROUND

Patients frequently do not adhere to essential medications, with substantial consequences to the public health.[1] Numerous studies have shown that patients with chronic conditions adhere only to 50–60% of medications as prescribed, despite evidence that medication therapy improves life expectancy and quality of life.[2,3] Non-adherence has been linked to worse health outcomes and more frequent hospitalizations,[4] contributing over $170 billion annually to United States health-care costs.[5] Interventions that stimulate better adherence to essential medications, even slightly, may meaningfully improve the public health.

Patients' confusion about a medical regimen and lack of knowledge of their disease state are among the many factors that adversely affect adherence.[6,7] Ideally, patients would receive necessary information about safe and appropriate medication use when communicating with physicians or pharmacists, but studies indicate that those discussions are often incomplete,[8,9] and frequently forgotten.[10] As a result, patients likely receive some of their education about how to administer and use a medication from the label on the medication bottle.[11]

Unfortunately, many patients have difficulty reading and understanding medication container labels.[12,13] The quality of medication labels is highly variable, and frequently labels are not patient-centered.[14] Improvements in the medication container label may enhance patient understanding about the medication and safe use, and may encourage better adherence. While previous reviews suggest that simple interventions

This work was supported by the Pioneer Award from the Robert Wood Johnson Foundation. Dr. Shrank is supported by a career development award from the National Heart, Lung and Blood Institute (K23HL090505-01). Dr. Brookhart is supported by a career development award from the National Institute of Health (AG-027400).
Received August 5, 2008
Revised December 23, 2008
Accepted January 29, 2009
Published online February 27, 2009

to improve adherence are generally less effective than complex, multi-disciplinary interventions,[15] any evidence that a simple, low-cost intervention can improve adherence would have important public health implications. Numerous studies have assessed how features of prescription drug labels affect their readability and patient understanding. However, a recent systematic review of the relevant literature did not identify any previous studies evaluating the relationship between label design and medication adherence or studies using administrative claims data to evaluate the effect of a labeling change on patient refills.[16]

In May of 2005, one national chain pharmacy, the Target Corporation, developed and implemented a newly designed prescription medication label largely consistent with published evidence to optimize labeling.[17] The goal of the new label, called ClearRx, was to improve the readability and understandability of prescription drug labels and encourage safe and appropriate prescription drug use. The new design uses a flattened bottle with increased surface area to present information about medication administration and warnings. The design employs a larger font, uses greater white space to separate content, and presents information in a logical sequence, as preferred by patients.[16] The label incorporates a built-in pouch where patients can store medication information leaflets, facilitating access to detailed information throughout the course of therapy. Each patient in a household is assigned a color, and all bottles filled for the patient include a ring of that color to reduce the chances of using medication prescribed for someone else. The new design has been widely recognized as an improvement from community-standard medication labels.[17] Such improvements could improve a patient's understanding about how to administer the medication or its potential benefit, which has been shown to improve adherence to chronic therapy.[6,7,18–20]

We sought to evaluate whether implementing an improved prescription medication label influences adherence to essential chronic medications. We used pharmacy claims to evaluate the effect of implementing the new label on the frequency that patients refilled their medications.

METHODS

We evaluated the effect of a new prescription medication label design employed by Target pharmacies on chronic medication adherence using pharmacy claims from two large commercial insurance plans. The new label was implemented, nationwide, on May 1, 2005. We conducted a pre-post evaluation to compare chronic medication adherence among new-users of chronic therapy at Target pharmacies and non-Target, community pharmacies. In prevalent users of chronic therapy, we conducted a controlled time-trend analysis using segmented linear regression to compare adherence in users of Target and non-Target pharmacies. Those who used Target pharmacies were considered exposed to the new label, and those who used non-Target pharmacies were not exposed.

SAMPLE

Our sample was derived from beneficiaries commercially insured by either Blue Cross Blue Shield of Minnesota (3,141,907 unique members with eligibility from July 1, 2003-May 1,2006) or Horizon Blue Cross Blue Shield of New Jersey (1,511,432 members under the age of 65 with eligibility from July 1, 2003-May 1, 2006). Patients 18 years old or greater who were continuously enrolled during the study period from January 2004-May 2006 were included. We classified exposures by identifying patients who, during the study period, filled a prescription at a Target pharmacy for a medication used to treat one of nine chronic diseases: atrial fibrillation, diabetes, hyperlipidemia, congestive heart failure, osteoporosis, hypertension, depression, coronary artery disease, and asthma. The medications used to identify these nine chronic diseases are listed by medication class in Appendix 1. Medication classes were determined by the first four digits of their generic product identifier (GPI) code. Patients were included if they filled a medication for one of the nine classes and had a medical claim with an ICD-9 code for an emergency room, inpatient or outpatient visit for one of the nine corresponding diagnoses of interest (listed in Appendix 2). Each patient was only included in the analysis once, even if they filled medications in multiple study classes, and only the first class filled was included in this study. Patients were considered exposed on the basis of the pharmacy where they filled their first prescription (index prescription); patients who filled their index prescriptions at Target pharmacies were considered "exposed" regardless of where they filled subsequent prescriptions. For each Target pharmacy user, ten unexposed, non-Target pharmacy users were matched with replacement. Unexposed were matched on gender, age in decades, medication acquired, and calendar quarter that the medication was acquired. Unexposed patients filled all their prescriptions at non-Target pharmacies and were excluded if they filled a single prescription at Target. We selected ten unexposed patients for each exposed in order to have sufficient numbers of new and prevalent users.

NEW AND PREVALENT USERS

New User Analysis. We identified "new users" of medications in any of the study classes as patients who filled index prescriptions either before or after implementation of the new label and who had filled no prescriptions in the class in the 6 months prior. We identified two cohorts: (1) pre-implementation of the new label (May 1, 2004–November 1, 2004) and (2) post-implementation (May 1, 2005–November 1, 2005) (Fig. 1). For the new user analysis, we excluded patients over the age of 65 because prescription coverage changed for a large proportion who enrolled in a prescription drug plan through Medicare Part D in January 2006. We removed Horizon beneficiaries from this analysis because very few met inclusion criteria, and they did not add substantively to the analysis.

Prevalent User Analysis. "Prevalent users" were identified as all patients with a prescription for one of the study medications between January 1, 2004 and January 31, 2005. We excluded exposed patients with index prescriptions after January 31, 2005 to eliminate the possibility of misclassification; unexposed patients were matched on calendar quarter of filling the index prescription, up to a 3-month difference from

the case, so we only included patients whose index prescription predated implementation of the new label by 3 months or more. We censored patients over the age of 65 at January 1, 2006 because prescription coverage changed for a large proportion who enrolled in a prescription drug plan through Medicare Part D.

OUTCOMES

We used data on filled prescriptions to calculate two different measures of adherence, an interval-based proportion of days covered (PDC) in new users and a monthly PDC in prevalent users. We evaluated new users separately because we hypothesized that the improved label may have the greatest effect on behavior when a patient initiates therapy, and may offer less benefit to a patient who has been taking the medication previously and has chosen to refill the prescription.

New User Analysis. We calculated the proportion of days that patients possessed a supply of any medication in the class of the index prescription during the relevant interval: pre-implementation (beginning with an index prescription between May 1, 2004–November 1, 2004 and concluding on May 1, 2005) and post-implementation (beginning with an index prescription filled between May 1, 2005–November 1, 2005 and concluding on May 1, 2006). The numerator was defined as the total days supplied for all prescriptions within the drug class during the interval. For prescriptions written near the end of the observation window that had more days supplied than in the observation window, we only included the days supplied between that prescription date and the end of the observation window, capping PDC at 100%.[21] The denominator was defined as the number of days between the index prescription and the end of the study interval. We subtracted from the denominator any days patients spent in hospital after the index date. The numerator was divided by the denominator to generate a single adherence score for each patient.

Prevalent User Analysis. We calculated a monthly PDC for each patient in the cohort. We created a coverage diary for each patient to identify the number of days supply the patient had in each month (the numerator) and days of membership in the month (denominator). We identified cohort entrance dates as the date the index prescription was filled during the recruitment period for those who were not using as of May 1, 2004; otherwise, the entrance date was set at May 1, 2004. We consolidated multiple prescriptions filled on the same day so that only one recorded fill per patient per date was included in order to account for patients taking two doses of the same medication concurrently. Monthly PDC was capped at 100%. We censored patients over the age of 65 on January 1, 2006 because many enrolled in Medicare Part D plans. We did not censor patients who did not refill their medications prior to the end of the study period, assuming that these medications are prescribed for chronic use. We conducted sensitivity analyses in which we censored patients after discontinuation in the study drug class for 60 days. We also performed stratified analyses by disease category to assess whether results varied by disease.

STATISTICAL ANALYSIS

New User Analysis. We performed a pre-post analysis using multivariable linear regression, with PDC as the outcome. Predictor variables included drug class measured, total number of prescriptions filled in the same month that the index prescription was filled (as a proxy for comorbidity), patient age, gender, an indicator to determine whether the patient was in the pre- or post-intervention cohort, and an exposure variable (an indicator identifying whether the index prescription was at a Target or non-Target pharmacy). The interaction between the pre-post indicator and the exposure variable was used to evaluate the effect of the intervention. We used a pre-post design for new users rather than a time-trend analysis to eliminate the contamination caused by the implementation of the new label in those who initiated therapy before implementation. We did not control for cost-sharing because we have no reason to believe that using Target pharmacies during the study period would influence cost-sharing differentially as compared to other community pharmacies. We conducted sensitivity analyses to adjust for the "dose" of exposure to Target pharmacies in the new-user analysis; we identified patients who filled (1) all their prescriptions at Target, (2) the first prescription at Target and at least one subsequent prescription at another pharmacy, and (3) who filled prescriptions only at non-Target pharmacies.

Prevalent User Analysis. Monthly adherence proportions were calculated and plotted for the Target pharmacy users and non-Target pharmacy users before and after the new label was implemented. We used segmented linear regression to estimate sudden changes in slopes or levels of monthly rates after implementation of the new Target label. To estimate changes in level and slope attributable to the implementation of the Target label, we used regression models that included a constant term, a linear time trend (months 0–24), a binary indicator for the post-intervention period starting at month 13, and linear time trends for the post-intervention period. Intervention effects were determined as interaction terms between intervention indicators and the level and slope parameters. We used a longitudinal repeated measures design controlling for patient gender, age, and total number of medications used during the time period and the class of medication that the patient initiated. We controlled for correlated error terms using generalized estimating equations assuming an autoregression covariance structure with a 1-month lag.[22]

This study was approved by the Brigham and Women's Institutional Review Board. Statistical analyses were performed with SAS 9.2 (Cary, NC).

RESULTS

After applying exclusion and inclusion criteria, we identified 23,745 Target pharmacy users and 162,368 patients who did not use Target pharmacies from which to derive our new user and prevalent user cohorts (Fig. 2). Exposed and unexposed patients were qualitatively similar; statstically significant but small differences were observed (Table 1). A total of 4,260 exposed and 29,373 unexposed patients were included in the new-user analysis and 16,421 exposed and 105,925

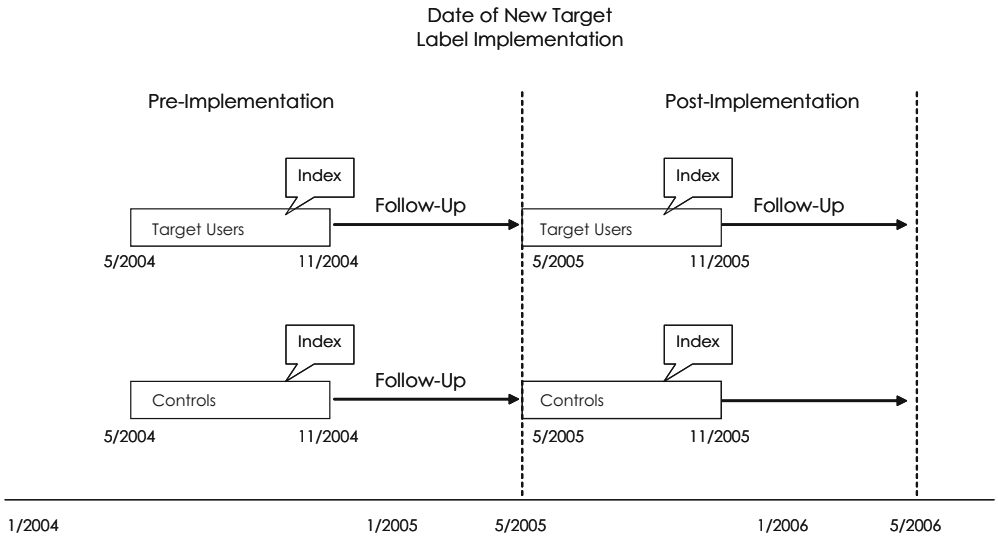

Figure 1. Study design in the new-user analysis.

unexposed patients were included in the prevalent-user analysis. A comparison of new-users of Target pharmacies before and after the implementation of the new label indicated little difference (Table 2). Patients were 1 year younger in the post-implementation period (43 vs. 42 years old, p=0.03), but there was no statistically significant difference in patient gender (62% female before and 61% after implementation; p=0.88) or number of medications used (5.9 medications used before and after, p=0.97).

New-User Analysis. Baseline mean adherence for Target pharmacy users and non-Target users in all study conditions in the year before implementation of the new Target label was 30% for asthma, 56% for atrial fibrillation, 57% for depression, 60% for congestive heart failure, 61% for diabetes and osteoporosis, and 62% for hyperlipidemia. In patients under the age of 65, after controlling for patient age, gender, number of medications filled, and medication class, we found no meaningful or statistically significant difference in adherence between users of Target or other community pharmacies (PDC 0.00374 lower in Target, p=0.644). Further, we found no meaningful or significant interaction between implementation of the new label at Target and the time period, indicating no effect of the intervention on adherence at Target users when compared to non-Target users (point estimate 0.00986; p=0.4415).

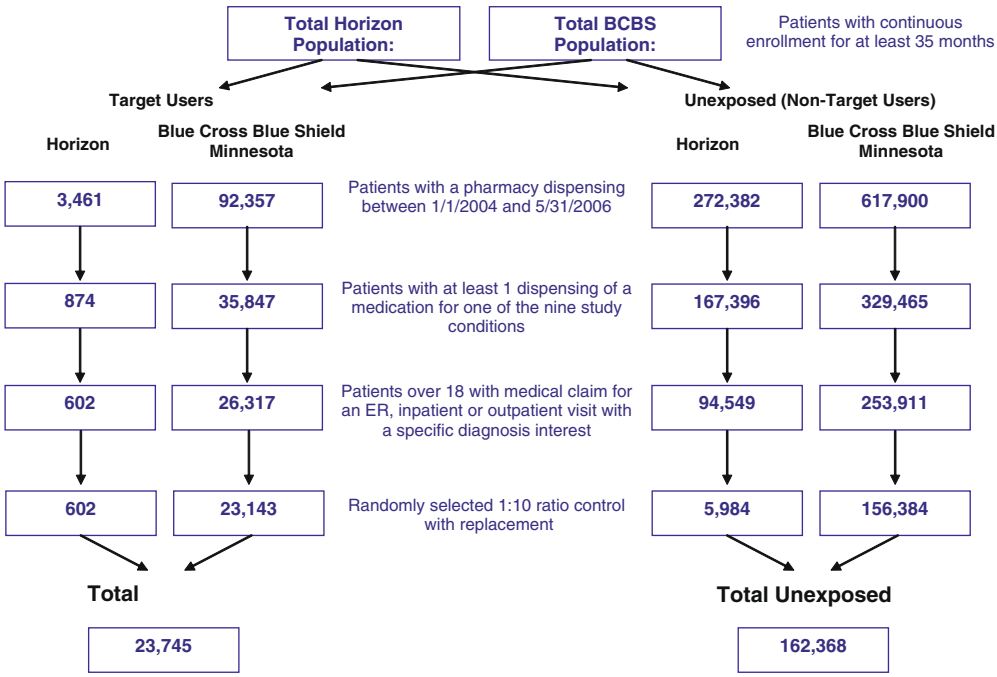

Figure 2. Study population.

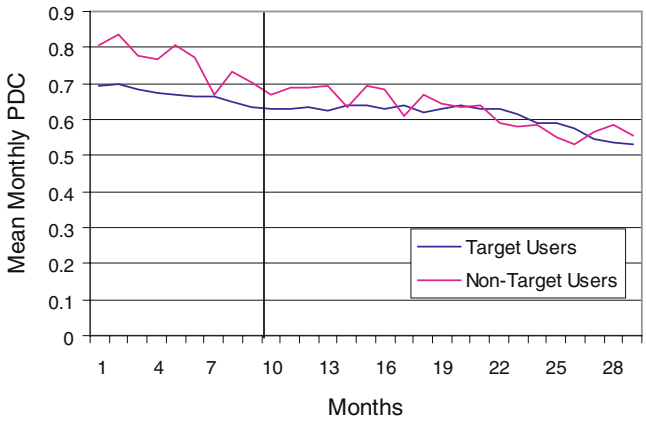

Figure 3. Monthly adherence plots before and after implementation of the new label in prevalent users.

Sensitivity analyses did not identify any significant relationship between the interaction between the labeling intervention and the "dose" of Target use (categorized as 100% Target users, less than 100% Target users who filled their index prescription at Target, and non-Target users) and medication adherence.

Prevalent User Analysis. Time-trend analysis of adherence in prevalent users of chronic medications before and after implementation of the Target label indicated very small effects of the intervention (Fig. 3). At baseline, Target users were approximately 1% more adherent than non-Target users (95% CI 0.0069–0.0151; p=0.015). After implementation of the new label, we found a 0.0069 percent reduction in the absolute level of adherence (95% CI −0.0138-0.0; p<0.001) in users of the Target pharmacies when compared with non-Target users. We found a 0.0007 percent increase in the slope (the monthly rate of change of adherence) after implementation of the new label (95% CI 0.0001–0.0013; p=0.001) in Target users as compared to non-Target users (Table 3). Sensitivity analyses censoring patients after discontinuation for 60 days indicated qualitatively similar results.

Sensitivity analyses stratified by chronic disease indicated no significant effect of the new Target label on adherence in four of the studied diseases. For patients with congestive heart failure and osteoarthritis, we found changes in adherence that were qualitatively similar to the overall sample; changes were inconsistent (a reduction in adherence level and increase in slope) and larger in magnitude than in the total sample. Among patients with asthma, we found no change in level, but a small improvement in slope of adherence change after implementation of the new label (0.001 increase in monthly PDC, p=0.04). In patients with hyperlipidemia and hypertension, we found no change in slope, but small reductions in level of adherence after implementation of the new label (0.01 reduction in PDC, p=0.02; 0.01 reduction in PDC, p=0.01, respectively).

DISCUSSION

To our knowledge, this analysis is the first claims-based evaluation of the effect of a prescription medication labeling change on medication adherence.[16] While Target pharmacies

Table 1. New- and Prevalent-User Characteristics by Treatment Group

	New users	New users	Prevalent users	Prevalent users
Characteristics	Target users (n=4,260)N (%)	Non-Target users (n=29,373)N (%)	Target users (n=16,421) N (%)	Non-Target users (n=105,925)N (%)
*Female	2,566 (60.2)	16,972 (57.8)		
Mean age	54.2 (16.9)	55.1 (16.1)	57.9 (15.7)	59.4 (14.9)
Diagnosis of				
**Atrial fibrillation	292 (6.9)	1,999 (6.8)	1,353 (8.2)	9,445 (8.9)
**Asthma	840 (19.7)	5,762 (19.6)	3,135 (19.1)	21,159 (20.0)
*CAD	598 (14.0)	4,587 (15.6)	2,811 (17.1)	20,521 (19.4)
*Congestive heart failure	233 (5.5)	1,838 (6.3)	1,160 (7.1)	8,938 (8.4)
*Depression	1,469 (34.5)	8,912 (30.3)	4,952 (30.2)	27,788 (26.2)
*Diabetes	629 (14.8)	4,794 (16.3)	3,193 (19.4)	23,609 (22.3)
*Hypertension	2,361 (55.4)	17,130 (58.3)	11,093 (67.6)	77,524 (73.2)
Hyperlipidemia	1,524 (35.8)	10,616 (36.1)	6,365 (38.8)	40,866 (38.6)
Osteoporosis	512 (12.0)	3,213 (10.9)	1,976 (12.0)	12,351 (11.7)
Calcium channel blockers	131 (3.1)	696 (3.3)	739 (4.5)	5,210 (4.9)
Warfarin	102 (2.4)	717 (2.4)	314 (1.9)	2,031 (1.9)
Digoxin	17 (0.4)	110 (0.4)	110 (0.7)	795 (0.8)
**Diabetes	242 (5.7)	1,706 (5.8)	709 (4.3)	5,085 (4.8)
Inhaled steroids	260 (6.1)	1,823 (6.2)	493 (3.0)	3,079 (2.9)
Bisphosphonates	274 (6.4)	1,663 (5.7)	806 (4.9)	4,931 (4.7)
Antiplatelet	40 (0.9)	250 (0.9)	102 (0.6)	791 (0.8)
Leukotriene modifiers	83 (2.0)	441 (1.5)	145 (0.9)	909 (0.9)
*Antidepressant	1,136 (26.7)	7,227 (24.6)	3,429 (20.9)	18,352 (17.3)
**Beta blocker	578 (13.6)	4,214 (14.4)	2,432 (14.8)	16,562 (15.64)
**ACE/ARB	471 (11.1)	3,593 (12.2)	2,326 (14.2)	15,954 (15.1)
Statin	581 (13.6)	4,170 (14.2)	1,722 (10.5)	11,534 (10.9)
Health-care utilization				
Mean number of unique medications (SD)	4.3 (4.1)	4.2 (4.2)	5.1 (4.7)	5.2 (4.9)

*p = <0.001
**p = <0.01

Table 2. Linear Regression Model to Evaluate Adherence in New Users, after Controlling for Medication Class

Variable	Parameter estimate	Standard error	t Value	Pr > |t|
Female	−0.01158	0.00464	−2.5	0.0126
Age	−0.00087243	0.00021826	−4	<0.0001
Number of medications	−0.00001534	0.00058126	−0.03	0.9789
Post- implementation	0.10302	0.00476	21.65	<0.0001
Target	−0.00374	0.0081	−0.46	0.644
Target*post	0.00986	0.01281	0.77	0.4415

have implemented a prescription medication label aimed at improving readability and understanding, we found little effect on medication adherence. When users of Target pharmacies were compared to patients who filled their prescriptions at non-Target pharmacies, we found no change in adherence in new users of chronic medications before and after implementation of the new label. Among prevalent users, we found changes in adherence that were small and inconsistent (a small reduction in the level of adherence and a small improvement in the monthly rate of change of adherence in the post-implementation period). The small magnitude and conflicting direction of these changes indicate that they are likely clinically unimportant.

These findings are not entirely surpirsing. Numerous studies have evaluated factors associated with medication non-adherence and have generally found adherence to be multi-factorial; cogntive, social, financial, and psychological explanations for non-adherence have been identified.[23] However, analyses of interventions to improve adherence have generally found that simple strategies are rather ineffective, and multi-factorial and complex inteventions are needed to influence behavior.[15,24] As a result, the change in labeling at Target pharmacies likely did not sufficiently address the multifactorial nature of medication non-adherence to affect meaningful behavioral change.

It may be that the label would be more likley to enhance medication safety than adherence. Some of the new features of the label, such as the colored rings to help patients identify which medication is for them, are focused on improving safety, and may have little effect on the quantity of medication purchased. Considering that the quality of pharmacologic care in the US is substandard,[25,26] and there is evidence of both over-use and under-use of essential medications,[25–27] improved labeling may encourage more appropriate use without measurably influencing adherence as we measured it.

While we did not find improved adherence in patients exposed to the new Target label, our claims-based methods for evaluating adherence may not have been sufficient to measure all aspects of adherence. Using claims to evaluate the frequency of refills is a commonly used approach to assess refill adherence with demonstrated validity; refill adherence using pharmacy claims correlates with other compliance measures as well as measures of drug presence (e.g., serum drug levels) or physiologic drug effects.[28] Studies of refill adherence are conditional on a patient filling an intial prescription. This is unlikely to be an important limitation, as we would only expect the label to influence a patient once they have purchased an initial prescription, after which the patient is first exposed to the label. However, our adherence measures were not sensitive enough to ascertain nuanced measures of appropriate medication use such as timing of administration or administration on an empty or full stomach as directed. Further, we were unable to determine whether patients exposed to the new label were more likely to adhere to written warnings and to avoid contraindications. Before concluding that the Target label offered no clinical benefit, more nuanced evaluation of medication use would be useful to evaluate the effect on adherence, and additional study of the effect of the new label on safety and adverse effects is needed.

Our study is limited by the sample we studied, commercially-insured patients. The label may have been more effective in improving understanding[15] and stimulating adherence in Medicaid beneficiaries or the uninsured, who often exhibit lower health literacy, and our study did not evaluate these populations. In addition, we censored data from all seniors on January 1, 2006 because we lost full records for a large percentage of patients after implementation of Medicare Part D. Shortening this window for analysis may also have limited our ability to identify changes in adherence in elderly patients, another population that may benefit from clearer labels and larger font. Further studies in elderly and low health literacy populations are needed before concluding that the Target label does not affect adherence.

Our obsevational methods were also unable to fully account for selection bias. It is possible that sicker or older patients selected Target pharmacies after learning about the new label designs. However, we matched exposed and unexposed patients on socio-demographic characteristics and adjusted for individual health characteristics in our models, and expect that the null finding in this study could not be explained by selection bias alone. We also saw a secular trend of improved adherence in the post period among new users, but we do not expect that it should have biased our study, and the difference-in-difference model controlled for these trends.

In conclusion, our evaluation of pharmacy claims in two large health plans did not find a clinically meaningful influence of an intervention to improve prescription medication labeling upon medication adherence. Further studies of the effect of the new label on medication safety and health outcomes are needed to assess the importance of label design on medication use. While we cannot rule out any benefit on adherence with the methods we used, these findings should inform pharmacies, insurers, and policy-makers, who may advocate for improved labeling. While efforts to improve labeling may enhance appropriate medication use, providers and payors should have reasonable expectations about how overall drug consumption will be affected. More importantly, these data

Table 3. Segmented Linear Regression Model of Adherence in Prevalent Users, Controlling for Drug Class

Parameter	Estimate	95% Confidence interval	
Female	0.0081	0.0073	0.0089
Age	−0.001	−0.001	−0.001
Time	0.0116	0.0114	0.0118
Target	0.011	0.0069	0.0151
Time*Target	−0.0006	−0.0012	−0.0001
Target*postMay05	−0.0069	−0.0138	0
Time*postMay05	−0.0274	−0.0276	−0.0272
Time*postMay05*Target	0.0007	0.0001	0.0013

should further encourage physicians to improve their communication with patients about medication use. They should not rely on patients to get their information from medication labels alone, even those with innovative designs, if appropriate adherence is the goal.

Acknowledgements: *This work was supported by a Pioneer Award from the Robert Wood Johnson Foundation.*

Dr. Shrank is supported by a career development award from the National Heart, Lung and Blood Institute (K23HL090505-01). Dr. Brookhart is supported by a career development award from the National Institute of Aging (AG-027400).

Drs. Shrank, Avorn, Choudhry, Schneeweiss, and Brookhart receive research funding from CVS Caremark for studies on medication adherence.

We would like to thank Joy Lee for her administrative and technical help with the project.

Conflict of Interest: *None disclosed.*

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APPENDIX 1: MEDICATIONS USED TO IDENTIFY PATIENTS WHO MIGHT HAVE ONE OF NINE CHRONIC DISEASES

(1) Atrial fibrillation
   (a) Warfarin (coumadin)
   (b) Beta-blockers: Acebutolol Hydrochloride, Atenolol, Betaxolol Hydrochloride, Bisoprolol Fumarate, Carteolol Hydrochloride, Esmolol Hydrochloride, Metoprolol Succinate, Metoprolol Tartrate, Nadolol, Penbutolol Sulfate, Pindolol, Propranolol Hydrochloride, Sotalol Hydrochloride, Timolol Maleate
   (c) Calcium channel blockers, nondihydropyridines: Diltiazem Hydrochloride, Diltiazem Malate, Mibefradil Dihydrochloride, Verapamil Hydrochloride

(2) Diabetes
   (a) Ace inhibitors: Benazepril Hydrochloride, Captopril, Enalapril Maleate, Enalaprilat, Enalaprilat Dihydrate, Fosinopril Sodium, Lisinopril, Moexipril Hydrochlo-

ride, Perindopril Erbumine, Quinapril Hydrochloride, Ramipril, Trandolapril
(b) Angiotensin receptor blocker: Candesartan, Cilexetil, Eprosartan Mesylate, Irbesartan, Losartan Potassium, Olmesartan Medoxomil, Telmisartan, Valsartan
(c) Metformin
(d) Sulfonureas: glipizide, glyburide, gliclazide, glimepiride,
(e) Glitazones: rosiglitazone, pioglitazone
(f) Insulin: insulin aspart, insulin glulisine, insulin lispro, regular, nph, lente, ultrelente, insulin detemir, insulin glargine, insulin mixtures (novolog 70/30, humalog 75/25, humulin 70/30, humulin 50/50, novolin 70/30—these are brand names)

(3) Asthma/COPD
(a) Beta agonists: albuterol, fenoterol, formoterol, fenotorol, levalbuterol, metaproteronol, pirbuterol, salmeterol, terbutaline
(b) Combos: advair, combivent, duoned, symbicort (these are brand names)
(c) Inhaled steroids: beclomethasone, budesonide, flunisolide, fluticasone, mometasone, triamcinolone
(d) Leukotriene inhibitors: montelukast, zafirlukast, zileuton
(e) Others: ipatropium, tiotropium

(4) Hypercholesterolemia/Hyperlipidemia
(a) Statins: atorvastatin, simvastatin, lovastatin, pravastatin, rosuvastatin, fluvastatin, vytorin
(b) Other: niacin, ezetimibe
(c) Bile acid sequestrants: cholestyramine, cholesevelam, colestipol
(d) Fibrates: fenofibrate, gemfibrozil, bezafibrate

(5) CHF (congestive heart failure)
(a) Ace inhibitors: Benazepril Hydrochloride, Captopril, Enalapril Maleate, Enalaprilat, Enalaprilat Dihydrate, Fosinopril Sodium, Lisinopril, Moexipril Hydrochloride, Perindopril Erbumine, Quinapril Hydrochloride, Ramipril, Trandolapril
(b) Loop diuretics: furosemide, bumetanide, torsemide
(c) Angiotensin receptor blocker: Candesartan, Cilexetil, Eprosartan Mesylate, Irbesartan, Losartan Potassium, Olmesartan Medoxomil, Telmisartan, Valsartan
(d) Aldosterone ant.: spironolactone, eplerenone
(e) Beta-blockers: Acebutolol Hydrochloride, Atenolol, Betaxolol Hydrochloride, Bisoprolol Fumarate, Carteolol Hydrochloride, Esmolol Hydrochloride, Metoprolol Succinate, Metoprolol Tartrate, Nadolol, Penbutolol Sulfate, Pindolol, Propranolol Hydrochloride, Sotalol Hydrochloride, Timolol Maleate
(f) Digoxin

(6) Osteoporosis
(a) Bisphosphonates: alendronate, clodronate, etidronate, ibandronate, pamidronate, risedronate, zoledronic acid

(7) Hypertension
(a) ACE Inhibitors: Benazepril Hydrochloride, Captopril, Enalapril Maleate, Enalaprilat, Enalaprilat Dihydrate, Fosinopril Sodium, Lisinopril, Moexipril Hydrochloride, Perindopril Erbumine, Quinapril Hydrochloride, Ramipril, Trandolapril
(b) Thiazide diuretics: Bendroflumethiazide, Benzthiazide, Chlorothiazide, Chlorothiazide Sodium, Chlorthalidone, Cyclothiazide, Hydrochlorothiazide, Hydroflumethiazide, Indapamide, Methyclothiazide, Metolazone, Polythiazide, Quinethazone, Trichlormethiazide
(c) Angiotensin receptor blocker: Candesartan, Cilexetil, Eprosartan Mesylate, Irbesartan, Losartan Potassium, Olmesartan Medoxomil, Telmisartan, Valsartan
(d) Beta-blockers: Acebutolol Hydrochloride, Atenolol, Betaxolol Hydrochloride, Bisoprolol Fumarate, Carteolol Hydrochloride, Esmolol Hydrochloride, Metoprolol Succinate, Metoprolol Tartrate, Nadolol, Penbutolol Sulfate, Pindolol, Propranolol Hydrochloride, Sotalol Hydrochloride, Timolol Maleate
(e) Calcium channel blockers:

- Nondihydropyridines: Diltiazem Hydrochloride, Diltiazem Malate, Mibefradil Di-Hydrochloride, Verapamil Hydrochloride
- Dihydropyridines: Amlodipine Besylate, Bepridil Hydrochloride, Felodipine, Isradipine, Nicardipine Hydrochloride, Nifedipine, Nimodipine, Nisoldipine

(f) Potassium-Sparing Agents: Amiloride Hydrochloride, Spironolactone, Triamterene
(g) Central Alpha-Antagonists: Clonidine Hydrochloride, Guanabenz Acetate, Guanfacine Hydrochloride, Methyldopa, Methyldopate Hydrochloride, Phenoxybenzamine Hydrochloride, Phentolamine Hydrochloride, Tolazoline Hydrochloride
(h) Alpha Blockers: Doxazosin Mesylate, Prazosin Hydrochloride, Terazosin Hydrochloride
(i) Combination Drugs

Beta Blockers And Diuretics

- Bendroflumethiazide/Nadolol
- Chlorthalidone/Atenolol
- Hydrochlorothiazide/Bisoprolol Fumarate
- Hydrochlorothiazide/Labetalol Hydrochloride
- Hydrochlorothiazide/Metoprolol Tartrate
- Hydrochlorothiazide/Propranolol
- Hydrochlorothiazide/Propranolol Hydrochloride
- Hydrochlorothiazide/Timolol

ACE Inhibitors And Diuretics

- Benazepril Hydrochloride/Hydrochlorothiazide
- Captopril/Hydrochlorothiazide
- Enalapril Maleate/Hydrochlorothiazide
- Fosinopril Sodium/Hydrochlorothiazide
- Lisinopril/Hydrochlorothiazide
- Moexipril Hydrochloride/Hydrochlorothiazide
- Quinapril Hydrochloride/Hydrochlorothiazide

Angiotensin II Receptor Antagonists And Diuretics

- Candesartan Cilexetil/Hydrochlorothiazide
- Irbesartan/Hydrochlorothiazide
- Losartan Potassium/Hydrochlorothiazide
- Telmisartan/Hydrochlorothiazide
- Valsartan/Hydrochlorothiazide

Calcium Antagonists And ACE Inhibitors

- Benazepril Hydrochloride/Amlodipine Besylate
- Enalapril Maleate/Diltazem Maleate
- Enalapril Maleate/Felodipine
- Trandolapril/Verapamil Hydrochloride

Other Combinations

- Bendroflumethiazide/Potassium Chloride
- Cryptenamine/Methylclothiazide
- Hydrochlorothiazide/Spironolactone
- Spironolactone/Hydrochlorothiazide
- Hydrochlorothiazide/Triamterene
- Hydrochlorothiazide/Amiloride Hydrochloride
- Clonidine Hydrochloride/Chlorthalidone
- Deserpidine/Hydrochlorothiazide
- Deserpidine/Methyclothiazide
- Guanethidine Sulfate/Hydrochlorothiazide
- Methyldopa/Chlorothiazide
- Methyldopa/Hydrochlorothiazide
- Reserpine/Benzthiazide
- Reserpine/Chlorothiazide
- Reserpine/Chlorthalidone
- Reserpine/Hydrochlorothiazide
- Reserpine/Hydroflumethiazide
- Reserpine/Methyclothiazide
- Reserpine/Polythiazide
- Reserpine/Quinethazone
- Reserpine/Trichlormethiazide
- Hydralazine Hydrochloride/Hydrochlorothiazide
- Hydralazine Hydrochloride/Reserpine
- Hydralazine Hydrochloride/Reserpine/Hydrochlorothiazide
- Hydralaz/Reserpine/Hydrochlorothiazide
- Hydralazine Hydrochloride/Hydrochlorothiazide
- Prazosin Hydrochloride/Polythiazide
- Methylclothiazide/Pargyline
- Rauwolfia Serpentina/Bendroflumethiazide
- Rauwolfia/Bendroflumethiazide/Potassium

Miscellaneous

- Diazoxide
- Metyrosine
- Reserpine/Mannitol Hexanitrate
- Acetazolamide

(8) Depression
   a) SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
   b) Others: buproprion, duloxetine, mirtazapine, venlafaxine

(9) Coronary Artery Disease
   (a) Ace inhibitors: Benazepril Hydrochloride, Captopril, Enalapril Maleate, Enalaprilat, Enalaprilat Dihydrate, Fosinopril Sodium, Lisinopril, Moexipril Hydrochloride, Perindopril Erbumine, Quinapril Hydrochloride, Ramipril, Trandolapril
   (b) Angiotensin receptor blocker: Candesartan, Cilexetil, Eprosartan Mesylate, Irbesartan, Losartan Potassium, Olmesartan Medoxomil, Telmisartan, Valsartan
   c) Beta-blockers: Acebutolol Hydrochloride, Atenolol, Betaxolol Hydrochloride, Bisoprolol Fumarate, Carteolol Hydrochloride, Esmolol Hydrochloride, Metoprolol Succinate, Metoprolol Tartrate, Nadolol, Penbutolol Sulfate, Pindolol, Propranolol Hydrochloride, Sotalol Hydrochloride, Timolol Maleate
   d) statins: atorvastatin, simvastatin, lovastatin, pravastatin, rosuvastatin, fluvastatin, vytorin
   e) anti-platelets: clopidogrel, aspirin, coumadin

APPENDIX 2: ICD-9 DIAGNOSTIC CODES USED TO IDENTIFY CHRONIC DISEASES

(1) Atrial Fibrillation (ICD-9 codes: 427.31)
(2) Diabetes (ICD-9 codes: 250.0x–250.9x)
(3) Asthma/COPD (ICD-9 codes: 494.xx, 496.xx)
(4) Hypercholesterolemia/Hyperlipidemia (ICD-9 codes: 272.0, 272.2)
(5) CHF (congestive heart failure) (ICD-9 codes: 428.xx)
(6) Osteoporosis (ICD-9 codes: 733.0)
(7) Hypertension (ICD-9 codes: 401.xx, 402.xx, 403.xx, 404.xx, 405.xx)
(8) Depression (ICD-9 codes: 296.2x, 296.3x, 300.4x, 309.0x, 309.1x, or 311.xx)
(9) Coronary Artery Disease (ICD-9 codes: 414.0x)