

# Synchronized Prescription Refills and Medication Adherence: A Retrospective Claims Analysis

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**P**oor medication adherence is a common problem among patients taking medications for a chronic condition.<sup>1</sup> For patients receiving multiple medications for the treatment of more than 1 chronic condition, the resulting complexity can be particularly challenging.<sup>2</sup> To address some of the practical burdens associated with long-term medication regimens, there has been increasing interest in whether synchronizing medication refill schedules—whereby all of a patient's maintenance medications are refilled at the same time—may be a promising, scalable approach to improving adherence.

A recent review of the synchronization literature revealed few major peer-reviewed studies of synchronization.<sup>3</sup> Holdford and Inocencio (2013) examined a convenience sample of patients at an independent retail pharmacy chain in the rural midwestern United States who were receiving new prescription medications, from 1 of 6 drug classes, to treat cardiovascular disease and diabetes.<sup>4</sup> Intervention patients (ie, those who were participating in an appointment-based medication synchronization program that included synchronization of refills) had higher adherence across all drug classes than a control group of patients receiving usual care. A second study by Holdford (2015) among commercially insured retail pharmacy patients in Ohio who had been using medications for 6 months or more found similar results.<sup>5</sup> Further, Choudhry et al (2011) used retrospective claims data from a large pharmacy benefit manager to examine therapeutic complexity in patients receiving refills for cardiovascular medications from a chain of retail and/or mail order pharmacies and found that less consolidated (ie, less synchronized) refill schedules were an independent predictor of worse medication adherence.<sup>2</sup> Although valuable, the generalizability of these studies may be limited due to their focus on either specific geographic regions, retail pharmacy users, commercially insured patients, and/or a limited set of drug classes.

Despite the absence of more generalizable evidence, there has been increasing adoption of medication synchronization programs across the nation.<sup>3</sup> According to the American Pharmacists Association Foundation, more than 23 pharmacy chains and approximately

## ABSTRACT

**OBJECTIVES:** Medication adherence is often suboptimal, especially among patients on multiple chronic medications. We examined the association between synchronized medication refill schedules—which typically reduce organizational effort and logistical demands—and adherence.

**STUDY DESIGN:** Retrospective study among patients enrolled in Medicare Advantage prescription drug plans.

**METHODS:** We used 2012 pharmacy, medical, and enrollment data linked with consumer meta-data for Medicare patients filling 2 or more maintenance prescriptions for antihypertensives, lipid-lowering agents, antidiabetic agents, antidepressants, and/or antiosteoporotic agents. Medication adherence for the year was measured using the proportion of days covered (PDC) at the drug class level. Patients were deemed adherent if drug class PDC was  $\geq 0.80$ . Outcomes were compared between 1:1 propensity score-matched patients on synchronized versus nonsynchronized refill schedules for maintenance medications.

**RESULTS:** The synchronized refill group showed better adherence than the control group, although the magnitude of effects varied by drug class and specific outcome measure. Mean PDC scores ranged from 0.02 higher for antihypertensives to 0.07 higher for antidepressants in the synchronized refill group relative to the control group ( $P < .01$ ). Further, compared with the control group, a larger proportion of synchronized refill group members were deemed adherent, ranging from 6 percentage points higher for antihypertensives to 15 percentage points higher for lipid-lowering agents ( $P < .01$ ). Differences between the synchronized and control groups were larger among exclusive users of retail versus mail order pharmacies for maintenance medications.

**CONCLUSIONS:** Synchronized medication refill schedules were associated with better medication adherence, particularly for patients filling maintenance medications exclusively at retail pharmacies.

*Am J Manag Care.* 2017;23(2):98-104

2000 independent pharmacies in the United States have implemented medication synchronization programs.<sup>6</sup> An increasing number of states have proposed or recently passed legislation to remove barriers to medication synchronization, such as requiring insurers to pro-rate co-payments for the partial refills that are often needed to synchronize existing prescriptions.<sup>6</sup> According to a recent national survey of 1000 adults 40 years or older who were receiving 1 or more medications for long-term medical conditions, about 1 in 8 patients were enrolled in a prescription synchronization program.<sup>7</sup> In light of the growing adoption of, and policy interest in, synchronization programs, there is a pressing need for additional evaluations of the effectiveness of synchronizing refill schedules.

In this study, we utilized existing claims data for a sample of individuals enrolled in Medicare Advantage prescription drug plans (MA-PDs) who were receiving antihypertensives, lipid-lowering drugs, antidiabetic agents, antidepressants, and/or antiosteoporotic agents, to examine adherence outcomes in patients with synchronized medications compared with those whose medications were not synchronized. We focused on the Medicare population for several reasons. First, an estimated 85% of US adults 65 years or older have at least 1 chronic health condition, and 60% have at least 2.<sup>8</sup> Second, given that forgetfulness and difficulties with transportation may increase with age, Medicare patients may be a particularly appropriate target population for interventions that reduce trips to the pharmacy and make it easier to manage prescription refills. Third, medication adherence for seniors has garnered increasing attention due to the CMS Five-Star Quality Ratings System program, which provides public ratings of Medicare Part D plans and ties performance to bonus payments.<sup>9</sup> The ratings incorporate several medication adherence measures and award an increasing number of stars based on the percentage of a Part D plan's members that meet adherence benchmarks.

## METHODS

### Data Source and Sample Selection

Using 2012 pharmacy, medical, and enrollment data from Humana Inc's top 50 (ie, highest enrollment) MA-PD plans linked with consumer meta-data files from the AmeriLINK Consumer Database,<sup>10</sup> we took a 20% random sample of individuals meeting the following study criteria: 1) continuous eligibility for pharmacy and medical benefits in the same plan throughout 2012; 2) filling 2 or more prescriptions for antihypertensives, lipid-lowering drugs, antidiabetic agents, antidepressants, and/or antiosteoporotic agents; 3) a record of at least 2 different prescription fill dates for those medications in

## TAKEAWAY POINTS

Prescription synchronization programs are popular, but evidence regarding their utility in improving adherence is limited. Our retrospective claims analysis of Medicare Advantage patients receiving multiple maintenance medications (ie, antihypertensives, lipid-lowering drugs, antidiabetic agents, antidepressants, and/or antiosteoporotic agents) compared patients with synced refill schedules to propensity score-matched patients without synced schedules.

- ▶ Compared with the nonsynced group, the synced group showed better adherence as measured by proportion of days covered. The magnitude varied by drug class.
- ▶ Differences between the synced and nonsynced groups were larger in patients exclusively using retail pharmacies compared with patients exclusively using mail order pharmacies.
- ▶ Synchronized prescription refills may facilitate adherence.

calendar year (CY) 2012; 4) exclusive use of either retail or mail order pharmacies to refill maintenance medications during the study year (ie, all prescriptions filled via 1 delivery channel); and 5) an equal number of unique maintenance drug classes in both the first half of the year and in the entire year (as a proxy for no major disruption in the maintenance drug regimen) to ensure that it would have been possible to maintain synced refill schedules throughout the year.

The primary study group consisted of individuals who had a synchronized refill schedule for all of their maintenance medications for the entire study year—defined as having refills for all medications at every refill date during the year. For example, a patient taking 4 maintenance medications would need to show refills for all 4 medications at each refill date in order to be classified in the synchronized medication refill group.

In sensitivity analyses, we applied alternate eligibility criteria for the study group, representing less restrictive definitions of synchronization. In the first sensitivity analysis, patients were classified in the synchronized refill group if they refilled all maintenance drugs at the same time at the first 2 fills in the year (ie, started as synced, but did not necessarily remain synced). In the second sensitivity analysis, the synchronized refill group consisted of patients who refilled all maintenance drugs at once at any 2 consecutive fill dates during the year, regardless of when in the year this occurred.

The control group, which remained the same for all analyses, included patients who did not have any 2 consecutive fill dates during the year where they refilled all their maintenance drugs at the same time. The study protocol was approved by the University of Pennsylvania Institutional Review Board.

### Outcomes

Our primary outcome was medication adherence at the drug class level, as measured by the proportion of days covered (PDC) for CY2012.<sup>11</sup> In keeping with CMS's technical guidance on measuring adherence to Star Rating medications, PDC was calculated as the proportion of days in the observation period (ie, 365 days in our study) with a day's supply of a medication available from at least 1 prescription in that drug class.<sup>12</sup> A continuous PDC measure was calculated for each of the 5 drug classes of interest among patients filling drugs for that class.

We also created indicators for whether a PDC measure was  $\geq 0.80$ , as this is a common cutoff for classifying a patient as adherent and also used by CMS for Part D Plan Star Ratings calculations.<sup>13</sup>

It should be noted that although some mail order pharmacies offer patients the option to receive automatic refills, CMS regulations require pharmacies to obtain consent from Medicare beneficiaries prior to shipping every refill. Thus, patients must take an action (eg, via initiating a refill order or responding to a call) before medication is sent. CMS has noted that this requirement would be expected to increase the value (ie, accuracy) of refill-related adherence measures.<sup>14</sup>

### Statistical Analysis

We applied propensity score matching to balance the synchronized refill group members with control members across a variety of characteristics. As a first step, we stratified the sample by 4 key variables likely to affect medication adherence in order to ensure that matched pairs were identical with respect to the following parameters: 1) type of pharmacy where maintenance medications were filled (exclusive use of retail pharmacy vs exclusive use of mail order pharmacy); 2) insurance plan identifier, to account for differences in insurance benefits structure, co-payment requirements, drug formulary and utilization management tools, and other plan-specific features; 3) total number of maintenance medications; and 4) combination of maintenance drug classes being used (eg, a synchronized refill group member taking only antihypertensives and lipid-lowering medications would be matched to a control group member taking only those 2 classes of maintenance drugs).

Only strata with at least 1 synchronized refill group member and 1 potential control were considered in the matching algorithm. Within each stratum, we matched along a wide range of 310 variables, including: 1) sociodemographic variables (eg, age, gender, marital status, Medicare Part D low-income subsidy status, disability status, geographic region, county-level percent on Medicare Advantage); 2) Census tract-level measures for variables including home ownership, education, household income, and home value; 3) clinical variables (ie, medical condition indicators and the CMS Hierarchical Condition Categories (CMS-HCC) score)<sup>15</sup>; 4) prescription cost variables, including total prescription costs for the year, total prescription costs for maintenance medications only, and total out-of-pocket costs; and 5) consumer meta-data variables used to characterize plan members, including estimated income, interests, hobbies, consumer personas (eg, young urban singles, struggling seniors), occupation (including retirement status), attitudes (eg, positive outlook, control seekers), and tendency to drink alcohol and/or smoke. These variables were obtained from and/or predicted based on demographics, purchasing behavior, public records, Census data, consumer surveys, and other primary sources.

The success of propensity score matching was evaluated by comparing the means of matched synchronized and control group members along the 310 variables used. We calculated Cohen's *d* to

estimate the size of any differences between the matched groups across all variables; any sample characteristic with a Cohen's *d*  $< 0.10$  was considered insignificant as per standard practice.<sup>16</sup>

Using the matched sample, we performed paired *t* tests for continuous outcomes and McNemar's tests for categorical outcomes. We also conducted subgroup analyses by type of pharmacy used to fill all maintenance medications (exclusively retail vs exclusively mail order). We then tested—via regression analyses with interaction terms for the continuous PDC scores and Mantel-Haenszel tests for the dichotomous adherence measure (PDC  $\geq 0.80$ )—whether the association between synchronized refills and medication adherence differed for exclusively mail order pharmacy users compared with exclusively retail pharmacy users.

In sensitivity analyses, we repeated the main analysis twice using the 2 alternate eligibility criteria for defining the study group. A final sensitivity analysis repeated the main analysis after excluding the consumer meta-data variables during the propensity-matching step. Statistical significance is reported at the  $\alpha = 0.05$  level and all hypothesis tests were 2-sided. Propensity score matching was conducted in SAS version 9.4 (SAS Institute Inc, Cary, North Carolina), whereas statistical analyses were performed in Stata version 13.1 (StataCorp LP, College Station, Texas).

## RESULTS

Our final sampling frame consisted of 42,162 individuals, of which 6544 (15.5%) had synchronized refill schedules (eAppendix Figure A [eAppendices available at [ajmc.com](http://ajmc.com)]). After applying the propensity score-matching algorithm, 6458 synchronized refill group members (99%) were successfully matched to 6458 control group members.

Table 1 provides key characteristics for the synchronized refill and control group members. Prior to propensity score matching, the 2 groups were similar with respect to demographics but differed on a number of clinical and treatment characteristics. For example, synchronized refill group members tended to have fewer medications, correspondingly lower prescription costs, and lower CMS-HCC scores. The matching process successfully reduced observable differences between groups, as demonstrated by Cohen's *d*  $< 0.10$  for each of the 310 variables used in the propensity score matching (eAppendix Table A).

The matched sample had a mean age of 75 years and just under half were female. A majority of the matched sample used antihypertensives (89.9%) and lipid-lowering drugs (60.5%), whereas fewer than 10% used antidiabetic agents, antidepressants, and antiosteoporotic agents. Approximately 82% were exclusive mail order pharmacy users.

Both adherence outcome measures showed higher adherence in the synchronized refill group compared with the control group, although the magnitude and significance of the association varied by the drug class and specific outcome measure (Table 2). Ab-

**TABLE 1.** Selected Sample Characteristics Before and After Propensity Score Matching

Variable	Unmatched Sample			Propensity Score-Matched Sample		
	Control (n = 36,703)	Synced (n = 6551)	d	Control (n = 6458)	Synced (n = 6458)	d
Age, years: mean (SD)	75.8 (8.2)	75.1 (7.7)	0.09	75.0 (7.3)	75.1 (7.6)	-0.01
Female	50.0%	46.9%	0.07	47.9%	47.2%	0.01
Married	51.2%	49.9%	0.03	52.5%	50.0%	0.05
Estimated income (\$1000s), mean (SD)	57.6 (51.1)	55.4 (48.7)	0.04	58.1 (50.5)	55.4 (48.8)	0.05
Medicare disabled	13.8%	12.2%	0.05	10.5%	12.1%	-0.05
Part D low-income subsidy	10.7%	10.0%	0.02	8.4%	10.0%	-0.05
Region						
West	10.1%	10.8%	-0.03	10.8%	10.9%	0.00
South	31.1%	32.2%	-0.02	31.8%	32.1%	-0.01
East	36.3%	30.7%	0.12	31.1%	30.6%	0.01
Central	22.5%	26.2%	-0.09	26.3%	26.3%	0.00
Exclusive mail order <sup>a</sup>	63.5%	81.6%	-0.39	81.5%	81.5%	0.00
Exclusive retail <sup>a</sup>	36.5%	18.4%	0.39	18.5%	18.5%	0.00
Number of maintenance drugs, mean (SD)	3.5 (1.3)	2.7 (1.0)	0.60	2.7 (1.0)	2.7 (1.0)	0.00
Number of nonmaintenance drugs, mean (SD)	3.0 (2.5)	2.2 (2.1)	0.33	2.3 (2.1)	2.2 (2.1)	0.05
Drug class, users						
Antihypertensives	90.1%	89.8%	0.01	89.9%	89.9%	0.00
Lipid-lowering agents	66.4%	60.3%	0.13	60.5%	60.5%	0.00
Antidiabetic agents	12.5%	9.3%	0.10	9.2%	9.2%	0.00
Antidepressants	8.2%	6.7%	0.05	6.6%	6.6%	0.00
Antiosteoporotic agents	2.9%	2.2%	0.05	2.2%	2.2%	0.00
Diagnosis						
Hypertension	92.7%	92.7%	0.00	92.3%	92.8%	-0.02
Hyperlipidemia	83.4%	79.5%	0.10	78.6%	79.6%	-0.03
Diabetes	22.8%	17.5%	0.13	16.9%	17.4%	-0.01
Depression	14.5%	10.6%	0.11	10.7%	10.5%	0.01
Osteoporosis	11.4%	8.7%	0.09	8.6%	8.7%	0.00
COPD	6.6%	2.7%	0.16	3.0%	2.7%	0.02
Congestive heart failure	4.8%	2.7%	0.10	2.1%	2.7%	-0.04
Cardiovascular disease	6.4%	4.1%	0.10	4.0%	4.1%	-0.01
End stage renal disease	4.0%	2.5%	0.08	2.4%	2.5%	-0.01
CMS-HCC score, mean (SD)	60.7 (20.1)	50.5 (16.0)	0.50	51.0 (15.7)	50.6 (16.0)	0.03
Total 2012 cost of all medications (\$), mean (SD)	1224.68 (2873.63)	650.38 (1354.30)	0.21	641.74 (1725.10)	651.58 (1357.13)	-0.01
Total 2012 cost of maintenance medications (\$), mean (SD)	888.26 (2258.87)	444.94 (869.01)	0.21	434.59 (1158.92)	445.18 (886.59)	-0.01
Total 2012 out-of-pocket costs (\$), mean (SD)	262.38 (424.41)	139.00 (259.27)	0.31	146.46 (231.80)	138.75 (257.87)	0.03

COPD indicates chronic obstructive pulmonary disease; CMS-HCC, CMS Hierarchical Condition Category; d, Cohen's d; SD, standard deviation.

<sup>a</sup>Refers to type of pharmacy used for maintenance medications.

solute differences in mean PDC scores ranged from 0.02 higher for antihypertensives to 0.07 higher for antidepressants in the synchronized refill group relative to the control group. Similarly, a larger proportion of synchronized refill group members were clas-

sified as adherent (PDC  $\geq$  0.80) compared with the control group, with absolute differences ranging from 6 percentage points higher among patients taking antihypertensives to 15 percentage points higher among patients taking lipid-lowering agents.

**TABLE 2.** Adherence Outcomes for Patients With Synchronized Refills Versus Propensity Score-Matched Controls

	Number of Matched Pairs	Synchronized Refill Group	Control Group	Absolute Difference	95% CI	P <sup>a</sup>
Continuous PDC, mean						
Antihypertensives	5726	0.94	0.92	0.02	(0.02-0.03)	<.01
Lipid-lowering agents	3444	0.91	0.85	0.06	(0.06-0.07)	<.01
Antidiabetic agents	547	0.90	0.87	0.03	(0.02-0.05)	<.01
Antidepressants	398	0.90	0.83	0.07	(0.04-0.09)	<.01
Antiestrogenic agents	123	0.85	0.81	0.04	(-0.01 to 0.10)	.11
Percent adherent (PDC ≥0.80)						
Antihypertensives	5726	92%	86%	6%	(5%-7%)	<.01
Lipid-lowering agents	3444	88%	72%	15% <sup>b</sup>	(13%-17%)	<.01
Antidiabetic agents	547	85%	75%	10%	(5%-15%)	<.01
Antidepressants	398	83%	70%	13%	(8%-19%)	<.01
Antiestrogenic agents	123	76%	65%	11%	(-2% to 23%)	.09

CI indicates confidence interval; PDC, proportion of days covered.

<sup>a</sup>P values are based on paired *t* tests for continuous PDC and McNemar’s test for percent adherent.

<sup>b</sup>Difference does not equal Synchronized minus Control due to rounding.

Examining subgroups by type of pharmacy revealed that the magnitude of the absolute differences in adherence between synced and nonsynced schedules were greater in patients utilizing retail pharmacies (Figure and eAppendix Figure B). Mean PDC score differences between the synchronized refill group and the control group ranged from 0.06 higher for antihypertensives to 0.15 higher for lipid-lowering agents in the retail pharmacy users, whereas they were 0.02 and 0.05 higher, respectively, for the mail order pharmacy users. Similarly, the absolute differences in the proportion of individuals who were adherent (PDC ≥0.80) between the synchronized refill group and the control group ranged from 12 percentage points for antihypertensives to 30 percentage points for lipid-lowering agents in the retail pharmacy subgroup, whereas the differences were 4 percentage points to 13 percentage points, respectively, for the mail order pharmacy subgroup. The magnitude of the association between synchronization and adherence was significantly larger in retail users for 3 of the 5 drug classes we examined (eAppendix Table B). All sensitivity analyses showed findings similar to those of our main analyses (eAppendix Table C).

## DISCUSSION

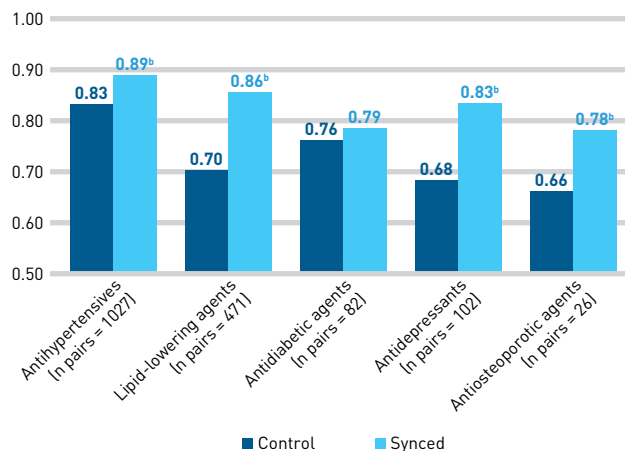
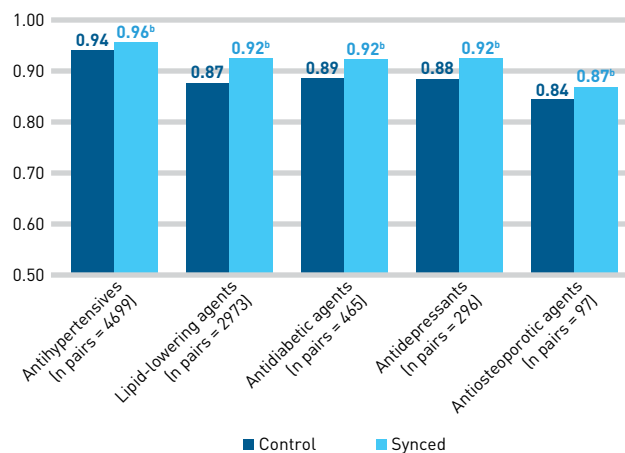
To our knowledge, this is the first retrospective analysis to examine the adherence benefits associated with synchronized medication refill schedules in a sample of individuals enrolled in MA-PDs and receiving a wide range of common maintenance medications. Our analyses revealed higher levels of adherence among those patients with synchronized refill schedules than those with unsynchronized schedules for both of our outcome measures: mean drug class PDC and percentage of patients meeting an adherence threshold of PDC ≥0.80. The magnitude of adherence advantages associated

with prescription synchronization varied by drug class, with the largest differences seen among lipid-lowering and antidepressant agents and the smallest differences seen among antihypertensives, where adherence was high even in the control group. Differences for antiosteoporotic agents did not reach statistical significance, likely due to the smaller sample size in that category.

Overall, the differences we observed were of sufficient magnitude to affect CMS Part D Plan Five-Star Rating criteria, particularly in regard to the percentage of patients in the plan meeting adherence criteria (ie, PDC ≥0.80) for lipid-lowering drugs and antidiabetic agents.<sup>9</sup> Further research is needed to determine whether some of the more modest adherence differences we observed would translate into improved health outcomes or economic savings, especially for patients with good baseline adherence. Nonetheless, it has been widely documented that sustaining long-term adherence is a complex behavior that poses challenges for most patients<sup>1</sup>; therefore, increased convenience may help to support maintenance of good adherence and reduce the risk of “adherence fatigue,” even in those who are already doing well.

In addition, we found that patients with synchronized refill schedules who were filling their maintenance medications exclusively through retail pharmacies had higher adherence than their nonsynced retail pharmacy counterparts. In comparison, smaller differences in adherence were seen for synced versus nonsynced schedules among patients exclusively using mail order pharmacies. This is not surprising given the greater time and travel demands associated with multiple trips to a retail store; reducing the number of pharmacy visits likely alleviates some of the burdens associated with obtaining refills.

It is notable that less than 20% of our final study population consisted of customers who exclusively used retail pharmacies for

**FIGURE.** Average PDC Score by Drug Class**(a)** Average PDC score by drug class, exclusive retail pharmacy users<sup>a</sup>**(b)** Average PDC score by drug class, exclusive mail order pharmacy users<sup>a</sup>

PDC indicates proportion of days covered.

<sup>a</sup>Patients with synchronized refill schedules versus propensity score-matched controls.<sup>b</sup>Indicates statistical significance at  $P < .05$ .

maintenance medications, perhaps reflecting the increasing use of mail order pharmacies for long-term prescriptions. Exclusively mail order patients were characterized by higher adherence overall compared with exclusively retail patients, which is consistent with other studies.<sup>17,18</sup> This may be because mail order pharmacies typically offer a 90-day supply of medication—often with lower co-pays than required in the retail setting—as well as the fact that home delivery reduces logistical demands. Nevertheless, the fact that we still observed higher adherence associated with synchronized refill schedules, despite high adherence levels among all mail order patients, highlights that multiple approaches to increasing adherence could have additive effects. Even when patients

have consistent medication regimens and use a consistent type of pharmacy, synchronization may be further reducing prescription refill management burdens and facilitating improved adherence.

Although our analyses controlled for baseline differences using propensity score matching, inspection of our study sample prior to matching offers insight into systematic differences between patients with synchronized maintenance medication refill schedules and those without them. For example, nonsynced patients had a higher mean number of both maintenance and nonmaintenance medications and higher CMS-HCC scores than patients with synced medications, suggesting that patients who might benefit most from simplified refill schedules are not necessarily on synchronized schedules. Synchronized refill schedules were also less common among patients using only retail pharmacies for their maintenance medications, despite the fact that having to pick up prescriptions in multiple trips is typically less convenient than having medication delivered to the home and that many existing synchronization programs are aimed at retail patients.

### Limitations

Several caveats deserve mention. First, given our cross-sectional design, our study documents associations but does not establish causal relationships between prescription synchronization and improved adherence. Second, although PDC has been shown to correlate with other indicators of medication adherence and is a widely used and generally accepted adherence measurement method,<sup>11,19</sup> it does not reflect whether a medication was actually taken as prescribed. Third, the potential for confounding, inherent in all observational studies, applies here. In particular, systematic unobserved patient-related differences could have confounded our findings; for example, it is possible that more highly organized patients would be both more likely to initiate synchronized schedules and to be adherent. We sought to offset these limitations by propensity score matching on a variety of patient demographic and clinical characteristics and also on an extensive series of consumer meta-data variables, including attitudes, lifestyles, and other health behaviors that are typically unobserved confounders in most retrospective claims analyses. Fourth, we observed high levels of adherence in our control group, perhaps due to our sample selection criteria and propensity-matching approach, which may have led to a ceiling effect in our analyses. Some analyses of individual medication classes (eg, antioosteoporotic agents, antidepressants) were also based on small sample sizes; hence, we should be cautious about estimates in those cases.

Finally, we also did not have access to information regarding how patients came to have synchronized refill schedules. Patients may have been participating in a medication synchronization program available at their retail pharmacy, have chosen to synchronize their medication of their own accord or on the advice of a healthcare provider or pharmacist (outside of a formal medication synchronization program), or ended up with a naturally

synchronized schedule if new prescriptions were required after switching physicians, health plans, or type of pharmacy (retail to mail order pharmacy or vice versa). Although this lack of detail is a limitation in some respects, it also allowed us to assess whether synchronized schedules in general are associated with improved adherence. Medication synchronization programs typically involve both synchronization and multiple touchpoints, where patients have contact with a pharmacy staff member who may also provide additional adherence support, such as early detection of adherence problems, problem-solving strategies, or encouragement. Because our sample would be expected to include individuals exposed to various medication synchronization programs in diverse contexts, our results can be seen as a general estimate of synchronization impact. As noted by others, future intervention research that permits disentangling of potentially active treatment components is needed to further understand the potential benefits of synchronization and associated support programs.<sup>4</sup>

## CONCLUSIONS

Our analyses demonstrate that propensity score matching can be applied to existing data sets to generate valuable insights into differences in medication adherence outcomes between patients on synchronized refill schedules and those whose refills are not synchronized. Thus, secondary datasets can serve as another source of information to inform policy debates while we wait for additional data to become available from prospective evaluations of prescription synchronization programs being implemented in the current marketplace. Several states have already passed legislation requiring insurance plans to permit partial, prorated refills for patients wishing to synchronize multiple prescriptions,<sup>6</sup> and CMS's beneficiary handbook now makes this option available to all Medicare beneficiaries.<sup>20</sup> More than a dozen states have introduced similar legislation.<sup>6</sup> Our findings add to the conversation regarding the utility of large-scale implementation of medication synchronization programs. ■

### Acknowledgments

The authors wish to thank Michael Relish, MS, Vicki L. Vogel, BA, Brian M. Lefeber, MS, MBA, George J. Spurlock, MBA, Brian Minichillo, BS, and Lara Wimmer, MBA, all of Humana Inc, for their support with this study. The authors also thank Amy R. Pettit, PhD, consultant and adjunct fellow, University of Pennsylvania Center for Public Health Initiatives, for her feedback on the manuscript and assistance with editing.

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**Source of Funding:** Humana, Inc.

**Author Disclosures:** At the time of the study, Dr Doshi reported serving as a consultant for Alkermes, Inc, Boehringer Ingelheim, Forest Laboratories (now Allergan), Ironwood Pharmaceuticals, and Shire; and had received grants from Humana, Inc, PhRMA, Pfizer Inc, Amgen Inc, Merck & Co, Inc, and the National Pharmaceutical Council. Her spouse holds stock in Merck & Co, Inc, and Pfizer Inc. Dr Young was employed by Humana, Inc, and held Humana stock at the time of the study. Dr Lawnicki is employed by Humana, Inc, and holds Humana stock. Dr Troxel is on the VAL Health Scientific Advisory Board. Dr Volpp is a consultant for and holds stock in VAL Health and has been a consultant for CVS Health. The remaining authors report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

**Authorship Information:** Concept and design (JD, RL, PL, PPY, VFL, KGV); acquisition of data (RL, VFL); analysis and interpretation of data (JD, RL, PL, VFL, ABT); drafting of the manuscript (JD, RL, PL); critical revision of the manuscript for important intellectual content (JD, RL, PL, PPY, ABT, KGV); statistical analysis (JD, RL, PL, ABT); obtaining funding (JD, KGV); administrative, technical, or logistic support (JD, RL); and supervision (JD, PPY, KGV).

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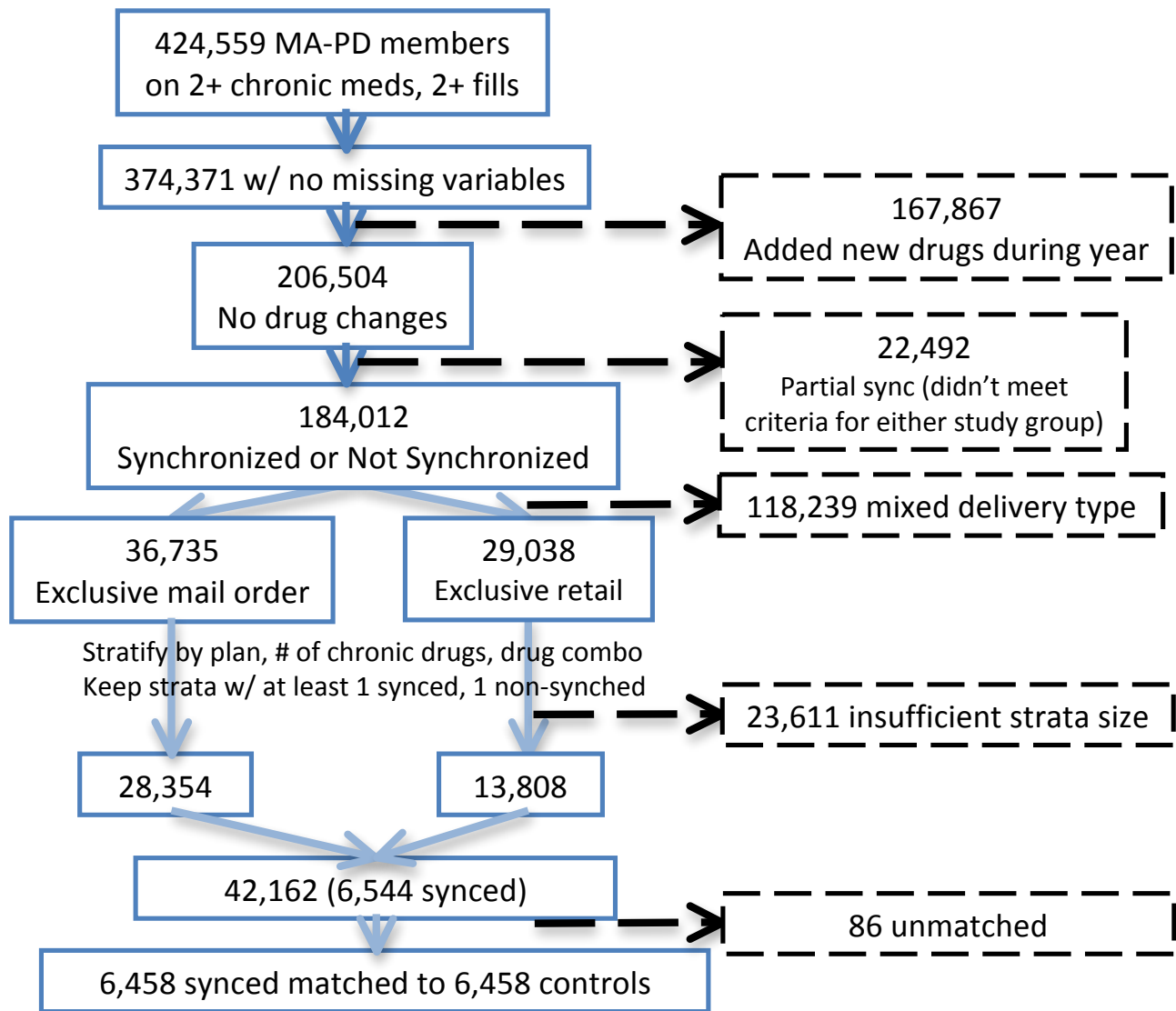
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eAppendix

eAppendix Figure A. Sample Flow Chart





**eAppendix Table A.** Full List of Variables Used in Propensity Score Matching

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Age in years, mean (SD)	75.8 (8.2)	75.1 (7.7)	0.09	75.0 (7.3)	75.1 (7.6)	-0.01
Female	50.0%	46.9%	0.07	47.9%	47.2%	0.01
Married	51.2%	49.9%	0.03	52.5%	50.0%	0.05
Estimated Income (\$1000s), mean (SD)	57.6 (51.1)	55.4 (48.7)	0.04	58.1 (50.5)	55.4 (48.8)	0.05
Medicare disability	13.8%	12.2%	0.05	10.5%	12.1%	-0.05
Part D Low-Income Subsidy	10.7%	10.0%	0.02	8.4%	10.0%	-0.05
Region: West	10.1%	10.8%	-0.03	10.8%	10.9%	0.00
Region: South	31.1%	32.2%	-0.02	31.8%	32.1%	-0.01
Region: East	36.3%	30.7%	0.12	31.1%	30.6%	0.01
Region: Central	22.5%	26.2%	-0.09	26.3%	26.3%	0.00
Exclusive mail order pharmacy users for maintenance meds	63.5%	81.6%	-0.39	81.5%	81.5%	0.00
Exclusive retail pharmacy users for maintenance meds	36.5%	18.4%	0.39	18.5%	18.5%	0.00
Number of maintenance medications	3.50	2.70	0.60	2.70	2.70	0.00
Number of nonmaintenance medications	3.00	2.20	0.33	2.30	2.20	0.05
Drug classes, users						
Antihypertensives	90.1%	89.8%	0.01	89.9%	89.9%	0.00
Lipid-lowering agents	66.4%	60.3%	0.13	60.5%	60.5%	0.00
Antidiabetic agents	12.5%	9.3%	0.10	9.2%	9.2%	0.00
Antidepressants	8.2%	6.7%	0.05	6.6%	6.6%	0.00
Antiosteoporotic agents	2.9%	2.2%	0.05	2.2%	2.2%	0.00
Diagnosis						
Hypertension	92.7%	92.7%	0.00	92.3%	92.8%	-0.02

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Hyperlipidemia	83.4%	79.5%	0.10	78.6%	79.6%	-0.03
Diabetes	22.8%	17.5%	0.13	16.9%	17.4%	-0.01
Depression	14.5%	10.6%	0.11	10.7%	10.5%	0.01
Osteoporosis	11.4%	8.7%	0.09	8.6%	8.7%	0.00
COPD	6.6%	2.7%	0.16	3.0%	2.7%	0.02
Congestive heart failure	4.8%	2.7%	0.10	2.1%	2.7%	-0.04
Cardiovascular disease	6.4%	4.1%	0.10	4.0%	4.1%	-0.01
End stage renal disease	4.0%	2.5%	0.08	2.4%	2.5%	-0.01
CMS-HCC score, mean (SD)	60.7 (20.1)	50.5 (16.0)	0.50	51.0 (15.7)	50.6 (16.0)	0.03
Total 2012 cost of all medications (\$), mean (SD)	1,224.68 (2,873.63)	650.38 (1,354.30)	0.21	641.74 (1,725.10)	651.58 (1,357.13)	-0.01
Total 2012 cost of maintenance medications (\$), mean (SD)	888.26 (2,258.87)	444.94 (869.01)	0.21	434.59 (1,158.92)	445.18 (866.59)	-0.01
Total 2012 out-of-pocket costs (\$), mean (SD)	262.38 (424.42)	139.00 (259.27)	0.31	146.46 (231.80)	138.75 (257.87)	0.03
Ethnicity-African American	7.0%	6.0%	0.04	5.2%	6.1%	-0.04
Ethnicity-Hispanic	7.4%	6.2%	0.05	5.5%	6.1%	-0.03
Ethnicity-Other	45.8%	51.6%	-0.12	52.5%	51.4%	0.02
Ethnicity-Caucasian	39.8%	36.2%	0.07	36.8%	36.4%	0.01
Language-English	89.9%	91.0%	-0.04	91.7%	91.0%	0.02
Language-Spanish	7.3%	5.9%	0.06	5.4%	5.9%	-0.02
Language-Other	2.8%	3.1%	-0.02	2.9%	3.1%	-0.01
Age of dwelling structure, years	37.47	37.32	0.01	36.93	37.29	-0.02
Email at a household level	12.8%	12.7%	0.00	13.2%	12.8%	0.01
Estimated income per adult (\$1000s), mean (SD)	30.5 (27.1)	29.6 (26.2)	0.04	30.6 (26.5)	29.6 (26.1)	0.04

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Estimated net worth per adult (\$1000s), mean (SD)	127.8 (166.7)	116.4 (157.7)	0.07	126.3 (159.9)	116.7 (157.6)	0.06
Estimated net worth divided by age (\$1000s), mean (SD)	3.0 (3.4)	2.8 (3.2)	0.07	3.0 (3.3)	2.8 (3.2)	0.08
Decile, Dual income likely	7.84	7.87	-0.03	7.86	7.88	-0.02
Credit active-main street retail	18.6%	17.2%	0.04	18.1%	17.2%	0.02
Credit active-groceries	0.1%	0.0%	0.01	0.0%	0.0%	0.01
Decile, healthcare response likely	2.68	2.71	-0.01	2.59	2.71	-0.05
Insurance mail order responder	13.2%	11.5%	0.05	11.9%	11.5%	0.01
Mail order buyer-multiple	65.3%	64.3%	0.02	66.6%	64.2%	0.05
Mail order buyer-probable	5.6%	5.7%	0.00	4.8%	5.7%	-0.04
Mail order buyer-single	23.0%	23.5%	-0.01	22.6%	23.6%	-0.02
Mail order responder-multiple	76.9%	76.2%	0.02	79.0%	76.2%	0.07
Mail order responder-single	14.7%	15.3%	-0.02	13.7%	15.2%	-0.04
Family position-brother	1.6%	1.5%	0.00	1.5%	1.5%	0.00
Family position-child	0.2%	0.2%	0.00	0.2%	0.1%	0.01
Family position-female head of household	18.6%	18.5%	0.00	17.7%	18.6%	-0.02
Family position-grandmother	8.7%	8.1%	0.02	7.8%	8.1%	-0.01
Family position-husband	25.6%	26.4%	-0.02	27.4%	26.3%	0.03
Family position-male head of household	11.2%	13.0%	-0.06	11.9%	12.9%	-0.03
Family position-grandfather	5.4%	5.9%	-0.02	5.5%	5.9%	-0.02
Family position-sister	1.2%	1.4%	-0.02	1.4%	1.3%	0.01
Family position-wife	20.0%	17.8%	0.06	19.6%	17.9%	0.04
Family member 18-19	0.2%	0.2%	-0.01	0.2%	0.2%	0.00

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Family member 20-29	4.1%	4.1%	0.00	4.0%	4.0%	0.00
Family member 30-39	9.4%	9.9%	-0.02	9.5%	10.0%	-0.01
Family member 40-49	17.7%	18.5%	-0.02	18.1%	18.4%	-0.01
Family member 50-59	14.8%	13.5%	0.04	12.9%	13.5%	-0.02
Family member 60-64	7.8%	7.3%	0.02	6.7%	7.3%	-0.02
Family member 65+	89.6%	90.3%	-0.02	91.2%	90.4%	0.03
Household-Married (husband and wife present) with children	10.4%	9.7%	0.02	10.0%	9.7%	0.01
Household-Married (husband & wife present) with no children	40.8%	40.2%	0.01	42.5%	40.2%	0.05
Household-Two persons, one male and one female- marital status unknown-with children present	1.0%	1.1%	0.00	0.9%	1.1%	-0.02
Household-Two persons, one male and one female- marital status unknown with no children present	3.9%	4.0%	-0.01	3.6%	4.0%	-0.02
Household-Male householder with one or more other persons of any gender with children present	0.9%	1.0%	-0.01	1.1%	1.0%	0.01
Household-Male householder with one or more persons of any gender with no children present	2.5%	2.8%	-0.02	2.4%	2.7%	-0.02
Household-Female householder with one or more other persons of any gender with children present	1.0%	1.0%	0.00	1.0%	1.0%	0.00

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Household-Female householder with one or more other persons of any gender with no children present	2.8%	2.7%	0.01	3.0%	2.7%	0.02
Household-One person (male householder) with children present	0.6%	0.6%	-0.01	0.5%	0.6%	-0.01
Household-One person (male householder) with no children present	9.0%	10.4%	-0.05	9.6%	10.3%	-0.03
Household-One person (female householder) with children present	0.8%	1.0%	-0.02	1.0%	1.0%	0.00
Household-One person (female householder) with no children present	15.5%	15.3%	0.00	14.6%	15.4%	-0.02
Occupation - Management	4.8%	4.9%	0.00	4.7%	4.8%	0.00
Occupation - Military/Govt	0.7%	0.8%	0.00	0.9%	0.7%	0.02
Occupation - Operate home	4.4%	4.5%	0.00	4.6%	4.5%	0.00
Occupation - Professional	8.9%	9.3%	-0.01	9.8%	9.2%	0.02
Occupation - Retired	28.6%	28.4%	0.00	30.4%	28.4%	0.04
Occupation – Sales/Marketing	5.1%	5.0%	0.01	5.3%	5.0%	0.01
Occupation - Self-employed	6.0%	6.1%	-0.01	6.3%	6.1%	0.01
Occupation - Student	0.8%	0.7%	0.01	0.8%	0.7%	0.01
Occupation - Tradesman	5.3%	6.2%	-0.04	6.2%	6.1%	0.00
Occupation code- Professional-Technical	10.9%	10.3%	0.02	12.2%	10.3%	0.06
Occupation code-Doctors	0.0%	0.0%	0.00	0.0%	0.0%	0.00
Occupation code-Lawyers	0.0%	0.0%	0.00	0.0%	0.0%	-0.01

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Occupation code-Teachers	0.2%	0.2%	-0.01	0.2%	0.2%	-0.01
Occupation code-Administration-Managerial	0.3%	0.1%	0.03	0.2%	0.1%	0.02
Occupation code-Management	6.0%	5.8%	0.01	6.2%	5.8%	0.02
Occupation code-Proprietors	2.3%	2.0%	0.02	2.2%	2.0%	0.01
Occupation code-Supervisors	0.1%	0.0%	0.01	0.0%	0.0%	-0.01
Occupation code-Sales/Services	2.8%	2.5%	0.02	2.3%	2.5%	-0.01
Occupation code-Clerical/White Collar	3.0%	3.2%	-0.01	3.1%	3.2%	0.00
Occupation code-Craftsman/Blue Collar	3.7%	4.2%	-0.03	3.6%	4.3%	-0.03
Occupation code-Foreman	0.0%	0.1%	-0.04	0.1%	0.1%	-0.01
Occupation code-Operatives/Blue Collar	0.3%	0.2%	0.02	0.3%	0.2%	0.01
Occupation code-Farm	0.0%	0.0%	0.01	0.0%	0.0%	0.00
Occupation code-Unskilled	0.1%	0.1%	0.00	0.1%	0.1%	0.00
Occupation code-Service Workers	0.2%	0.1%	0.01	0.1%	0.1%	0.00
Occupation code-Military	0.0%	0.0%	-0.03	0.0%	0.0%	0.02
Occupation code-Student	0.6%	0.7%	-0.01	0.7%	0.7%	0.00
Occupation code-Retired	25.3%	23.7%	0.04	24.7%	23.8%	0.02
Occupation code-Housewife	2.3%	2.4%	-0.01	2.8%	2.4%	0.02
Occupation code-Source given but not coded	1.1%	1.3%	-0.02	1.2%	1.3%	-0.01
Generations-Strapped Seniors	6.4%	9.0%	-0.10	8.3%	9.0%	-0.02
Generations-Rich Retirees	2.1%	2.0%	0.01	2.3%	2.1%	0.01

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Generations-Blooming in the Burbs	15.8%	16.1%	-0.01	16.6%	16.2%	0.01
Generations-Retired Renters	8.4%	8.0%	0.02	8.1%	8.0%	0.00
Generations-Minorities in the Majority	6.5%	5.6%	0.04	4.8%	5.7%	-0.04
Generations-Indulgent Intellectuals	20.2%	19.6%	0.02	21.1%	19.5%	0.04
Generations-Family Friendly	4.2%	5.5%	-0.06	4.8%	5.5%	-0.03
Generations-Retirement Retreats	6.0%	5.0%	0.05	4.9%	5.0%	0.00
Generations-Urban Upper Crust	7.6%	6.3%	0.05	6.9%	6.3%	0.02
Generations-Boomerang Bohemians	8.3%	7.9%	0.01	8.0%	7.9%	0.00
Generations-Small Town Traditionalists	0.1%	0.2%	-0.01	0.1%	0.2%	-0.03
Generations-Gold'n'Gray	0.2%	0.2%	-0.01	0.1%	0.2%	-0.02
Generations-Small Town Singles	0.6%	0.9%	-0.03	0.7%	0.8%	-0.02
Generations-Mainstream Matures	0.9%	0.8%	0.01	0.7%	0.8%	0.00
Generations-American Bedrock	0.8%	0.8%	0.00	0.7%	0.8%	-0.01
Generations-Urban Mix	0.4%	0.3%	0.01	0.4%	0.3%	0.01
Generations-Urban Blues	0.2%	0.3%	-0.03	0.2%	0.3%	-0.03
Generations-Credit Commandos	1.3%	1.4%	-0.01	1.6%	1.3%	0.02
Generations-Blue Collar Strugglers	0.5%	0.6%	-0.01	0.5%	0.6%	-0.01
Generations-Settled Suburbanites	1.5%	1.7%	-0.01	1.9%	1.7%	0.01

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Generations-Classic Rockers	1.8%	2.1%	-0.02	2.0%	2.0%	0.00
Generations-All-American On Line	0.3%	0.4%	-0.02	0.3%	0.4%	0.00
Generations-Rural Outsiders	0.1%	0.1%	-0.01	0.1%	0.1%	-0.01
Generations-Family Transitionals	0.8%	0.7%	0.01	0.7%	0.7%	0.00
Generations-Urban Outsiders	0.1%	0.0%	0.03	0.1%	0.0%	0.02
Generations-Suburban Mainstream	0.2%	0.1%	0.02	0.2%	0.1%	0.02
Generations-Metro Influentials	0.0%	0.0%	0.00	0.0%	0.0%	0.00
Generations-Wired Wanderers	0.0%	0.0%	0.00	0.1%	0.0%	0.01
Generations-Urban Sophisticates	0.0%	0.0%	0.01	0.0%	0.0%	0.00
Generations-Suburban Strivers	0.2%	0.2%	0.01	0.2%	0.2%	0.00
Generations-Empty Nest Caregivers	0.2%	0.2%	0.00	0.2%	0.2%	0.00
Generations-American Family Up-and-Coming	0.3%	0.2%	0.02	0.2%	0.2%	-0.01
Generations-Blue Collar Blend	0.0%	0.0%	0.00	0.0%	0.0%	-0.01
Generations-Urban Strugglers	0.2%	0.2%	0.00	0.1%	0.2%	-0.02
Generations-Large Extended Families	0.3%	0.4%	-0.02	0.2%	0.3%	-0.02
Generations-Urban Singles	0.1%	0.0%	0.01	0.0%	0.0%	0.01
Generations-Established & Settling In	0.1%	0.1%	0.00	0.1%	0.1%	0.01
Generations-Rural & Barely Making It	0.2%	0.3%	0.00	0.2%	0.3%	-0.01



Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Generations-Married with Children	0.1%	0.0%	0.03	0.0%	0.0%	0.00
Generations-Struggling in Suburbia	0.1%	0.1%	0.00	0.0%	0.1%	-0.02
Generations-Ethnically Diverse Urbanites	0.0%	0.0%	0.01	0.0%	0.0%	-0.02
Generations-Moving on a Steady Course	0.1%	0.1%	0.01	0.1%	0.1%	0.00
Generations-Big Bucks in the Big Cities	0.0%	0.0%	0.00	0.0%	0.0%	0.00
Generations-Ethnic Second-City Strugglers	0.1%	0.0%	0.01	0.0%	0.0%	-0.01
Generations-Young, Single & Mobile	0.0%	0.0%	0.01	0.0%	0.0%	0.02
Generations-Set Up House & Settle Down	0.1%	0.1%	0.00	0.1%	0.1%	0.00
Generations-Start-Ups in the Country	0.0%	0.1%	-0.02	0.0%	0.0%	0.00
Generations-Parents on the Go	0.2%	0.1%	0.02	0.1%	0.1%	0.01
Generations-Living Off Mom & Dad	0.0%	0.0%	0.00	0.0%	0.0%	-0.01
Generations-Chronic Responders	0.1%	0.1%	-0.02	0.1%	0.1%	-0.02
Generations-Young Singles in the City	0.0%	0.0%	0.00	0.0%	0.0%	0.01
Generations-Family First	0.1%	0.1%	0.00	0.1%	0.1%	0.00
Interest-Art/Antique Collecting	4.1%	3.8%	0.02	4.2%	3.8%	0.02
Interest-Automotive Work	19.6%	19.5%	0.00	20.4%	19.5%	0.02
Interest-Bible Reading	26.2%	26.6%	-0.01	27.4%	26.6%	0.02
Interest-Bicycling	7.3%	7.3%	0.00	8.1%	7.2%	0.03

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Interest-Book Reading	65.7%	65.7%	0.00	67.8%	65.7%	0.04
Interest-Boating/Sailing	13.0%	13.8%	-0.02	14.6%	13.7%	0.03
Interest-Buy Videos	14.3%	13.5%	0.02	14.2%	13.5%	0.02
Interest-Own a Cat	16.3%	17.1%	-0.02	18.0%	16.9%	0.03
Interest-Own CD Player	15.6%	14.4%	0.03	15.6%	14.4%	0.03
Interest-Donate Charity	49.1%	48.0%	0.02	50.4%	48.0%	0.05
Interest-Camping/Hiking	10.7%	12.0%	-0.04	12.4%	11.9%	0.01
Interest-Collectibles	32.0%	32.2%	0.00	33.2%	32.1%	0.02
Interest-Crafts	32.6%	33.4%	-0.02	35.4%	33.3%	0.04
Interest-Career Activities	1.3%	1.2%	0.01	1.1%	1.1%	-0.01
Interest-Cable TV	3.0%	2.7%	0.02	2.8%	2.6%	0.01
Interest-Cultural/Art Events	11.3%	9.3%	0.06	10.2%	9.3%	0.03
Interest-Current Affairs	0.6%	0.6%	0.00	0.5%	0.6%	-0.01
Interest-Civic Activities	0.8%	0.9%	0.00	0.8%	0.8%	0.00
Interest-Own a Dog	22.6%	23.8%	-0.03	24.4%	23.5%	0.02
Interest-Dieting/Weight Control	25.0%	24.4%	0.01	26.4%	24.3%	0.05
Interest-Electronics	54.9%	54.9%	0.00	57.3%	54.9%	0.05
Interest-Fashion Clothing	4.9%	4.5%	0.02	4.6%	4.5%	0.01
Interest-Physical Fitness	38.9%	38.4%	0.01	40.9%	38.4%	0.05
Interest-Home Furnishing/Decorating	32.1%	32.4%	-0.01	33.8%	32.3%	0.03
Interest-Fishing	23.7%	25.1%	-0.03	25.9%	24.9%	0.02
Interest-Travel Foreign	12.3%	10.3%	0.06	11.4%	10.3%	0.03
Interest-Gardening	46.1%	46.5%	-0.01	49.1%	46.3%	0.05
Interest-Grandchildren	36.2%	35.5%	0.02	37.6%	35.4%	0.05
Interest-Golf	18.0%	16.9%	0.03	18.9%	16.9%	0.05
Interest-Casino Gambling	14.4%	14.7%	-0.01	14.6%	14.6%	0.00
Interest-Gourmet/Foods	17.0%	15.5%	0.04	16.5%	15.5%	0.03

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Interest-Nations Heritage	1.6%	1.6%	0.00	1.8%	1.6%	0.02
Interest-Health/Natural Foods	12.7%	12.0%	0.02	12.8%	11.9%	0.03
Interest-Hunting/Shooting	16.3%	18.7%	-0.06	18.5%	18.5%	0.00
Interest-Home PC	3.0%	3.0%	0.00	2.9%	3.0%	0.00
Interest-Houseplants	1.1%	1.2%	-0.01	1.1%	1.1%	0.00
Interest-Self-Improvement	12.1%	11.2%	0.03	12.0%	11.2%	0.03
Interest-Mail Order Buyer	54.4%	53.8%	0.01	56.2%	53.8%	0.05
Interest-Motorcycling	3.5%	3.7%	-0.01	3.7%	3.6%	0.00
Interest-Money Opportunities	3.6%	3.4%	0.01	3.6%	3.3%	0.02
Interest-Military Veteran	8.1%	7.7%	0.02	8.1%	7.7%	0.01
Interest-Power Boating	1.8%	1.8%	0.00	2.1%	1.8%	0.02
Interest-Household Pets	31.4%	32.2%	-0.02	33.2%	31.9%	0.03
Interest-Photography	12.0%	12.2%	-0.01	13.2%	12.1%	0.03
Interest-Stereo/Records	9.9%	9.0%	0.03	9.5%	9.0%	0.02
Interest-Real Estate	2.3%	1.8%	0.03	2.1%	1.8%	0.02
Interest-Running/Jogging	2.0%	1.8%	0.02	2.0%	1.8%	0.01
Interest-Recreational Vehicle	9.7%	9.7%	0.00	10.5%	9.7%	0.03
Interest-Sailing	0.6%	0.4%	0.02	0.5%	0.4%	0.01
Interest-Stamp/Coin Collection	3.1%	3.4%	-0.02	3.6%	3.4%	0.01
Interest-Sewing	16.3%	16.4%	0.00	17.6%	16.3%	0.03
Interest-Science Fiction	1.2%	1.1%	0.01	1.2%	1.1%	0.01
Interest-Snow Skiing	2.3%	2.2%	0.01	2.3%	2.2%	0.01
Interest-Stocks/Bonds	6.6%	6.0%	0.02	6.5%	5.9%	0.02
Interest-Sports on TV	11.5%	11.0%	0.01	11.8%	10.9%	0.03
Interest-Sweepstakes	34.8%	34.2%	0.01	34.9%	34.2%	0.01

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Interest-Science/Technology	7.5%	7.1%	0.02	7.8%	7.1%	0.03
Interest-Tennis	1.1%	0.9%	0.03	1.0%	0.8%	0.02
Interest-Travel in USA	35.1%	34.2%	0.02	36.8%	34.2%	0.05
Interest-Home Video Games	0.3%	0.2%	0.01	0.2%	0.2%	0.00
Interest-Home Video Recording	4.2%	3.6%	0.03	3.8%	3.5%	0.02
Interest-Wines	9.9%	9.3%	0.02	9.5%	9.3%	0.01
Interest-Home Workshop	11.6%	11.3%	0.01	13.0%	11.3%	0.05
Interest-Wildlife/Environment	4.5%	4.3%	0.01	4.8%	4.3%	0.02
Interest-Walking/Health	26.9%	26.5%	0.01	28.6%	26.5%	0.05
Attitude-Creative Talent	0.2%	0.2%	0.01	0.2%	0.2%	0.00
Attitude-Altruists	33.8%	32.0%	0.04	33.6%	32.1%	0.03
Attitude-Alternative Medicine Embracer	7.6%	7.6%	0.00	8.1%	7.7%	0.02
Attitude-Book Worms	1.0%	1.3%	-0.03	1.2%	1.3%	-0.01
Attitude-Adventure Seekers	0.0%	0.0%	0.01	0.0%	0.0%	-0.02
Attitude-Biotech Embracers	5.3%	4.4%	0.04	5.1%	4.4%	0.03
Attitude-Cooking Enthusiasts	24.5%	21.7%	0.07	22.3%	21.8%	0.01
Attitude-Control Seekers	0.1%	0.1%	0.02	0.1%	0.1%	0.01
Attitude-Competitive	0.1%	0.1%	-0.01	0.1%	0.0%	0.01
Attitude-DIYers	0.3%	0.3%	0.01	0.2%	0.3%	-0.02
Attitude-Early Embracers	0.1%	0.1%	0.00	0.0%	0.0%	0.00
Attitude-Family Devoted	0.5%	0.4%	0.02	0.4%	0.4%	0.01
Attitude-Fitness Fans	0.6%	0.4%	0.02	0.5%	0.4%	0.01
Attitude-Intellectuals	2.2%	2.3%	-0.01	2.5%	2.3%	0.02
Attitude-Info Seekers	1.6%	1.5%	0.00	1.7%	1.5%	0.01
Attitude-Environmentalists	22.4%	21.1%	0.03	22.2%	21.2%	0.02

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Attitude-Optimists	18.7%	16.1%	0.07	17.9%	16.2%	0.05
Attitude-Organizers	0.1%	0.2%	0.00	0.1%	0.2%	-0.01
Attitude-Patriotic Loyalists	34.9%	35.6%	-0.01	36.2%	35.5%	0.01
Attitude-Romantics	5.5%	6.3%	-0.03	5.7%	6.3%	-0.03
Attitude-Risk Takers	0.0%	0.0%	-0.01	0.0%	0.0%	-0.01
Attitude-Sports Enthusiasts	0.2%	0.2%	0.00	0.1%	0.2%	-0.02
Attitude-Savvy Investor	18.8%	15.2%	0.09	17.4%	15.2%	0.06
Attitude-Sophisticates	8.8%	7.9%	0.03	8.4%	7.9%	0.02
Attitude-Simplicity Seekers	0.3%	0.2%	0.01	0.1%	0.2%	-0.02
Attitude-Technology Leaders	0.7%	0.8%	-0.01	0.8%	0.8%	0.00
Attitude-Traditionalists	41.3%	41.3%	0.00	41.4%	41.3%	0.00
Attitude-Trend Setters	0.1%	0.1%	0.00	0.1%	0.1%	0.00
Attitude-Youth Chasers	0.0%	0.0%	0.00	0.0%	0.0%	0.00
Tends to be very focused on themselves	4.58	4.57	0.01	4.64	4.57	0.03
Tends to trust health insurance company & sales reps	6.04	6.14	-0.04	6.04	6.14	-0.03
Tends not to be frugal	5.31	5.35	-0.01	5.16	5.35	-0.07
Tends to not be a print and mass media user	2.11	2.22	-0.05	2.04	2.22	-0.08
Tends to not be a caregiver	5.34	5.27	0.03	5.27	5.29	-0.01
Tends not to feel overwhelmed	5.33	5.11	0.08	5.20	5.13	0.03
Tends to not be as focused on themselves	4.06	4.15	-0.04	4.10	4.15	-0.02
Tends to report eating health foods	3.10	3.11	0.00	2.98	3.11	-0.06
Tends to not have a positive outlook	5.66	5.85	-0.08	5.73	5.84	-0.05

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Tends to struggle with medical language	5.73	5.94	-0.07	5.72	5.93	-0.07
Tends to be dependent on others	7.11	7.21	-0.05	7.07	7.20	-0.06
Tends to not use the internet	7.30	7.37	-0.04	7.27	7.37	-0.05
Tends to use the internet	3.19	3.18	0.00	3.32	3.18	0.05
Living well	3.13	3.13	0.00	3.07	3.12	-0.05
Predicted: BMI <sup>a</sup>	28.28	28.37	-0.04	28.26	28.36	-0.05
Predicted: Health Score <sup>a</sup>	74.12	74.08	0.01	74.35	74.09	0.05
Predicted: To use alternative medicine <sup>a</sup>	0.34	0.34	-0.02	0.34	0.34	-0.01
Predicted: To be on a diet <sup>a</sup>	0.16	0.16	0.03	0.15	0.16	-0.02
Predicted: To be discipline in living well/lifestyle choices <sup>a</sup>	0.24	0.23	0.06	0.23	0.23	0.01
Predicted; To see doctor regularly <sup>a</sup>	0.23	0.23	-0.03	0.23	0.23	-0.04
Predicted: To drink alcohol heavily <sup>a</sup>	0.10	0.10	-0.03	0.09	0.10	-0.03
Predicted: To be sedentary <sup>a</sup>	0.29	0.29	-0.01	0.28	0.29	-0.04
Predicted: To be physically active <sup>a</sup>	0.66	0.66	0.01	0.67	0.66	0.05
Predicted: To be a smoker <sup>a</sup>	0.33	0.33	-0.04	0.32	0.33	-0.07
Predicted: Other <sup>a</sup>	0.30	0.29	0.03	0.30	0.29	0.02
Predicted: BMI (Decile) <sup>a</sup>	4.81	4.69	0.05	4.85	4.70	0.06
Predicted: Health Score (Decile) <sup>a</sup>	5.31	5.35	-0.02	5.19	5.35	-0.07
Predicted: To use alternative medicine (Decile) <sup>a</sup>	5.31	5.25	0.02	5.30	5.26	0.02
Predicted: To be on a diet (Decile) <sup>a</sup>	5.25	5.31	-0.03	5.38	5.32	0.03

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Predicted: To be discipline in living well/lifestyle choices (Decile) <sup>a</sup>	5.48	5.66	-0.07	5.63	5.66	-0.01
Predicted; To see doctor regularly (Decile) <sup>a</sup>	7.13	7.07	0.03	7.16	7.09	0.05
Predicted: To drink alcohol heavily (Decile) <sup>a</sup>	6.61	6.55	0.03	6.62	6.56	0.03
Predicted: To be sedentary (Decile) <sup>a</sup>	3.90	3.89	0.01	4.03	3.90	0.05
Predicted: To be physically active (Decile) <sup>a</sup>	2.10	2.12	-0.01	2.02	2.12	-0.05
Predicted: To be a smoker (Decile) <sup>a</sup>	3.81	3.74	0.03	3.91	3.75	0.07
Predicted: Other (Decile) <sup>a</sup>	3.56	3.66	-0.03	3.59	3.65	-0.02
Census Median Household Effective Buying Income	42.54	42.39	0.01	43.40	42.42	0.07
Census Geounit Quality Score	78.45	77.94	0.04	78.85	77.99	0.07
Census Median Household Income (\$1000s)	50.13	49.94	0.01	51.24	49.98	0.06
Census Median Home Value (\$1000s)	165.04	160.99	0.05	166.41	161.35	0.06
Census Education Level-Less than 9th Grade	0.0%	0.0%	0.01	0.0%	0.0%	0.00
Census Education Level-Less than 12th Grade	0.3%	0.3%	0.00	0.2%	0.3%	-0.03
Census Education Level-High School Diploma	42.3%	45.6%	-0.07	42.3%	45.3%	-0.06
Census Education Level-Some College	44.3%	42.1%	0.04	44.2%	42.4%	0.04
Census Education Level-Associate's Degree	6.7%	5.9%	0.03	6.3%	6.0%	0.01

Variable	Unmatched Sample		Cohen's d	Matched Sample		Cohen's d
	Control (n=36,703)	Synced (n=6,551)		Control (n=6,458)	Synced (n=6,458)	
Census Education Level- Bachelor's Degree	6.4%	6.0%	0.02	7.0%	6.0%	0.04
Census Education Level- Master's Degree	0.0%	0.0%	0.01	0.0%	0.0%	0.00
Census Average Number of Automobiles	1.7	1.8	-0.09	1.8	1.8	0.04
Census % White	76.54	77.19	-0.03	78.46	77.13	0.06
Census % Black	14.40	13.56	0.04	12.42	13.61	-0.06
Census % Hispanic	14.74	13.63	0.06	13.07	13.64	-0.03
Census % Married	47.19	47.88	-0.05	48.64	47.84	0.06
Census % Divorced or Separated	17.08	16.78	0.05	16.52	16.80	-0.05
Census % Single Family Dwelling	70.44	71.22	-0.03	71.84	71.19	0.03
Census % Household with Children	30.21	30.80	-0.05	30.63	30.77	-0.01
Census % Homeowner	64.25	64.25	0.00	64.84	64.22	0.03
Census % Motor vehicle ownership	92.33	92.39	-0.01	92.75	92.39	0.05
Cnty%-Medicare Advantage	43.37	42.06	0.08	41.71	42.10	-0.02

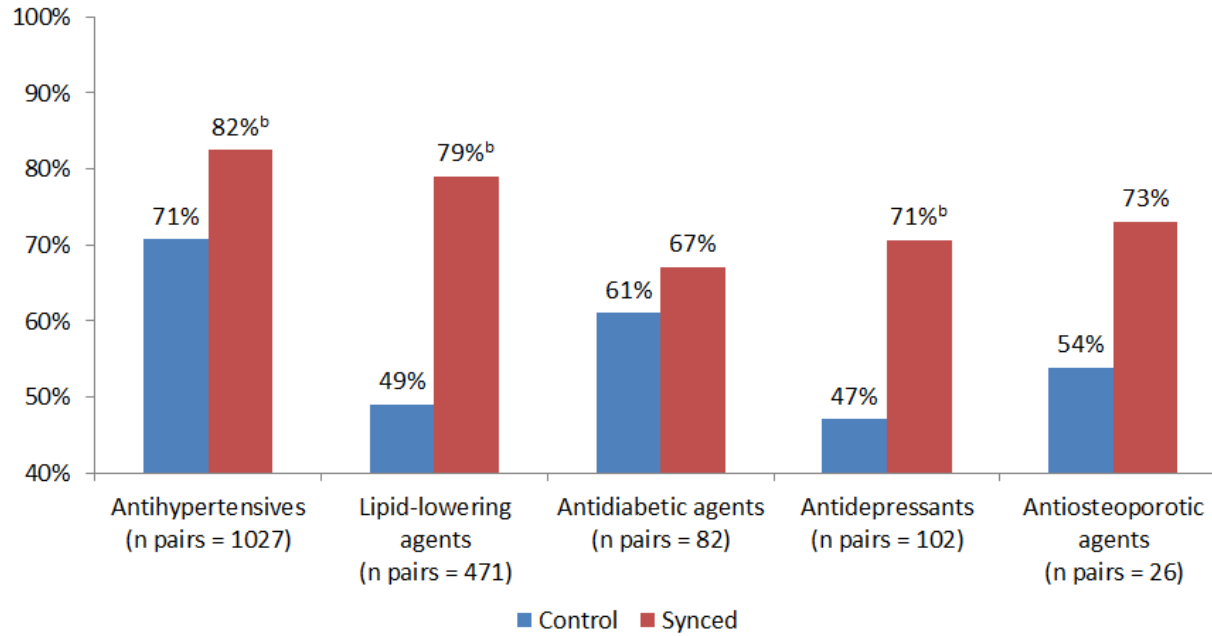
COPD indicates chronic obstructive pulmonary disease.

<sup>a</sup> Predicted BMI is a continuous scale. Predicted Health Score is a 0-100 scale. The remaining predicted values are on a 0-1 scale.

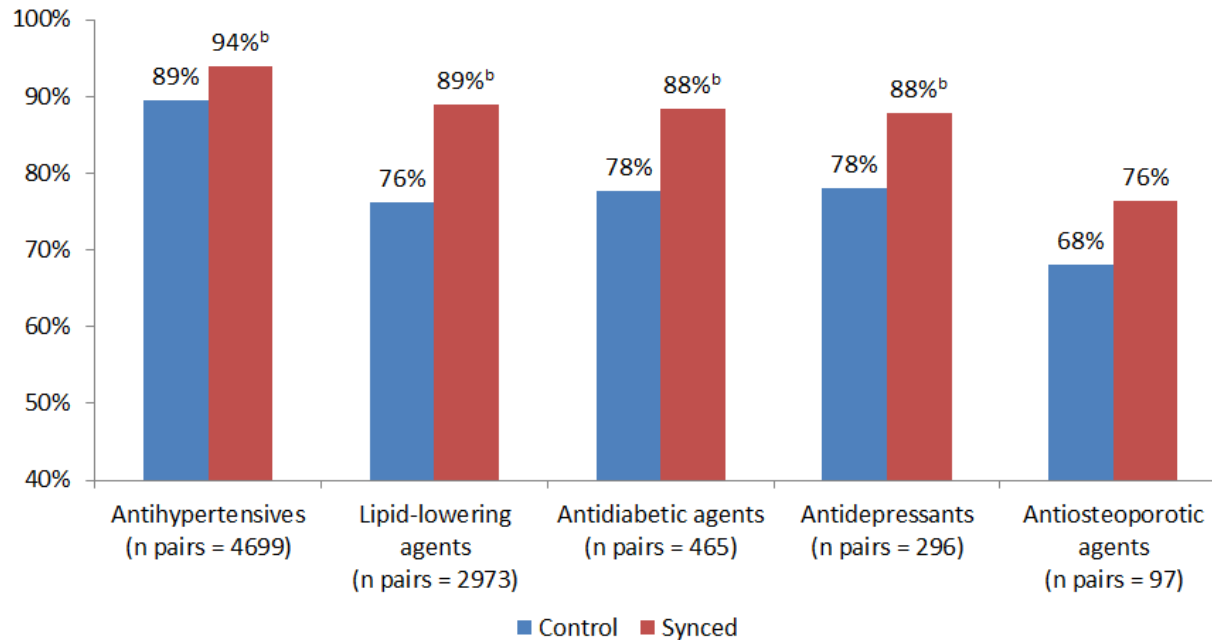


**eAppendix Figure B. Percent Adherent (PDC  $\geq 0.80$ ) by Drug Class**

**(a) Percent adherent (PDC  $\geq 0.80$ ) by drug class, exclusive retail pharmacy users<sup>a</sup>**



(b) Percent adherent (PDC  $\geq 0.80$ ) by drug class, exclusive mail order pharmacy users<sup>a</sup>



PDC indicates proportion of days covered.

<sup>a</sup>Patients with synchronized refill schedules vs propensity score-matched controls.

<sup>b</sup>Indicates statistical significance at  $P < .05$ .

**eAppendix Table B.** Adherence Outcomes for Patients with Synchronized Refills vs. Propensity Score-Matched Controls, Subgroup Analysis for Retail vs. Mail Order Pharmacy Patients

	Exclusive Retail			Exclusive Mail Order			Retail vs. Mail Order
	N Pairs <sup>a</sup>	Absolute Difference	95% CI	N Pairs	Absolute Difference	95% CI	p-value <sup>c</sup>
Continuous PDC							
Antihypertensives	1,027	0.06 <sup>b</sup>	(0.04,0.08)	4,699	0.02 <sup>b</sup>	(0.01,0.02)	<0.01
Lipid-lowering agents	471	0.15 <sup>b</sup>	(0.12,0.18)	2,973	0.05 <sup>b</sup>	(0.04,0.06)	<0.01
Antidiabetic agents	82	0.02	(-0.06,0.10)	465	0.04 <sup>b</sup>	(0.02,0.05)	0.73
Antidepressants	102	0.15 <sup>b</sup>	(0.08,0.22)	296	0.04 <sup>b</sup>	(0.02,0.06)	<0.01
Antiestrogens	26	0.12	(-0.08,0.32)	97	0.02	(-0.02,0.07)	0.38
% Adherent (PDC≥0.8)							
Antihypertensives	1,027	0.12 <sup>b</sup>	(0.08,0.15)	4,699	0.04 <sup>b</sup>	(0.03,0.06)	0.56
Lipid-lowering agents	471	0.30 <sup>b</sup>	(0.24,0.36)	2,973	0.13 <sup>b</sup>	(0.11,0.15)	0.01
Antidiabetic agents	82	0.06	(-0.10,0.22)	465	0.11 <sup>b</sup>	(0.06,0.16)	0.16
Antidepressants	102	0.24 <sup>b</sup>	(0.10,0.37)	296	0.10 <sup>b</sup>	(0.04,0.16)	0.39
Antiestrogens	26	0.19	(-0.17,0.55)	97	0.08	(-0.05,0.22)	0.52

CI indicates confidence interval.

<sup>a</sup> Patients with synchronized refill schedules vs. propensity score-matched controls.

<sup>b</sup> Difference between synchronized refill group and propensity score-matched controls was statistically significant at p<0.05.

<sup>c</sup> P-values indicate the significance level at which the effect for the exclusive retail subgroup differs from the effect for the exclusive mail order subgroup.

**eAppendix Table C. Sensitivity Analyses**

	Synced (Beginning) <sup>a</sup>			Synced (Any) <sup>b</sup>			Synced (No Meta-Data) <sup>c</sup>		
	N	Absolute	95% CI	N	Absolute	95% CI	N	Absolute	95% CI
Continuous PDC	Pairs	Difference	95% CI	Pairs	Difference	95% CI	Pairs	Difference	95% CI
Antihypertensives	9,978	0.04	(0.03,0.04)	15,329	0.04	(0.04,0.05)	5,525	0.03	(0.02,0.03)
Lipid-lowering agents	6,109	0.07	(0.07,0.08)	9,510	0.07	(0.07,0.08)	3,341	0.07	(0.06,0.07)
Antidiabetic agents	952	0.05	(0.03,0.06)	1,487	0.05	(0.04,0.06)	465	0.03	(0.01,0.05)
Antidepressants	670	0.07	(0.05,0.09)	1,096	0.10	(0.08,0.11)	332	0.05	(0.03,0.08)
Antiosteoporotic agents	198	0.02	(-0.02,0.06)	305	0.04	(0.01,0.07)	104	0.02	(-0.03,0.07)
% Adherent (PDC $\geq$ 0.8)	N	Absolute	95% CI	N	Absolute	95% CI	N	Absolute	95% CI
	Pairs	Difference	95% CI	Pairs	Difference	95% CI	Pairs	Difference	95% CI
Antihypertensives	9,978	0.08	(0.07,0.09)	15,329	0.09	(0.08,0.09)	5,525	0.07	(0.06,0.08)
Lipid-lowering agents	6,109	0.16	(0.14,0.17)	9,510	0.15	(0.14,0.17)	3,341	0.16	(0.14,0.18)
Antidiabetic agents	952	0.11	(0.08,0.15)	1,487	0.12	(0.09,0.15)	465	0.09	(0.04,0.14)
Antidepressants	670	0.15	(0.10,0.20)	1,096	0.19	(0.16,0.23)	332	0.14	(0.07,0.21)
Antiosteoporotic agents	198	0.06	(-0.04,0.16)	305	0.09	(0.01,0.16)	104	0.06	(-0.08,0.20)
% Adherent (PDC $\geq$ 0.8)	N	OR	95% CI	N	OR	95% CI	N	OR	95% CI
	Pairs	OR	95% CI	Pairs	OR	95% CI	Pairs	OR	95% CI
Antihypertensives	9,978	2.26	(2.05,2.49)	15,329	2.53	(2.34,2.75)	5,525	2.09	(1.83,2.38)
Lipid-lowering agents	6,109	2.64	(2.40,2.91)	9,510	2.61	(2.42,2.82)	3,341	2.86	(2.50,3.29)
Antidiabetic agents	952	2.09	(1.64,2.68)	1,487	2.37	(1.92,2.93)	465	1.86	(1.30,2.68)
Antidepressants	670	2.32	(1.76,3.07)	1,096	3.08	(2.45,3.89)	332	2.18	(1.48,3.27)
Antiosteoporotic agents	198	1.32	(0.85,2.06)	305	1.54	(1.06,2.24)	104	1.27	(0.70,2.33)

CI indicates confidence interval; OR, odds ratio.

<sup>a</sup> Study group includes individuals who refilled all maintenance drugs at the same time at the first 2 fills in the year (ie, started as synced but did not necessarily remain synced).

<sup>b</sup> Study group includes individuals who refilled all maintenance drugs at the same time at any 2 consecutive fill dates in the year, regardless of when in the year this occurred.

<sup>c</sup> Repeats the main analysis except during the propensity score matching processes, no consumer meta-data variables were used (ie, matching variables included age, gender, marital status, estimated income, disability status, low-income subsidy, geographic region, clinical health condition indicators, CMS-HCC score, total prescription cost, total prescription cost for maintenance medications, and total out-of-pocket cost).