Measuring Medication Adherence Associated Medical Care Savings Using Commercially Insured Members' Real-World Data

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BACKGROUND

- Increasing medication adherence is a pharmacy practice and quality metric cornerstone, which relies on medical cost offsets to quantify value.
- Adherence improvement programs typically report medical cost savings associated with medication adherence improvement and use these estimates to justify specific programs' costs or the value of managed care pharmacy services.
- Most evidence supporting medical cost offsets from adherence is outdated, employs naïve methods, and frequently does not include the key populations of interest. For example, one frequently cited paper assesses the cross-sectional relationship between adherence and medical costs and uses data from 1997-1999.[1]
- The three adherence-related studies[2-4] cited in the Medicare National Impact Assessment of the Centers for Medicare and Medicaid Services Quality Measure[5] use data that is 10–15 years old, include subpopulations not relevant to managed care adherence improvement programs, and do not adequately account for confounding and bias.

OBJECTIVE

To estimate the relationship between medication adherence improvement and medical spending reduction for a commercially insured population across a range of conditions.

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METHODS

Study Design

- Retrospective analysis of integrated medical and pharmacy claims from over 16 million commercially insured members across a 4-year period (2018 – 2021). **(Figure 1)**
- Two separate analytic samples were identified; each separate analytic population consisted of a 3-year measurement period (2018 – 2020 and 2019 – 2021) and used identical analytic methods. The two separate analytic populations were combined in the statistical assessment.

Inclusion/Exclusion

- Members were continuously enrolled in commercial line of business for 3 years (Pre 12-month period, Base 12-month period, and Post 12-month period).
- For each medication adherence measure, members were required to have at least 2 fills of qualifying drugs in the measure-specific drug category with the first fill at least 90 days before the end of the year for both Pre and Base years. This aligns with the method used by the Pharmacy Quality Alliance for its endorsed adherence measures.[6] Additionally, for antidepressants, antipsychotics, non-insulin diabetes medications, members were required to meet measure eligibility criteria for the Base year further defined below.
- Members were required to be nonadherent in the Pre year, with proportion of days covered (PDC) less than 80% for all adherence measures except for the antiretroviral adherence measure, which required members to have PDC less than 90%.
- Members were required to have >$0 medical claim spending in Base year and Post year.

Statistical Analysis

- Adherence Measures
  - The primary independent variable was the change in annual dichotomous adherence PDC value between the Pre period and Base period for each measure-specific drug category.
  - Separate multivariable regression models were created for each of the following drug category adherence measures for each Base year (i.e., 2019 and 2020):
    - Antidepressants
    - Antihypertensives
    - Antipsychotics
    - Antiretrovirals
    - Non-insulin diabetes medications (NIDM)
    - Statins
    - Renin-angiotensin system antagonists (RASA)
  - Adherence was dichotomized into nonadherent versus adherent using standardized PDC threshold of 80% or more for all measures except for antiretrovirals, which required a PDC value of 90% or more to be considered adherent.
  - For antihypertensives, antiretrovirals, statins and renin-angiotensin system antagonists, members who were measure-eligible (i.e., 2+ fills over 91 days or more before the end of the period) in the Pre year were considered nonadherent in the Base year if they were not measure-eligible but were continuously enrolled and had medical spending. This was done to ensure that members who discontinued medication use were not dropped from analysis, under the assumption that all of these medications are intended for long-term use.
  - For antidepressants, antipsychotics and non-insulin diabetes medications, members who were measure-eligible in the Pre year but not in the Base year were excluded from analysis. For antipsychotics and antidepressants, the decision was made not to assume nonadherence since these medications can have short-term indications. For non-insulin diabetes medications, members who initiate insulin were removed from the measure, therefore making the assumption of nonadherence was inappropriate.
- Medical Cost Outcome
  - The dependent variable across all models was the change in annual medical costs between the Base period and the Post period, winsorized at 99th percentile due to skewed data.
  - Annual medical costs were calculated by summing the allowed amounts (which include member share and take into account network discounts) for all medical claims and adjusted to 2021 dollars using the medical services consumer price index (CPI).[7]
- Model Covariates
  - Age, gender, change in Charlson Comorbidity Index score[8] (first difference and lagged first difference), and enrolled Blue Plan.
- Modeling Approach **(Figure 1)**
  - Two Base years were used for this study: 2019 and 2020.
  - Following a lagged first difference approach for panel data analysis,[9] the change in PDC from the Pre year to Base year (e.g., 2018 to 2019) was correlated with changes in medical costs from the Base year to the Post year (e.g., 2019 to 2020).
  - Change in PDC was categorized into two groups based on the trend in adherence from the Pre year to the Base year: Nonadherent→Adherent, Nonadherent→Nonadherent. The primary comparison of interest was differences in the cost outcome between members in the Nonadherent→Adherent group and the Nonadherent→Nonadherent group, with Nonadherent→Nonadherent as the reference.
  - Both sets of Base years were combined into a single linear regression model controlling for demographic and clinical differences to estimate changes in average medical cost associated with changes in PDC.

RESULTS

- Of the more than 16 million commercially insured members enrolled in a given year, 12.8 million were enrolled for the 3-year period with 2019 as the Base year and 12.8 million for the 2020 Base year.
- Applying inclusion criteria reduced the sample to 1.85 million unique members fully eligible in either Base year 2019 or 2020. These 1.85 million members represent 5.9 million total member-drug category measure-year combinations. **(Figure 2)**
- Across all drug categories, there were fewer members in the Nonadherent→Adherent group than the Nonadherent→Nonadherent group, with the Nonadherent→Adherent group comprising 5.2% to 11.5% of the total measure-eligible members compared to 10.7% to 15.1% for the Nonadherent→Nonadherent group.
- Members in the Nonadherent→Adherent group were older than their reference Nonadherent→Nonadherent group and had a smaller change in Charlson Comorbidity Index score between the Base and Post years.
- Base and Post spending varied by measure and by group, with the lowest spending observed for members in the Nonadherent→Nonadherent group for the antidepressant measure in the Pre year ($9,685) and the highest spending was observed for the same group and year for the members eligible for the antipsychotics adherence measure ($16,474).
- The greatest unadjusted winsorized spending differences in total allowed medical costs between Base and Pre years were observed for the Nonadherent→Nonadherent group, which had increases in spending ranging from $144 for members eligible for the antipsychotics adherence measure to $1,321 for the NIDM measure. By contrast, changes in medical cost for the Nonadherent→Adherent group ranged from $658 for the antipsychotics measure to $760 for RASA.
- Compared to members remaining non-adherent, members becoming adherent were associated with statistically significant lower annual medical costs ranging from $292 to $947, among 6 of 7 drug categories assessed. **(Figure 3)**

TABLE 1

Demographics, Clinical Characteristics and Analytic Results

Variable	Group	Antidepressants	Antihypertensives	Antipsychotics	Antiretrovirals	NIDM	Statins	RASA
N	Full Sample	1,054,840 (100%)	1,895,574 (100%)	74,244 (100%)	32,553 (100%)	494,747 (100%)	1,098,294 (100%)	1,284,883 (100%)
	Nonadherent→Adherent	115,492 (11.0%)	156,035 (8.2%)	8,560 (11.5%)	1,699 (5.2%)	53,386 (10.8%)	111,744 (10.2%)	112,480 (8.8%)
	Nonadherent→Nonadherent	128,456 (12.2%)	213,366 (11.3%)	10,993 (14.8%)	3,476 (10.7%)	55,518 (11.2%)	165,366 (15.1%)	155,240 (12.1%)
Age, Mean (95% CI)	Nonadherent→Adherent	46.3 (46.2 to 46.4)**	52.5 (52.5 to 52.6)**	43.4 (43.1 to 43.7)**	46.3 (45.8 to 46.8)**	53.4 (53.3 to 53.5)**	56.1 (56.1 to 56.2)**	54.2 (54.1 to 54.3)**
	Nonadherent→Nonadherent	45.1 (45.1 to 45.2)**	49.4 (49.4 to 49.5)**	42.0 (41.7 to 42.2)**	43.3 (42.9 to 43.7)**	51.5 (51.4 to 51.6)**	54.8 (54.7 to 54.8)**	52.6 (52.5 to 52.6)**
Gender (% Female)	Nonadherent→Adherent	83,166 (72.0%)**	79,538 (51.0%)**	5,326 (62.2%)*	379 (22.3%)**	26,567 (49.8%)**	46,353 (41.5%)**	47,768 (42.5%)**
	Nonadherent→Nonadherent	91,845 (71.5%)**	120,928 (56.7%)**	6,905 (62.8%)*	670 (19.3%)**	29,366 (52.9%)**	71,871 (43.5%)**	70,660 (45.5%)**
CCI Score Difference, Base to Pre, Mean (95% CI)	Nonadherent→Adherent	0.04 (0.03 to 0.05)	0.10 (0.09 to 0.11)**	0.04 (-0.01 to 0.08)	0.26 (0.18 to 0.35)**	0.13 (0.11 to 0.14)**	0.06 (0.05 to 0.07)**	0.09 (0.08 to 0.10)**
	Nonadherent→Nonadherent	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)**	0.04 (0.00 to 0.08)	0.09 (0.03 to 0.16)**	0.12 (0.10 to 0.13)**	0.06 (0.05 to 0.06)**	0.05 (0.04 to 0.06)**
CCI Score Difference, Post to Base, Mean (95% CI)	Nonadherent→Adherent	0.02 (0.01 to 0.03)**	0.04 (0.03 to 0.05)**	0.05 (0.01 to 0.09)	-0.08 (-0.16 to 0.00)	0.04 (0.03 to 0.06)**	0.06 (0.05 to 0.07)**	0.07 (0.06 to 0.08)**
	Nonadherent→Nonadherent	0.03 (0.02 to 0.04)**	0.07 (0.06 to 0.08)**	0.07 (0.03 to 0.11)	0.01 (-0.05 to 0.07)	0.07 (0.06 to 0.09)**	0.08 (0.07 to 0.08)**	0.09 (0.08 to 0.10)**
Total Unadjusted Allowed Medical Cost, Base Year, Mean (95% CI)	Nonadherent→Adherent	$11,030 ($10,820 to $11,241)**	$11,580 ($11,358 to $11,803)**	$16,434 ($15,637 to $17,232)**	$9,375 ($7,548 to $11,203)**	$10,598 ($10,309 to $10,887)**	$10,906 ($10,649 to $11,163)**	$9,874 ($9,674 to $10,075)**
	Nonadherent→Nonadherent	$9,685 ($9,479 to $9,892)**	$10,923 ($10,712 to $11,133)**	$16,474 ($15,564 to $17,384)**	$11,591 ($9,755 to $13,427)**	$10,140 ($9,819 to $10,462)**	$10,503 ($10,290 to $10,717)**	$12,325 ($12,063 to $12,587)**
Total Unadjusted Allowed Medical Cost, Post Year, Mean (95% CI)	Nonadherent→Adherent	$11,159 ($10,933 to $11,385)**	$11,777 ($11,531 to $12,023)**	$15,715 ($14,893 to $16,537)**	$11,415 ($7,113 to $15,717)**	$11,557 ($11,202 to $11,913)**	$11,452 ($11,155 to $11,749)**	$11,109 ($10,863 to $11,354)**
	Nonadherent→Nonadherent	$10,216 ($10,007 to $10,426)**	$12,103 ($11,880 to $12,325)**	$16,451 ($15,385 to $17,517)**	$12,980 ($10,557 to $15,403)**	$11,850 ($11,464 to $12,237)**	$11,849 ($11,609 to $12,089)**	$13,472 ($13,187 to $13,757)**
Change in Total Unadjusted Allowed Medical Cost Difference, Post to Base truncated at 99th Percentile, Mean (95% CI)	Nonadherent→Adherent	$46 (-$73 to $166)**	$99 (-$19 to $216)**	-$658 (-$1,234 to -$82)**	-$41 (-$911 to $828)	$623 ($422 to $825)**	$255 ($117 to $393)**	$760 ($626 to $894)**
	Nonadherent→Nonadherent	$489 ($383 to $595)**	$1,050 ($954 to $1,146)**	$144 (-$358 to $646)**	$496 (-$112 to $1,104)	$1,322 ($1,127 to $1,517)**	$1,109 ($1,000 to $1,218)**	$1,060 ($938 to $1,181)**

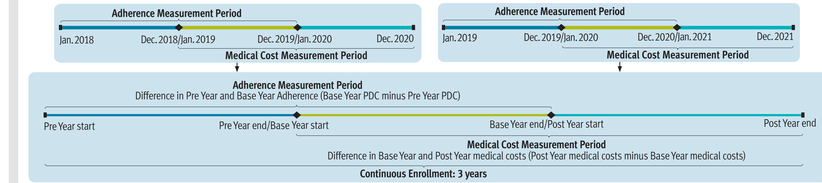
Statistical comparisons across exposure levels were comprised of analysis of variance (ANOVA) for continuous outcomes and chi-square tests for categorical outcomes. * = p<0.05; ** = p<0.01.
Measure N is the total count of member-year (e.g., members fully eligible for a measure in the 2019 Base year and 2020 Base year are counted twice). CI = confidence interval; PDC = Proportion of Days Covered; CCI = Charlson Comorbidity Index; NIDM = Non-insulin Diabetes Medications; RASA = Renin-angiotensin System Antagonists

LIMITATIONS

- Generalizability is limited to members who were continuously enrolled for 3 years and had at least some medical spending in Base and Post year.
- Members who were not measure-eligible, nonpersistent or had only one fill in the Base year for antidepressants, antipsychotics, and non-insulin diabetes medications were not included in the study.
- Findings are limited to commercially insured members and may not be representative of members insured through government programs.
- While the methods employed eliminate time-invariant confounders (e.g., healthy adherer effect), potential bias may remain due to time-varying unobserved confounders.

FIGURE 1

Study Schema



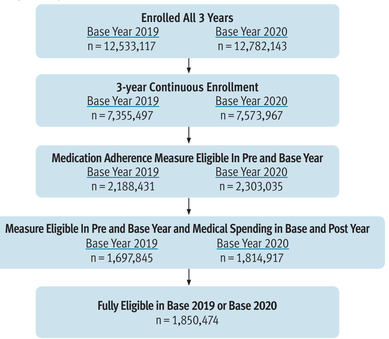
PDC = Proportion of Days Covered[6]

CONCLUSIONS

- Using a robust study design and statistical methodology, this study finds moving from non-adherent to adherent correlating to $292 to $947 in annual medical cost savings for 6 out of the 7 drug categories assessed. The small analytic population for antiretrovirals contributes to lack of statistical significance found.
- Time lagging the relationship between medication adherence and medical spending lessens reverse causality concerns and better aligns with time over which adherence is expected to influence health care spending for most chronic conditions.
- Fixed effects account for time-invariant unobservable variables such as the healthy adherer effect and reduces estimate bias.
- These results support ongoing adherence programs within commercially insured populations. For example, if a 10,000-member population had 190 members who were nonadherent to a statin, and a clinical program that would prompt 20 of them to become adherent, this would result in $16,490 in estimated total savings (20 members x $847 annual medical care savings per member), equating to $0.14 PMPM.

FIGURE 2

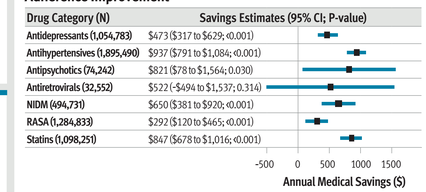
Analytic Population Identification Flow Diagram



Unique member N is the count of members eligible for at least one measure in at least one Base year; Unique member-measure-year is the total unique combinations of members by measure and year.

FIGURE 3

Associated Medical Spending Reduction from Medication Adherence Improvement



PDC = Proportion of Days Covered; NIDM: Non-insulin Diabetes Medications; RASA: Renin-angiotensin System Antagonists; Medical costs adjusted to 2021 dollars; Estimates obtained from lagged-first multivariate regression models controlling for age, gender, Blue Plan and change in Charlson Comorbidity Index score[8]

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