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Comparison of a new three-item self-reported measure of adherence to medication with pharmacy claims data in patients with cardiometabolic disease

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Abstract

Background: Less than half of patients with cardiometabolic disease consistently take prescribed medications. While health insurers and some delivery organizations use claims to measure adherence, most clinicians do not have access during routine interactions. Self-reported scales exist, but their practical utility is often limited by length or cost. By contrast, the accuracy of a new 3-item self-reported measure has been demonstrated in individuals with HIV. We evaluated its concordance with claims-based adherence measures in cardiometabolic disease.

Methods: We used data from a recently-completed pragmatic trial of patients with cardiometabolic conditions. After 12 months of follow-up, intervention subjects were mailed a survey with the 3-item measure that queries about medication use in the prior 30 days. Responses were linearly transformed and averaged. Adherence was also measured in claims in Month 12 and

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Months 1–12 of the trial using proportion of days covered (PDC) metrics. We compared validation metrics for non-adherence for self-report (average<0.80) compared with claims (PDC<0.80).

Results: Of 459 patients returning the survey (response rate: 43.5%), 50.1% were non-adherent in claims in Month 12 while 20.9% were non-adherent based on the survey. Specificity of the 3-item metric for non-adherence was high (Month 12: 0.83). Sensitivity was relatively poor (Month 12: 0.25). Month 12 positive and negative predictive values were 0.59 and 0.52, respectively.

Conclusions: A three-item self-reported measure has high specificity but poor sensitivity for non-adherence versus claims in cardiometabolic disease. Despite this, the tool could help target those needing adherence support, particularly in the absence of claims data.

Keywords

hypertension; hyperlipidemia; adherence; survey

BACKGROUND

Long-term adherence to evidence-based medications for chronic diseases remains poor.^{1–6} On average, less than half of patients with a cardiometabolic condition consistently take their prescribed medications.^{4,7,8} Suboptimal adherence leads to substantial increases in preventable morbidity and mortality and an estimated \$300 billion in excess spending in the US annually.^{9,10}

While healthcare organizations employ numerous methods to measure adherence, administrative pharmacy claims data and patient self-report are most commonly used.^{11–13} Even though claims data are accurate measures of long-term medication-taking and are not subject to recall bias, they may not be available for most clinicians at the point of care.¹⁴ Even for population health management programs, there is also often an administrative lag in accessing claims data, limiting their use for real-time decision-making.^{1,14} Existing self-reported adherence measures range from one-item questions inquiring about frequency of missed doses to longer multi-item assessments evaluating beliefs associated with adherence.^{13,15–20} The practicability of these measures is often limited by their cost (e.g., licensing fees) or length (e.g., patient burden).

One promising measure is the recent 3-item self-report scale by Wilson et al., which queries patients about how many days they missed medications and overall consistency over the last 30 days.^{21,22} Unlike other measures, this 3-item scale is short, easy to administer, and does not involve licensing fees. The 30-day recall also matches the most common interval for prescription dispensing by retail pharmacies (e.g., 30 days) and would therefore hypothetically align well with claims.²³ The accuracy of a 3-item self-reported adherence measure has been demonstrated in individuals with HIV compared to data collected from electronic pill bottles. However, despite this measure's growing acceptance²⁴, this metric has not been compared directly with pharmacy claims data, nor studied in cardiometabolic disease.

Therefore, using data from a recently-completed pragmatic trial,^{25,26} we compared adherence collected via this three-item self-reported metric²² versus pharmacy claims data

as the referent in patients with cardiometabolic disease. We also explored the extent to which self-report adherence measures correspond with different claims-based adherence levels and thresholds and examined patient factors that might affect agreement between the measures.

METHODS

Study design and patient population

We used data from the Study of a Tele-pharmacy Intervention for Chronic diseases to (2) Improve Treatment adherence (STIC2IT) pragmatic trial.^{25,26} This two-arm trial was conducted at a large integrated delivery network in Massachusetts between August 2015 and August 2017. Subjects were included in the trial if they demonstrated suboptimal hyperlipidemia, hypertension, or diabetes disease control and were non-adherent to prescribed medications for these conditions.^{25,26} Patients were excluded from the trial if they had <6 months of plan enrollment or were <18 or >85 years of age before randomization. In total, 2,038 patients were randomized to the intervention arm. As previously described^{25,26}, the central intervention component was a clinical pharmacist consultation. Patients were excluded from the present analysis if they lost continuous enrollment in the 12-month follow-up. The overall study design is in Appendix Figure 1.

Measuring self-reported adherence through the 3-item scale

Patients in the intervention arm who received 1 clinical pharmacist consultation were administered a mailed survey 12 months after randomization to assess adherence. The survey consisted of a cover letter written on behalf of the patient's primary care provider and a second page with the 3-item adherence measure. The cover letter also provided details on how to complete the survey online through Qualtrics, a web-based survey platform. The surveys were otherwise anonymized and contained scrambled patient identifiers to link with claims data. Individuals not returning the survey within 30 days were sent a second copy with a \$5 gift card. In the rare event that patients returned both rounds, we included only the first round in the analyses.

The three self-report items queried patients about the number of days on which medication was taken, frequency of use, and overall ratings of adherence, respectively, as follows:

1. Days Taken: "In the last 30 days, on how many days did you miss at least one dose of any of your medications?" (number of days:0–30). As previously done, this item was converted to "days taken" by subtracting the number of days missed from 30.²¹
2. Frequency: "In the last 30 days, how often did you take your medications in the way you were supposed to?" (never/rarely/sometimes/usually/almost always/always)
3. Overall Rating: "In the last 30 days, how good a job did you do at taking your medications in the way you were supposed to?" (very poor/poor/fair/good/very good/excellent)

As done in previously-published studies, we linearly transformed the three self-reported items to a 0–100 scale, with zero being the lowest adherence, and 100 being the best.²¹ This means, for example, that the Frequency and Overall Rating items that had 6 levels were transformed to 0, 20, 40, 60, 80, and 100, respectively and that the Days Taken item was transformed to units of 3.33 for each (i.e., 100/30), so Days Taken=29 was transformed to 96.67%. An average was then calculated as a mean of the three individual items on this 0–100 scale.²¹ If there was missing data (<4%) for any individual item, we took the mean of the non-missing items.

Pharmacy claims-based adherence

We created a drug supply diary from prescription claims data from the date of randomization until the end of the 12-month follow-up for each medication used for any of the three study conditions.²⁷ Medications in the same therapeutic class were considered interchangeable (e.g., two beta-blockers). Supply for overlapping fills could accumulate up to 180 days excess supply. From these supply diaries, for each eligible medication, we then measured the proportion of days that patients had medications available, or the proportion of days covered (PDC) within each month of follow-up and the entire 12-month period.²⁸ Using an “average of averages” approach, we averaged this PDC across all medications used to treat a single condition (e.g., hypertension) and then calculated an overall average adherence across each patient’s eligible conditions.^{28,29}

We used this “average of averages” calculation to generate two different continuous measures of claims-based adherence, including 1) PDC in the 12 months after randomization (“PDC in Months 1–12”) and 2) PDC in the 12th month after randomization because this period overlapped with the measurement by self-report (“PDC in Month 12”). The three-item survey and claims-based metrics both measure the implementation phase of adherence.³⁰

Covariates

We used claims and electronic health record (EHR) data to measure potential predictors of adherence during the 365 days before randomization. If patients had less than one year of insurance eligibility, covariates were measured upon enrollment. Using EHR data, we measured age, sex, race/ethnicity (classified as “white”/“non-white”), marital/partner status, Body Mass Index (BMI), and current tobacco use. Using International Classification of Disease 9th edition (ICD-9) or 10th edition (ICD-10) codes in medical claims data, we measured comorbidities, a combined comorbidity score (measure of overall health status),^{31,32} number of outpatient physician office visits, hospitalizations, and emergency room (ER) visits. Using pharmacy claims data, we measured the number of unique medications each patient filled.²⁷ By definition, no factors measured in claims were missing because insurance coverage was a trial criterion.^{25,33} While the overall proportion missing BMI was low (<5%), we imputed using mean values for those without one.³³

Statistical analyses

We first described characteristics of survey responders and non-responders and calculated absolute standardized differences. Then, we examined distributions of adherence measured

in claims by levels of self-reported adherence on the three self-reported items using box plots. As in prior work, we aggregated adjacent categories when there were a small number of responses in a given category (e.g., Very Poor/Poor).²¹

To enable dichotomous comparisons, in claims data, we classified patients with a mean PDC<0.80 as “non-adherent”, the most commonly-used threshold for “non-adherence”.³⁴ In the survey data, we classified patients who self-reported as having taken medication on<24 days per month as “non-adherent” (i.e., the analogue to PDC=0.80, 24/30=0.80).²¹ Similarly, we classified patients who responded with “almost always/always” for frequency and “very good/excellent” for overall ratings as “adherent”. For the average 3-item score, we classified patients <80% as “non-adherent”.

We used these cutpoints to calculate validation metrics using non-adherence using claims measures as the standard. Sensitivity provides the ability of self-report to identify “true positives” (i.e., proportion non-adherent in the survey measure of those non-adherent in claims). Specificity provides the ability of self-report to identify “true negatives” (i.e., proportion adherent in the survey measure of those adherent in claims). We also calculated positive and negative likelihood ratios and positive and negative predictive values (PPV, NPV). We also examined patient characteristics by their concordance and for these analyses stratified age into 3 categories (<55, 55–64, 65 years), BMI as <30 or ≥30, combined comorbidity score 1 or <1, office visits as <2 or ≥2, and unique medications as <5, 5–10, ≥10.³² We also conducted exploratory subgroup analyses by chronic condition qualifying the patient for trial entry.

Finally, we conducted sensitivity analyses, including restricting to those who returned the first survey and excluding those with a PDC=0 in the measurement window to reduce the possibility of inaccurate claims for that patient.³⁵ To explore the optimal definition of “non-adherence”, we varied the thresholds for “non-adherence” for the average 3-item score and claims. Analyses were conducted using SAS 9.4 (Cary, NC). The Institutional Review Board of Brigham and Women’s Hospital approved this study. The trial is registered on [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02512276) (NCT02512276).

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RESULTS

In the trial, 1,069 intervention patients received the initial pharmacist consultation and were mailed the survey (52.4% of intervention group). Of these 1,069, 465 patients (43.5%) returned the surveys; >50% within 1 week. Of these, 6 (1.3%) surveys did not contain usable study identifiers to link their responses to claims data and were excluded. As a result, 459 patient surveys were included in analyses.

The mean age of those who responded was 64 years, and 57% were male (Appendix Table 1). Compared with non-responders, patients who returned the survey were slightly older, more likely to be white, have a partner, have a diagnosis of hyperlipidemia or osteoporosis,

and visit the ER in the prior 12 months. PDC adherence was also slightly higher among responders.

In Month 12, mean claims-based PDC was 56.8 (SD:43.4), median 76.7 (IQR: 0.0–96.7). Over Months 1–12, mean PDC was 57.7 (SD:32.9), median 65.5 (IQR: 33.2–85.5). For the 3-item score, the mean was 87.4 (SD:13.8), median 91.1 (IQR: 83.3–100.0). The distribution of responses to each survey question is shown in Appendix Table 2. The percentages of patients classified as “non-adherent” by self-report and pharmacy claims is in Figure 1. In Month 12, fewer patients were classified as “non-adherent” by patient self-report (20.9%) than claims (50.1%).

The raw self-reported items and PDC measures for each item level are compared in Figure 2. Mean PDC generally increased as self-reported adherence increased. The notable exception is that mean PDC in Months 1–12 was slightly higher in those reporting taking 29 days of medication versus those taking all 30 days. Patients who did not report adherence were much less likely to be adherent in claims.

Validation metrics for identifying non-adherence are shown in Table 1. Sensitivity was relatively low for identifying non-adherence (e.g., 0.25 for average of the 3-item score for Month 12). By contrast, specificity was high for identifying non-adherence (i.e., 0.83 for all comparisons). PPV and NPV were modest (e.g., 0.59 and 0.25, respectively for Month 12). These metrics were similar when comparing self-report with adherence measured in claims across both intervals (Month 12 and Months 1–12), although PPV was higher for Months 1–12 (0.80). For the self-reported items individually, the “Days Taken” metric appeared to perform best versus claims.

Baseline characteristics of patients by whether their survey and Months 1–12 claims-based PDC agree are shown in Appendix Table 3. In general, patients who were classified as optimally adherent by both measures tended to be male and older. Patients who were non-adherent by both measures tended to be younger, non-white, single/unpartnered, and have had fewer office visits. However, these inferences were limited by small sample size.

Exploratory subgroup analyses by eligible study condition are shown in Appendix Table 4. There were no substantial differences across subgroups, but conclusions were limited by small sample size. Restricting to patients who returned the surveys in the first round slightly improved but did not materially change concordance (Appendix Table 5).

Variations of the 3-item self-reported score and claims thresholds for non-adherence suggest that accuracy may improve with alternative cutpoints (Appendix Table 6). Specificity was extremely high for all claims-based thresholds at survey thresholds at or below <70% (Figure 3).

DISCUSSION

In this study of patients with cardiometabolic disease, we observed that self-reported adherence was consistently higher than claims-based adherence. In addition, patients reporting non-adherence were much less likely to be adherent in claims. Using pharmacy

claims as the referent, the 3-item self-report measure had high specificity but very low sensitivity for non-adherence; PPV and NPV suggest that there may be false positives or negatives, depending on prevalence of non-adherence. Survey metrics were similar for short (1-month) and longer (12-month) claims measurement windows.

To our knowledge, this is the first study to directly compare this self-report metric with pharmacy claims in patients with cardiometabolic disease. This item has become quickly embraced by many in the HIV community, but has not been studied to our knowledge in cardiometabolic diseases or in claims.²⁴ Previously-developed metrics have been limited by their length, difficulty of administration, or licensing fees.¹³ Concerns have been raised about other metrics that query about the extent of non-adherence while also asking about reasons for non-adherence.^{13,24} Other metrics ask about use during shorter time windows, yet prior work has suggested that a 1-month recall window may best approximate adherence – i.e., the recall window in this 3-item metric.^{36,37}

These results have several important insights relevant to clinical care. First, patients who self-identify with any degree of non-adherence also appeared to have suboptimal adherence in claims. This finding is not necessarily surprising given the overall tendency of patients to over-report adherence. The creators of the 3-item scale do not advocate for specific levels at which patients should be considered sub-optimally adherent, so any admission of non-perfect adherence could therefore prove potentially actionable.²¹ Sensitivity analyses of non-adherence cutpoints support this. The thresholds themselves therefore may not perfectly mirror claims data calculations, as for example, patients using multiple medications may report differently than how adherence was calculated in claims.²⁹ The 3-item scale also appears to perform similarly for patients' average adherence in the prior year as in the prior month.

While some metrics are modest, this brief 3-item self-report scale is inexpensive to administer and could be a useful tool in clinical care or population health management. Its strong specificity for identifying non-adherence may lend itself to some desirable properties, especially when pharmacy claims data may be unavailable or delayed. In clinical care, this self-report scale could be best used as a brief screening tool to identify patients with suboptimal adherence who would be candidates for more in-depth discussion about how to address their barriers. In patients with suspected non-adherence, due to the poor sensitivity, it may also be useful to assume non-adherence and then use the survey to confirm non-adherence. Of course, if employed as is, resulting false positive and false negative rates may still misclassify patients. Implementation strategies would need to recognize that because of the low sensitivity, many potential candidates would not be identified. Given that non-adherence to cardiometabolic medications is highly prevalent in real-world practice, identifying even a subset of patients for intervention represents an improvement. This scale could, for example, be used within a clinic questionnaire, or within population health outreach. In this study, the survey was mailed because it was delivered within a larger trial that did not require study-specific visits to increase generalizability and reduce any contamination with the intervention.

Our results largely corroborate the diagnostic parameters observed in prior examinations of other self-reported metrics.^{13,20} For example, our finding that self-reported adherence was higher than adherence measured in pharmacy claims is consistent with evaluations of other tools.^{15,16,38,39} It is impossible to distinguish whether the higher estimation by self-report in general is reflective of social desirability bias or perhaps an underestimation of adherence by claims.^{35,40,41} Regardless, prior research has shown that while adherence measured via self-report and claims may not correlate well with each other, both are separately correlated with blood pressure control, suggesting that the measures provide complementary information about patients' medication-taking.⁴²

The modest associations observed in this work and others could be explained in several ways. First, the metrics could functionally be measuring different things; for example, pharmacy claims-based adherence measures long-term adherence, whereas self-report measures short-term behaviors. Second, the results could be a function of how claims-based adherence is averaged, yet adherence changes over time and therefore standard deviations are fairly wide.^{43,44} Third, while these data are used regularly for quality improvement, the "gold standard" here was adherence measured in claims, which may have had their own inaccuracies, such as potential for missing claims when filled outside insurance; for example, excluding patients with PDC=0 slightly improved metrics.^{35,40,45} Prior work has shown that calibrating to the specific comparison data source can improve accuracy of self-reported scales by reducing overall overestimation by self-report.²¹ Of note, the metrics studied here were for "non-adherence"; if applied to identifying "optimal" adherence (e.g., PDC 0.80), they would be reversed. Finally, the scale does not perform as well in cardiometabolic disease as HIV at the threshold used in prior studies but may perform better at alternative cutpoints.

Several limitations should be acknowledged. First, patients were part of a larger quality improvement trial conducted in one region, eastern Massachusetts, and patients had to have a pharmacist consultation, prior non-adherence and poor control to receive a survey, potentially reducing generalizability. However, trial patients with these characteristics may be a key population of interest for this scale), and patients who participated in the consultation were generally similar to those in the parent trial.²⁵ A 44% response rate is modest; those responding may be more subject to social desirability bias, which may affect generalizability.⁴¹ Finally, sample sizes by study conditions were small.

CONCLUSION

This new three-item self-reported adherence metric had high specificity but poor sensitivity versus pharmacy claims data in patients with cardiometabolic disease. Patients who self-report any degree of non-adherence in this metric are also highly likely to be non-adherent based on claims data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

Appendix Figure 1.
Overall design of this study

Appendix Table 1.

Patient characteristics by survey responders and non-responders

	Responders (n=459)	Non-responders (n=610)	Absolute standardized difference
Demographic			
Male, n (%)	264 (57.5)	351 (57.5)	0.00
Age, mean (SD)	64.3 (9.8)	58.7 (11.3)	0.05
Non-white race/ethnicity, %			
Black, n (%)	120 (26.1)	227 (37.2)	0.24
Other, n (%)	53 (11.6)	119 (19.5)	0.22
Single, n (%)	186 (40.5)	290 (47.5)	0.14
Clinical			
Coronary artery disease, n (%)	28 (6.1)	35 (5.7)	0.02
Congestive heart failure, n (%)	17 (3.7)	19 (3.1)	0.03
Chronic kidney disease, n (%)	28 (6.1)	42 (6.9)	0.03
COPD/Asthma, n (%)	25 (5.5)	25 (4.1)	0.07
Depression, n (%)	24 (5.2)	41 (6.7)	0.06
Diabetes, n (%)	150 (32.7)	242 (44.6)	0.25
Hyperlipidemia, n (%)	154 (33.6)	173 (28.4)	0.11
Hypertension, n (%)	144 (31.4)	166 (27.2)	0.09

	Responders (n=459)	Non-responders (n=610)	Absolute standardized difference
Osteoporosis, n (%)	32 (7.0)	18 (3.0)	0.18
Tobacco use, n (%)	175 (38.1)	196 (32.1)	0.13
BMI, mean (SD)	29.6 (6.2)	31.4 (6.3)	0.05
Comorbidity score, mean (SD)	0.8 (1.6)	0.8 (1.6)	0.03
Resource utilization			
ER visit, n (%)	30 (6.5)	23 (3.8)	0.12
No. PCP visits, mean (SD)	1.8 (4.3)	1.0 (3.7)	0.04
Hospitalization, n (%)	30 (6.5)	34 (5.6)	0.04
No. unique drugs, mean (SD)	8.1 (5.4)	8.3 (5.6)	0.01
Medication adherence			
All patients			
Month 12 PDC, mean (SD)	56.8 (43.5)	46.7 (43.1)	0.01
Months 1–12 PDC, mean (SD)	57.7 (32.9)	50.8 (32.5)	0.01
Patients with hypertension			
Month 12 PDC, mean (SD)	50.3 (44.7)	43.5 (43.7)	0.00
Months 1–12 PDC, mean (SD)	50.1 (35.3)	46.1 (32.1)	0.00
Patients with diabetes			
Month 12 PDC, mean (SD)	44.7 (44.7)	42.9 (40.6)	0.01
Months 1–12 PDC, mean (SD)	47.2 (33.9)	40.3 (29.9)	0.00
Patients with hyperlipidemia			
Month 12 PDC, mean (SD)	59.7 (42.6)	46.3 (43.1)	0.01
Months 1–12 PDC, mean (SD)	60.6 (31.3)	47.5 (32.5)	0.01

Abbreviations: SD, Standard Deviation; COPD, Chronic obstructive pulmonary disease; BMI, Body Mass Index; ER, Emergency room; PCP, Primary Care Provider

Appendix Table 2.

Distribution of responses to each of the three self-reported adherence items

Survey item	Responses, N (%)
Days Taken	
Missing	16 (3.5%)
<24 days	27 (5.9 %)
24–26 days	42 (9.2%)
27–28 days	98 (21.4%)
29 days	83 (18.1%)
30 days	193 (42.0%)
Frequency	
Never	2 (0.4%)
Rarely	0 (0.0%)
Sometimes	9 (2.0%)
Usually	39 (8.5%)
Almost always	180 (39.2%)

Survey item	Responses, N (%)
Always	229 (49.9%)
Overall rating	
Very poor	5 (1.1%)
Poor	3 (0.7%)
Fair	21 (4.6%)
Good	66 (14.4%)
Very good	169 (36.8%)
Excellent	195 (42.5%)
Average adherence	
0 to <40%	7 (1.5%)
40 to <60%	13 (2.8%)
60 to <80%	76 (16.6%)
80 to 100%	363 (79.1%)

Appendix Table 3.

Patient characteristics and agreement between patient self-reported adherence and 12-month pharmacy claims-based adherence

Patient factors	Agreement		Non-Agreement	
	Optimally adherent by survey and claims (n=124)	Non-adherent by survey and claims (n=77)	False negatives: Non-adherent by claims but not survey (n=239)	False positives: Non-adherent by survey but not claims (n=19)
Demographic				
Male, n (%)	84 (67.7)	40 (52.0)	129 (54.0)	11 (57.9)
Age, n (%)				
<55 years	9 (7.3)	16 (20.8)	33 (13.8)	5 (26.3)
55–64 years	44 (35.5)	29 (37.7)	92 (38.5)	6 (31.6)
65 years	71 (57.3)	32 (41.6)	114 (47.7)	8 (42.1)
Non-white race/ethnicity, n (%)	35 (28.2)	41 (53.3)	89 (37.2)	8 (42.1)
Single, n (%)	47 (37.9)	37 (48.1)	95 (39.8)	7 (36.8)
Clinical				
Coronary artery disease, n (%)	7 (5.7)	0 (0.0)	19 (8.0)	2 (10.5)
Congestive heart failure, n (%)	8 (6.5)	2 (2.6)	6 (2.5)	1 (5.3)
Chronic kidney disease, n (%)	5 (4.0)	4 (5.2)	18 (7.5)	1 (5.3)
COPD/Asthma, n (%)	4 (3.2)	1 (1.3)	19 (8.0)	1 (5.3)
Depression, n (%)	7 (5.7)	2 (2.6)	12 (5.0)	3 (15.8)
Diabetes, n (%)	27 (21.8)	27 (35.1)	87 (36.4)	9 (47.4)
Hyperlipidemia, n (%)	44 (35.5)	15 (19.5)	90 (37.7)	5 (26.3)
Hypertension, n (%)	39 (31.5)	18 (23.4)	81 (33.9)	6 (31.6)
Tobacco use, n (%)	50 (40.3)	22 (28.6)	98 (38.9)	10 (52.6)

	Agreement		Non-Agreement	
Patient factors	Optimally adherent by survey and claims (n=124)	Non-adherent by survey and claims (n=77)	False negatives: Non-adherent by claims but not survey (n=239)	False positives: Non-adherent by survey but not claims (n=19)
BMI 30, n (%)	50 (40.3)	35 (45.5)	112 (46.9)	9 (47.4)
Comorbidity score 1, n (%)	38 (30.7)	17 (22.1)	85 (35.6)	5 (26.3)
Resource utilization				
ER visit, n (%)	10 (8.1)	4 (5.2)	15 (6.3)	1 (5.3)
Office visits 2, n (%)	36 (29.0)	15 (19.5)	64 (26.8)	4 (21.1)
Hospitalization, n (%)	10 (8.1)	1 (1.3)	16 (6.7)	3 (15.8)
No. unique drugs filled, n (%)				
<5	36 (29.0)	21 (27.3)	69 (28.9)	3 (15.8)
5–10	55 (44.4)	31 (40.3)	100 (41.8)	8 (42.1)
10	33 (26.6)	25 (32.5)	70 (29.3)	8 (42.1)
By study condition, mean (SD)				
No. hypertension drugs filled	1.3 (0.7)	1.4 (0.8)	1.7 (0.8)	1.6 (0.8)
No. hyperlipidemia drugs filled	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)
No. diabetes drugs filled	2.0 (0.0)	1.3 (0.8)	1.6 (0.8)	1.8 (1.0)

Abbreviations: CI, Confidence Interval; COPD, Chronic obstructive pulmonary disease; BM. I, Body Mass Index; ER, Emergency room Note: Adherence in pharmacy claims measured in Months 1–12

Appendix Table 4.

Diagnostic parameters for defining non-adherence between average patient self-report and pharmacy claims-based adherence: Exploratory subgroup analyses

	Claims PDC	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Average 3-item score							
<i>Month 12, n</i>							
	<i>Non-adherent</i>	<i>Adherent</i>					
<i>Non-adherent</i>	14	5	0.29	0.88	2.40	0.81	0.74
<i>Adherent</i>	35	37	(0.17–0.43)	(0.75–0.96)	(0.94–6.11)	(0.66–1.00)	(0.52–0.88)
Hypertension (n=91)							
<i>Months 1–12, n</i>							
	<i>Non-adherent</i>	<i>Adherent</i>					
<i>Non-adherent</i>	19	0	0.28	1.00	-	0.72	1.00
<i>Adherent</i>	50	22	(0.18–0.39)	(0.85–1.00)		(0.63–0.84)	(1.00–1.00)
Average 3-item score							
<i>Month 12, n</i>							
	<i>Non-adherent</i>	<i>Adherent</i>					
<i>Non-adherent</i>	40	31	0.23	0.84	1.41	0.92	0.56

		Claims PDC		Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
	<i>Adherent</i>	137	162	(0.17– 0.29)	(0.78– 0.89)	(0.92– 2.12)	(0.83– 1.02)	(0.46– 0.66)	(0.52– 0.57)
Hyperlipidemia (n=370)	Months 1–12, n								
		<i>Non- adherent</i>	<i>Adherent</i>						
	<i>Non- adherent</i>	55	16	0.22	0.87	1.73	0.89	0.77	0.36
	<i>Adherent</i>	191	108	(0.17– 0.28)	(0.80– 0.92)	(1.04– 2.89)	(0.81– 0.98)	(0.67– 0.85)	(0.34– 0.38)
Average 3-item score	Month 12, n								
		<i>Non- adherent</i>	<i>Adherent</i>						
	<i>Non- adherent</i>	5	6	0.23	0.50	0.45	1.55	0.45	0.26
	<i>Adherent</i>	17	6	(0.08– 0.45)	(0.22– 0.79)	(0.17– 1.18)	(0.84– 2.84)	(0.24– 0.68)	(0.16– 0.39)
Diabetes (n=34)	Months 1–12, n								
		<i>Non- adherent</i>	<i>Adherent</i>						
	<i>Non- adherent</i>	7	4	0.26	0.43	0.45	1.73	0.64	0.13
	<i>Adherent</i>	20	3	(0.11– 0.46)	(0.10– 0.82)	(0.18– 1.12)	(0.71– 4.18)	(0.41– 0.81)	(0.06– 0.27)

Abbreviations: PDC, PDC, Proportion of days covered; CI, Confidence Interval; LR+, Positive Likelihood Ratio; LR-, Negative Likelihood Ratio Note: Three item score linearly transformed to 0–100 scale and then averaged. “Non-adherence” was defined as follows: Claims PDC<80% and Average 3-item score<80%.

Appendix Table 5.

Diagnostic parameters for defining non-adherence between average patient self-report and pharmacy claims: Sensitivity analyses

		Claims PDC		Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Average 3-Item score	Month 12, n								
		<i>Non- adherent</i>	<i>Adherent</i>						
	<i>Non- adherent</i>	26	16	0.24	0.87	1.82	0.87	0.62	0.56
	<i>Adherent</i>	82	105	(0.16– 0.32)	(0.81– 0.93)	(1.03– 3.21)	(0.77– 0.99)	(0.48– 0.74)	(0.53– 0.59)
Round 1 only	Months 1–12, n								
		<i>Non- adherent</i>	<i>Adherent</i>						
	<i>Non- adherent</i>	33	9	0.22	0.88	1.89	0.88	0.79	0.37
	<i>Adherent</i>	118	69	(0.15– 0.28)	(0.81– 0.96)	(0.96– 3.76)	(0.79– 0.99)	(0.65– 0.88)	(0.34– 0.40)

		Claims PDC		Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Average 3-item score	Month 12, n								
		<i>Non-adherent</i>	<i>Adherent</i>						
	<i>Non-adherent</i>	26	39	0.30	0.83	1.78	0.84	0.40	0.76
Excluding those with claims- based PDC=0	<i>Adherent</i>	60	190	(0.21– 0.40)	(0.78– 0.88)	(1.15– 2.73)	(0.72– 0.98)	(0.30– 0.51)	(0.73– 0.79)
	Months 1–12, n								
		<i>Non-adherent</i>	<i>Adherent</i>						
	<i>Non-adherent</i>	67	19	0.26	0.87	1.95	0.85	0.78	0.39
	<i>Adherent</i>	191	124	(0.21– 0.31)	(0.81– 0.92)	(1.23– 3.12)	(0.78– 0.94)	(0.69– 0.85)	(0.37– 0.42)

Abbreviations: PDC, PDC, Proportion of days covered; CI, Confidence Interval; LR+, Positive Likelihood Ratio; LR-, Negative Likelihood Ratio Note: Three item score linearly transformed to 0–100 scale and then averaged. “Non-adherence” was defined as follows: Claims PDC<80% and Average 3-item score<80%.

Appendix Table 6.

Accuracy of self-reported non-adherence compared with pharmacy claims by cutpoint to define non-adherence

Average 3-item score				Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Month 12		Claims PDC							
		<80%							
<90%		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	116	103	0.50	0.55	1.12	0.90	0.53	0.53
	<i>Adherent</i>	114	126	(0.44– 0.57)	(0.48– 0.62)	(0.93– 1.36)	(0.76– 1.07)	(0.48– 0.58)	(0.48– 0.57)
		<80%							
<100%		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	168	153	0.73	0.33	1.09	0.81	0.52	0.55
	<i>Adherent</i>	62	76	(0.66– 0.79)	(0.27– 0.40)	(0.97– 1.23)	(0.61– 1.08)	(0.49– 0.55)	(0.48– 0.61)
		<70%							
<80%		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	55	41	0.26	0.84	1.60	0.88	0.57	0.58
	<i>Adherent</i>	154	209	(0.20– 0.33)	(0.78– 0.88)	(1.12– 2.30)	(0.80– 0.97)	(0.48– 0.66)	(0.55– 0.60)
		<60%							
<80%		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>								

Average 3-item score				Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
	<i>Non-adh</i>	51	45	0.26	0.83	1.56	0.89	0.53	0.61
	<i>Adherent</i>	142	221	(0.20–0.33)	(0.78–0.87)	(1.09–2.23)	(0.80–0.98)	(0.44–0.62)	(0.58–0.63)
<80%	<40%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	43	53	0.25	0.82	1.38	0.91	0.45	0.65
	<i>Adherent</i>	127	236	(0.19–0.33)	(0.77–0.86)	(0.77–0.86)	(0.83–1.01)	(0.36–0.54)	(0.62–0.67)
Months 1–12		Claims PDC							
<90%	<80%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	162	57	0.51	0.60	1.29	0.81	0.74	0.36
	<i>Adherent</i>	154	86	(0.46–0.57)	(0.52–0.68)	(1.02–1.62)	(0.68–0.97)	(0.69–0.73)	(0.32–0.40)
<100%	<80%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	229	92	0.72	0.36	1.13	0.77	0.71	0.37
	<i>Adherent</i>	87	51	(0.67–0.77)	(0.28–0.44)	(0.98–1.30)	(0.58–1.03)	(0.68–0.74)	(0.31–0.44)
<80%	<70%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	66	30	0.26	0.85	1.79	0.87	0.69	0.48
	<i>Adherent</i>	187	176	(0.21–0.32)	(0.80–0.90)	(1.21–2.65)	(0.79–0.95)	(0.60–0.76)	(0.46–0.51)
<80%	<60%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	55	41	0.27	0.84	1.68	0.87	0.57	0.59
	<i>Adherent</i>	149	214	(0.21–0.34)	(0.79–0.88)	(1.17–2.40)	(0.79–0.96)	(0.48–0.66)	(0.57–0.61)
<80%	<40%								
	<i>Non-adh</i>	<i>Adherent</i>							
	<i>Non-adh</i>	32	64	0.25	0.81	1.27	0.94	0.33	0.73
	<i>Adherent</i>	98	265	(0.17–0.33)	(0.76–0.85)	(0.87–1.84)	(0.84–1.05)	(0.26–0.42)	(0.71–0.75)

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Highlights

- Most patients with cardiometabolic disease do not take medications as prescribed.
- Existing measures for measuring adherence at point of care are suboptimal.
- A new 3-item self-reported tool shows some promise in cardiometabolic disease.
- This tool could help target those needing adherence support in clinical practice.

Figure 1.
Percentage of patients classified as non-adherent by different measures

A. Self-reported 3-item adherence: Days Taken item

B. Self-reported 3-item adherence: Frequency item

C. Self-reported 3-item adherence: Overall Rating item

D. Self-reported 3-item adherence: Average

Figure 2.
Adherence measured in pharmacy claims by levels of the 3-item patient self-reported adherence score

Figure 3. Specificity of non-adherence across different thresholds for non-adherence

Specificity of self-reported non-adherence in the average 3-item score compared with pharmacy claims in Month 12 across different thresholds for non-adherence in both data sources. PDC, Proportion of Days Covered

Table 1.

Accuracy of self-reported non-adherence compared with pharmacy claims

		Claims PDC		Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Days Taken item	<i>Month 12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	31	12	0.13	0.95	2.57	0.91	0.72	0.52
	<i>Adherent</i>	199	217	(0.09–0.18)	(0.91–0.97)	(1.36–4.88)	(0.86–0.97)	(0.58–0.83)	(0.51–0.54)
	<i>Months 1–12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	36	7	0.11	0.95	2.33	0.93	0.84	0.33
	<i>Adherent</i>	280	136	(0.08–0.15)	(0.92–0.99)	(1.06–5.10)	(0.88–0.98)	(0.70–0.92)	(0.32–0.34)
Frequency	<i>Month 12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	31	19	0.13	0.92	1.62	0.94	0.62	0.51
	<i>Adherent</i>	199	210	(0.09–0.18)	(0.88–0.95)	(0.95–2.79)	(0.88–1.01)	(0.49–0.74)	(0.50–0.53)
	<i>Months 1–12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	40	10	0.13	0.93	1.81	0.94	0.80	0.33
	<i>Adherent</i>	276	133	(0.09–0.16)	(0.89–0.97)	(0.93–3.52)	(0.88–1.00)	(0.67–0.89)	(0.31–0.34)
Overall rating	<i>Month 12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	73	22	0.23	0.85	1.50	0.91	0.77	0.33
	<i>Adherent</i>	243	121	(0.18–0.28)	(0.79–0.91)	(0.97–2.32)	(0.83–1.00)	(0.68–0.84)	(0.31–0.35)
	<i>Months 1–12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	55	40	0.24	0.83	1.37	0.92	0.58	0.52
	<i>Adherent</i>	175	189	(0.18–0.29)	(0.78–0.87)	(0.95–1.97)	(0.84–1.01)	(0.49–0.66)	(0.50–0.54)
Average 3- item score	<i>Month 12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	57	39	0.25	0.83	1.46	0.91	0.59	0.52
	<i>Adherent</i>	173	190	(0.19–0.31)	(0.77–0.88)	(1.01–2.09)	(0.82–1.00)	(0.50–0.68)	(0.50–0.55)
	<i>Months 1–12, n</i>								
		<i>Non-adh</i>	<i>Adherent</i>						
	<i>Non-adh</i>	77	19	0.24	0.87	1.83	0.87	0.80	0.34
	<i>Adherent</i>	239	124	(0.20–0.29)	(0.80–0.92)	(1.16–2.91)	(0.80–0.95)	(0.72–0.87)	(0.32–0.36)

Abbreviations: PDC, PDC, Proportion of days covered; Non-adh, Non-adherent; CI, Confidence Interval Note: Three item score linearly transformed to 0–100 scale and then averaged. “Non-adherence” was defined as follows: Claims PDC<80%, Days Taken<24, Frequency: Never/Rarely/Sometimes/Usually, Overall Rating: Very poor/Poor/Fair/Good, and Average 3-item score<80%.

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