Patient Preference and Adherence

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Patient Pill Organization Strategies and Adherence Measured in a Cross-Sectional Study of Hypertension

Matthew P Genelin[1], Laura J Helmkamp[2], John F Steiner[1,3], Julie A Maertens[2], Rebecca Hanratty[1,4], Suma Vupputuri[5], Edward P Havranek[1,4,6], L Miriam Dickinson[1,2], Irene V Blair[7], Stacie L Daugherty[1–3,6]

[1]University of Colorado School of Medicine, Aurora, CO, USA; [2]Adult and Child Consortium for Outcomes Research and Delivery Sciences (ACCORDS), University of Colorado, Aurora, CO, USA; [3]Institute for Health Research, Kaiser Permanente Colorado, Denver, CO, USA; [4]Department of Medicine, Denver Health and Hospital Authority, Denver, CO, USA; [5]Mid-Atlantic Permanente Research Institute, Kaiser Permanente Mid-Atlantic States, Rockville, MD, USA; [6]Department of Medicine, Division of Cardiology, University of Colorado School of Medicine, Aurora, CO, USA; [7]Department of Psychology and Neuroscience, University of Colorado Boulder, Boulder, CO, USA

Correspondence: Matthew P Genelin, University of Colorado School of Medicine, 3500 Rockmont Drive, #15-209, Denver, CO, 80202, USA, Email matthew.genelin@cuanschutz.edu

Background: The strategies patients use to organize medications (eg, pill dispenser) may be reflected in adherence measured at follow-up. We studied whether medication organization strategies patients use at home are associated with adherence measured using pharmacy-fills, self-report, and pill counts.

Design: Secondary analysis of data from a prospective randomized clinical trial.

Setting: Eleven US safety-net and community primary care clinics.

Patients: Of the 960 enrolled self-identified non-Hispanic Black and White patients prescribed antihypertensive medications, 731 patients reported pill organization strategies and were included.

Variable: Patients were asked if they use any of the following medication organization strategies: finish previous refills first; use a pill dispenser; combine same prescriptions; or combine dissimilar prescriptions.

Outcomes: Adherence to antihypertensive medications using pill counts (range, 0.0–1.0% of the days covered), pharmacy-fill (proportion of days covered >90%), and self-report (adherent/non-adherent).

Results: Of the 731 participants, 38.3% were men, 51.7% were age ≥65, 52.9% self-identified as Black or African American. Of the strategies studied, 51.7% finished previous refills first, 46.5% used a pill dispenser, 38.2% combined same prescriptions and 6.0% combined dissimilar prescriptions. Median (IQR) pill count adherence was 0.65 (0.40–0.87), pharmacy-fill adherence was 75.7%, and self-reported adherence was 63.2%. Those who combined same prescriptions had significantly lower measured pill count adherence than those who did not (0.56 (0.26–0.82) vs 0.70 (0.46–0.90), $p<0.01$) with no significant difference in pharmacy-fill (78.1% vs 74%, $p=0.22$) or self-reported adherence (63.0% vs 63.3%, $p=0.93$).

Conclusion: Self-reported medication organization strategies were common. Combining same prescriptions was associated with lower adherence as measured using pill counts but not pharmacy-fills or self-report. Clinicians and researchers should identify the pill organization strategies used by their patients to understand how these strategies may influence measures of patient adherence.

Trial Registration: ClinicalTrials.gov NCT03028597; https://clinicaltrials.gov/ct2/show/NCT03028597 (Archived by WebCite at http://www.webcitation.org/72vcZMzAB).

Keywords: hypertension, medication adherence, management strategies, organization strategies, medication management behaviors, chronic disease, pill count, pharmacy-fill, self-reported adherence

Introduction

Medication adherence is measured in clinical practice and research studies to enhance clinicians' and researchers' understanding of a patient's medication taking behavior. Poor medication adherence is associated with higher rates of adverse

Received: 15 December 2022
Accepted: 7 March 2023
Published: 23 March 2023

clinical events.[1–9] Patients managing chronic disease, such as hypertension, often take multiple medications and may receive new medication supplies before completing current supplies.[10] To organize their multiple pills and bottles, patients may use pill organization strategies such as placing medications for the coming week into a pill dispenser or combining same prescriptions into one bottle when a new prescription arrives. How often patients use these different strategies or whether they are associated with commonly used measures of medication adherence is not well known.

Despite the importance of medication adherence, there is no agreed upon gold standard for measuring adherence in clinical practice or research. Common measures of adherence include 1) manual pill counts, whereby all pills in a patient's medication bottle are counted and compared to the expected quantity of pills based on their most recent medication dispensing date, dose, and consumption frequency; 2) pharmacy refill data which measures medication supply obtained, typically over a longer period of observation, using the proportion of days covered (PDC); and 3) self-reported surveys of recent medication taking behavior.[5] Importantly, none of these measures of adherence account for how patients organize their medications once they receive them. Patient organization strategies may produce variable effects on adherence measures; for instance, pill count adherence may be overestimated when doses are not ingested but moved to another container or may be underestimated due to combining same medications into the same container. Therefore, it is important to determine the frequency of organization strategies and how these organization strategies are associated with different medication adherence measures.

We addressed these gaps in knowledge by studying patient pill organization strategies among participants enrolled in the HYpertension and VALUEs (HYVALUE) pragmatic clinical trial. The HYVALUE trial enrolled patients with uncontrolled hypertension who were taking at least one antihypertensive.[11,12] The primary objective of this sub-study of the larger trial was to determine the prevalence of selected patient strategies for organizing their pills, and to evaluate the association between these strategies and three common measures of adherence (pill counts, pharmacy-fills, and self-report). Understanding the different organization strategies patients use and how these strategies relate to adherence estimates in pragmatic clinical trials may inform treatment plans or study designs researchers and clinicians should consider when measuring patient adherence.

Methods

Trial Design, Setting, and Patient Population

Participants were selected as part of the HYpertension and VALUEs (HYVALUE) randomized controlled trial, which tested the utility of a values affirmation intervention to lessen the negative effect of stereotype threat on individuals with uncontrolled hypertension.[11,12] The study enrolled self-identified African American or Black patients and White patients who sought healthcare in 1 of 11 safety-net or community primary care clinics in Colorado and Maryland. Patients were eligible for enrollment in the HYVALUE trial if they had uncontrolled blood pressure, defined as a systolic blood pressure ≥140 mm Hg and diastolic ≥90 mm Hg at least once during the preceding 12 months, and a primary or secondary ICD-10 diagnosis code for hypertension in the previous 24 months. Because adherence was the primary outcome of the trial, patients were eligible if they filled their medications within the participating health system pharmacies. A total of 960 patients were enrolled between February 2017 and December 2019.[12]

This sub-study is a secondary analysis of data from a prospective randomized clinical trial. We excluded 229 participants from the HYVALUE Trial who did not complete the survey measures. The characteristics of those excluded from this sub-study were similar except they were older and included a higher proportion who self-identified as Black or African American (Table S1).

Patient Medication Organization Strategy Survey

The survey included patient pill organization strategies based on common themes participants enrolled early in the trial self-reported for how they organize their pills at home. Based on this work, a survey was created asking all patients whether they did or did not 1) finish previous refills first; 2) use a pill dispenser; 3) combine same prescriptions; or 4) combine dissimilar prescriptions. To understand other factors that may influence adherence measures, patients were also asked if they: took pills as needed because of clinician instructions; took a different dose because of doctor orders; took a different dose chosen oneself; or shared pills with others. Response options for all questions were limited to either yes or no. The survey was first introduced in November 2017 (8 months into enrollment) and all participants enrolled after this date were asked to complete the survey.

Outcomes: Adherence Measurements

We used three approaches to measure patient adherence to their medications. Pill count adherence was calculated as the proportion of the actual over the expected number of pills taken since the last recorded refill.[13,14] Participants were asked to bring all of their pill bottles to the enrollment visit and pill counts were performed by research staff. Pharmacy-fill adherence used health system data to determine the medication supply obtained over 12 months before the index visit using the proportion of days covered (PDC) by medication.[15,16] Pill count and pharmacy-fill adherence were averaged across all antihypertensives a patient was taking.[16] Finally, self-reported adherence asked patients to identify their pill-taking behavior over the previous 7 days using a validated 3-item survey with any positive response (eg, "I missed or skipped at least 1 dose") indicating non-adherence.[11,14,17,18]

Statistical Analysis

Analyses of demographics, patient pill organization strategies, and adherence used descriptive statistics: percentages for categorical variables, means and standard deviations for normally distributed continuous variables, and medians and interquartile ranges for non-normally distributed continuous variables. Among the larger HYVALUE trial population, we compared the characteristics of those included and excluded from this sub-study. (Table S1) Pharmacy-fill adherence was skewed and was dichotomized in our study as more than 90% PDC (adherent) or 90% or less PDC (nonadherent). Correlation between the three measures was assessed using Spearman correlation coefficients (ρ). Adherence between patients who used or did not use each medication organization strategy was compared using chi-square tests for the pharmacy-fill and self-report dichotomous adherence measures, and Wilcoxon-Mann–Whitney tests for the continuous pill count measure. The study was approved by the institutional review board. All statistical analysis used SAS version 9.4.

Results

Of the 731 participants included in our sub-study, 38.3% self-identified as male gender, 51.7% were aged 65 or older, and 52.9% self-identified as Black or African American race (Table 1).

Table 1 Characteristics of Study Population

Study Demographics*	% (N)
Gender (self-report)	
Male	38.3% (279)
Female	61.3% (447)
Transgender	0.3% (2)
Non-Binary	0.1% (1)
Age (years)	
<45	7.3% (53)
45–54	12.3% (90)
55–64	28.7% (210)
65–74	32.4% (237)
75+	19.3% (141)
Race (self-report)	
White or Caucasian	47.1% (344)
Black or African American	52.9% (387)

(*Continued*)

Table 1 (Continued).

Study Demographics*	% (N)
Highest Level of Education	
Less than High School	4.4% (32)
High School Diploma or equivalent	22.3% (162)
Some College, no degree	25.5% (185)
College Degree	47.8% (347)
Employment Status	
Employed	37.8% (275)
Unemployed	5.1% (37)
Retired	45.3% (329)
Disabled	11.8% (86)
Insurance Status	
Medicaid	16.7% (121)
Medicare	34.3% (248)
Commercial (High-deductible, Self-funded)	36.9% (267)
Uninsured/Self-Pay	0.3% (2)
Other	5.4% (39)
Medicaid and Medicare	6.5% (47)
Marital Status	
Married/Partnered	43.3% (311)
Unmarried	56.7% (407)
Living Status	
Lives Alone	32.5% (235)
Lives with other(s)	67.5% (488)
Difficulty in Paying for Basic Necessities	
Very Difficult	11.1% (77)
Somewhat Difficult	26.5% (184)
Not Difficult at All	62.4% (434)
Number of Blood Pressure Medications	
One	54.0% (391)
Two	28.3% (205)
Three	11.7% (85)
Four or more	5.9% (43)

(*Continued*)

Table 1 (Continued).

Study Demographics*	% (N)
Number of Pill Organization Strategies Used	
0	17.5% (128)
1	34.2% (250)
2	37.4% (273)
3	10.3% (75)
4	0.7% (5)

Notes: *Less than 2% of the participants were missing data on gender, highest level of education, employment status, insurance status, marital status, living status, and number of blood pressure medications. "Difficulty paying for basic necessities" is missing for 5% of the participants.

The majority (82.5%) of participants reported using at least one of four medication organization strategies, and 48.3% reported using two or more strategies (Table 1). Of the strategies studied, 51.7% reported finishing previous refills first before opening a new bottle, 46.5% move pills into a pill dispenser, 38.2% combine same prescriptions and 6.0% combine dissimilar prescriptions. Patients rarely endorsed the other factors that may influence adherence with the most common being "taking a different dose than bottle instructs per doctor's order" (9.3% of the participants) (Table 2).

Although not all participants had all three measures of adherence for analysis, all participants had at least one adherence measurement. Data for adherence measurement were available for 595 (81.4%) patients by pill counts, 674 (92.2%) patients by pharmacy-fill, and 720 (98.5%) by self-report. Adherence levels at enrollment varied by measurement: pill count adherence median 0.65 (IQR 0.45–0.87), pharmacy-fill 75.7% adherent, and self-report 63.2% adherent. The adherence measures were not strongly correlated with one another (All $\rho < 0.15$).

When assessing the association of pill organization strategies with adherence, patients who combined same prescriptions had lower adherence by pill count compared to those who did not (Median [IQR] 0.56 [0.26–0.82], vs 0.70 [0.46–

Table 2 Pill Organization Survey Questions and Response Frequency

Pill Organization Strategies	Response Frequency* (N=731)
Finish previous refills first: "I get a new refill but continue taking leftover pills from a previous refill until they are used up before starting the new bottle"	51.7% (378)
Use a pill dispenser: "I move pills into a pill dispenser, sorter, or other container"	46.5% (340)
Combine same prescriptions: "I combine new pills with pills from a prior refill of the same medicine"	38.2% (279)
Combine dissimilar prescriptions: "I combine pills from multiple prescriptions/medicines"	6.0% (44)
Other Factors That May Influence Adherence	**Response Frequency* (N=731)**
Took pills as needed because of clinician instructions: "My doctor told me to take my pills as needed, or to achieve a specific blood pressure target"	5.6% (41)
Shares pills: "I sometimes share my pills with others"	0.4% (3)
Takes different dose than bottle instructs, doctor's order: "My doctor told me to take my pills differently than the prescription/pill bottle states (for example, they told me to double the pills or cut pills in half)"	9.3% (68)
Takes different dose than bottle instructs, self-choice: "I typically take a different dose (for example, a different number of pills) than what my doctor told me to take"	3.7% (27)

Notes: *Each participant could select multiple strategies and the frequencies will total over 100%.

0.90], P<0.01). No association was seen between combining same prescriptions and pharmacy-fill adherence (78.1% adherence in those who used strategy vs 74.0% in others, p=0.22) or self-reported adherence (63.0% adherence in those who used strategy vs 63.3% in others, p = 0.93). No significant relationships were found between the other pill organization strategies and the three adherence measures (Table 3).

Among the other measured factors that may influence adherence, participants who endorsed taking a different dose than the bottle instructs per their choice had significantly lower pharmacy-fill adherence than those who did not report

Table 3 Adherence by Pill Organization Strategy

Strategies to Organize Pills	Survey Response	Pill Count Median*	Pharmacy- Fill % Adherent†	Self-Report % Adherent‡
Combine Same Prescriptions	Yes	0.56	78.1%	63.0%
	No	0.70	74.0%	63.3%
		P = <0.01	P = 0.22	P = 0.93
Finish Previous Pills First	Yes	0.64	74.7%	63.1%
	No	0.67	76.7%	63.3%
		P = 0.81	P = 0.54	P = 0.94
Combine Dissimilar Prescriptions	Yes	0.66	69.8%	54.5%
	No	0.65	76.1%	63.8%
		P = 0.72	P = 0.35	P = 0.22
Move Pills into Pill Dispenser	Yes	0.64	75.9%	65.2%
	No	0.66	75.5%	61.5%
		P = 0.21	P = 0.91	P = 0.30
Other Effects on Adherence Measurement	**Survey Response**	**Pill Count Median***	**Pharmacy-Fill % Adherent†**	**Self-Report % Adherent‡**
Shares Pills	Yes	0.45	66.7%	50.0%
	No	0.65	75.7%	63.2%
		P = 0.46	P = 0.57	P = >0.99
Takes Pills as Needed, Doctor's Order	Yes	0.67	74.3%	61.5%
	No	0.64	75.7%	63.3%
		P = 0.68	P = 0.84	P = 0.83
Takes Different Dose Than Bottle Instructs, Doctor's Order	Yes	0.68	73.4%	68.7%
	No	0.64	75.9%	62.6%
		P = 0.67	P = 0.66	P = 0.33
Takes Different Dose Than Bottle Instructs, Self-Choice	Yes	0.67	54.2%	48.1%
	No	0.65	76.5%	63.8%
		P = 0.45	P = 0.01	P = 0.10

Notes: *Median of group measured 0.0–1.0 calculated as ratio of pills present over predicted. †Dichotomous variable of proportion of days covered (PDC), Adherent = ≥90%, non-Adherent = <90%. ‡Self-report adherence: calculated based on 7-day average adherence to medication, self-reported by 3-question adherence survey (VOILS).

this behavior (54.2% versus 76.5%, P=0.01). Self-reported adherence tended to be lower in this group but was not statistically significant (48.1% vs 63.8%, p = 0.10). No difference in pill count adherence was associated with this or other behaviors (Table 3).

Discussion

In a trial examining medication adherence in patients with hypertension, our findings highlight that 1) patient pill organization strategies are common; 2) adherence varies according to the measure of adherence used; and 3) patient pill organization strategies are largely unrelated to adherence measures with a few important exceptions. The most common strategies of finishing a previous bottle before starting the next and moving pills to a pill dispenser were not associated with differences in adherence measures. Yet the third most common strategy, combining same prescriptions into a single bottle, was associated with significantly lower pill count adherence but not pharmacy or self-reported adherence. Finally, when examining other possible factors that may influence adherence, patients who reported taking a different dose than the bottle instructs per their choice (3.7% of the participants) had significantly lower pharmacy-fill adherence and tended to have lower self-reported adherence that was not statistically significant. Our findings highlight the importance of understanding how patients organize their medications at home as these strategies are associated with some adherence measures but not others.

Like prior studies, we found that adherence estimates are dependent on the method used and each has limitations.[5,19] As our findings highlight, pill counts can be underestimated when patients combine same prescriptions into a single bottle. Pill counts also rely on patients bringing their bottles to appointments and was missing in 19% of our participants. Pharmacy-fill information is another objective way to measure adherence but is affected by structural influences of the health care system (eg, refill reminders, automated refills, access to care) and cannot account for medication which was refilled but not ingested.[5,20–22] Self-reported adherence relies on a 7-day recall for behavior and may be significantly influenced by social desirability and recall biases.[23] Similar to other studies, we found no strong association between our three measures of adherence.[24] Studies have shown that prescription fill records and electronic medication bottle lids (records each opening of the bottle) were in higher agreement compared to self-reported adherence.[14] Yet, a review of 31 different studies evaluating medication adherence in hypertension found most studies had used self-reported adherence.[25] Taken together, our findings and others highlight the importance of considering the advantages and disadvantages of different medication adherence estimates.[5,26]

To our knowledge, our study is one of the first to evaluate patient pill organization strategies and their associations with common adherence measures used in clinical practice and pragmatic research studies. We demonstrated that common pill organization strategies are not associated with most measures of adherence with a few important exceptions. Combining same prescriptions was associated with significantly lower adherence measured by pill count but was not significantly associated with pharmacy-fill or self-reported adherence. This finding is not unexpected as combining prescriptions results in an artificially inflated pill count (ie, extra pills added to new bottle resulting in more pills than expected) despite a patient still taking the correct dose each day. Combining prescriptions would not be expected to influence pharmacy refill estimates of adherence given the longer duration (eg, 30- to 90-day window) of observed behavior for typical pharmacy refills. Further, self-report would not be influenced by combining prescriptions into a single bottle as in the end, the patient would still report taking the same number of pills over that 7-day window. It is harder to speculate why taking a different dose per patient choice was only significantly associated with lower pharmacy-fill adherence and no other measures, possibly secondary to different periods of observation (pharmacy-fill being longer). This same behavior was associated with lower self-report adherence, although not significantly. Overall, this behavior was not common (3.7% of the participants), and we are likely underpowered to find significant differences. Notably, we found no significant association with any of the medication organization strategies and self-reported adherence, one of the most common measures of medication adherence.[27,28] Our findings highlight the possibility that self-reported adherence may be impervious to certain pill organizing strategies because the patient takes this into account in their report, indicating a possible advantage of self-reported adherence over other measures.

Limitations

The strengths of this study include an assessment of the interplay between patient pill organization strategies and different adherence measurements; however, its limitations should be noted. The study was observational and cross-sectional, with the assessment of pill organization strategies and medication adherence occurring at the same time, disallowing causal conclusions. While this study examined four common strategies and other factors thought to influence adherence, other less common yet important strategies may be missed. We did not include other common measures of adherence, such as electronic medication monitors. Lastly, while we highlight the association of patient pill organization strategies with adherence, the significance of patient pill organization strategies on other clinical outcomes was not assessed.

Conclusion

In summary, among participants in a clinical trial, over 80% used at least one pill organization strategy. Pill organization strategies were not associated with most measures of adherence with a few important exceptions. Combining same prescriptions was associated with significantly lower pill count measured adherence. Taking a different dose than prescribed, per patient choice was significantly associated with lower pharmacy-fill adherence. No pill organization strategy was significantly associated with self-reported adherence suggesting this measure may have certain advantages over pill count and pharmacy fill measured adherence. Our study highlights the importance of considering the ways in which patients organize their medications at home when estimating patient adherence to treatment. Future studies are needed to assess whether medication organization strategies have clinically significant effects on treatment outcomes of chronic disease.

Data Sharing Statement

Upon request, we will make the a deidentified limited dataset available to users only under a data-sharing agreement between participating institutions that provides for 1) a commitment to using the data only for research purposes and not to identify any individual participant; 2) a commitment to securing the data using appropriate computer technology; and 3) a commitment to destroying or returning the data after analyses are completed. The data used in this study may include confidential or proprietary information of participating health systems which may not be publicly shared or disclosed. The data sharing agreement will assure that health system privacy policies are followed and the analysis being proposed is appropriate given the design and data available. Please contact Dr Stacie Daugherty at Stacie.L.Daugherty@kp.org regarding access to the additional data.

Study Ethics and Informed Consent

The principal investigators ensured the conduct of and oversight for the study according to the National Institutes of Health (NIH) and national policies. The institutional review boards (IRBs) for the University of Colorado School of Medicine and Denver Health (the Colorado Multiple Institutional Review Board), Kaiser Permanente Colorado, and Kaiser Permanente Mid-Atlantic States reviewed and approved the study.

Prior to study commencement, patient informed consent was obtained in a clinic examination room or other private area to allow the process to be private and confidential. Following discussion of the nature, risks, and possible benefits of the study, patient participants were asked to sign written informed consent as approved by the IRB for their respective health system. The consent process explicitly stated the decision on whether to participate in the study will in no way affect current or future care. The consent process was carried out by research staff, not clinical personnel, further decoupling the research and patients' usual care.

Previous Presentation

Poster: Society of General Internal Medicine Annual Conference; April 21, 2021

Author Contributions

All listed authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. We would also like to acknowledge the contribution from the following individuals: Cozette Boakye, Cassandra Bryant, Suzanne Dircksen, Hilde Heyn, Jennifer McCance, Courtney Anderson, Amanda Skenadore, Christine Truong, and Leslie Wright. We would like to thank the participants of the HYVALUE (HYpertension and VALUEs) Trial. Dr Stacie L. Daugherty and Ms Laura Helmkamp had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

This study and all authors are supported by R01 HL133343 from the National Heart, Lung, and Blood Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosure

Dr Stacie L. Daugherty is also supported by NIH grant DC0169065, NIH grant HL164106, a grant from PCORI and serves on a DSMB for another NHBLI funded trial; also reports royalties for review of cardiovascular risk factors in women from UpToDate. Dr John F. Steiner is supported by research funding from the National Institute of Diabetes, Digestive and Kidney Diseases (grant # P30DK092923) and by internal research funding from Kaiser Permanente. Dr Suma Vupputuri is supported by research funding from Sanofi, Inc. All other authors report no additional conflicts in relation to this manuscript.

References

1. Al-Noumani H, Wu JR, Barksdale D, Knafl G, AlKhasawneh E, Sherwood G. Health beliefs and medication adherence in omanis with hypertension. *J Cardiovasc Nurs*. 2018;33(6):518–526. doi:10.1097/JCN.0000000000000511
2. Shang P, Liu GG, Zheng X, et al. Association between medication adherence and 1-year major cardiovascular adverse events after acute myocardial infarction in China. *J Am Heart Assoc*. 2019;8(9):e011793. doi:10.1161/JAHA.118.011793
3. Shahin W, Kennedy GA, Stupans I. The impact of personal and cultural beliefs on medication adherence of patients with chronic illnesses: a systematic review. *Patient Prefer Adherence*. 2019;13:1019–1035. doi:10.2147/PPA.S212046
4. Levy AE, Huang C, Huang A, Michael HP. Recent approaches to improve medication adherence in patients with coronary heart disease: progress towards a learning healthcare system. *Curr Atheroscler Rep*. 2018;20(1):5. doi:10.1007/s11883-018-0707-0
5. Lam WY, Fresco P. Medication adherence measures: an overview. *BioMed Res Int*. 2015;2015:217047. doi:10.1155/2015/217047
6. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation*. 2009;119(23):3028–3035. doi:10.1161/CIRCULATIONAHA.108.768986
7. Kini V, Ho PM. Interventions to improve medication adherence: a review. *JAMA*. 2018;320(23):2461–2473. doi:10.1001/jama.2018.19271
8. Ferdinand KC, Yadav K, Nasser SA, et al. Disparities in hypertension and cardiovascular disease in blacks: the critical role of medication adherence. *J Clin Hypertens*. 2017;19(10):1015–1024. doi:10.1111/jch.13089
9. Basu S, Garg S, Sharma N, Singh MM. Improving the assessment of medication adherence: challenges and considerations with a focus on low-resource settings. *Ci Ji Yi Xue Za Zhi Tzu-Chi Med J*. 2019;31(2):73–80. doi:10.4103/tcmj.tcmj_177_18
10. Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of literature. *J Behav Med*. 2008;31(3):213–224. doi:10.1007/s10865-007-9147-y
11. Daugherty SL, Helmkamp L, Vupputuri S, et al. Effect of values affirmation on reducing racial differences in adherence to hypertension medication: the HYVALUE randomized clinical trial. *JAMA Netw Open*. 2021;4(12):e2139533. doi:10.1001/jamanetworkopen.2021.39533
12. Daugherty SL, Vupputuri S, Hanratty R, et al. Using values affirmation to reduce the effects of stereotype threat on hypertension disparities: protocol for the multicenter randomized Hypertension and Values (HYVALUE) trial. *JMIR Res Protoc*. 2019;8(3):e12498. doi:10.2196/12498
13. Choo PW, Rand CS, Inui TS, et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. *Med Care*. 1999;37(9):846–857. doi:10.1097/00005650-199909000-00002
14. Hansen RA, Kim MM, Song L, Tu W, Wu J, Murray MD. Adherence: comparison of methods to assess medication adherence and classify nonadherence. *Ann Pharmacother*. 2009;43(3):413–422. doi:10.1345/aph.1L496
15. Steiner JF, Prochazka AV. The assessment of refill compliance using pharmacy records: methods, validity, and applications. *J Clin Epidemiol*. 1997;50(1):105–116. doi:10.1016/S0895-4356(96)00268-5
16. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records. Description and validation. *Med Care*. 1988;26(8):814–823. doi:10.1097/00005650-198808000-00007
17. Voils CI, Maciejewski ML, Hoyle RH, et al. Initial validation of a self-report measure of the extent of and reasons for medication nonadherence. *Med Care*. 2012;50(12):1013–1019. doi:10.1097/MLR.0b013e318269e121
18. Steiner JF. Self-reported adherence measures: what do they assess and how should we use them? *Med Care*. 2012;50(12):1011–1012. doi:10.1097/MLR.0b013e318270abaf
19. Wu P, Johnson BA, Nachega JB, et al. The combination of pill count and self-reported adherence is a strong predictor of first-line ART failure for adults in South Africa. *Curr HIV Res*. 2014;12(5):366–375. doi:10.2174/1570162x1205141121102501

20. Polinski JM, Schneeweiss S, Levin R, Shrank WH. Completeness of retail pharmacy claims data: implications for pharmacoepidemiologic studies and pharmacy practice in elderly patients. *Clin Ther*. 2009;31(9):2048–2059. doi:10.1016/j.clinthera.2009.09.009
21. Fontanet CP, Choudhry NK, Isaac T, et al. Comparison of measures of medication adherence from pharmacy dispensing and insurer claims data. *Health Serv Res*. 2021;57(3):524–536. doi:10.1111/1475-6773.13714
22. Haramiova Z, Stasko M, Hulin M, Tesar T, Kuzelova M, Morisky DM. The effectiveness of daily SMS reminders in pharmaceutical care of older adults on improving patients' adherence to antihypertensive medication (SPPA): study protocol for a randomized controlled trial. *Trials*. 2017;18(1):334. doi:10.1186/s13063-017-2063-8
23. Stirratt MJ, Dunbar-Jacob J, Crane HM, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. *Transl Behav Med*. 2015;5(4):470–482. doi:10.1007/s13142-015-0315-2
24. Durand H, Hayes P, Harhen B, et al. Medication adherence for resistant hypertension: assessing theoretical predictors of adherence using direct and indirect adherence measures. *Br J Health Psychol*. 2018;23(4):949–966. doi:10.1111/bjhp.12332
25. Bochkareva EV, Butina EK, Kim IV, et al. Adherence to antihypertensive medication in Russia: a scoping review of studies on levels, determinants and intervention strategies published between 2000 and 2017. *Arch Public Health*. 2019;77:43. doi:10.1186/s13690-019-0366-9
26. Grymonpre RE, Didur CD, Montgomery PR, Sitar DS. Pill count, self-report, and pharmacy claims data to measure medication adherence in the elderly. *Ann Pharmacother*. 1998;32(7–8):749–754. doi:10.1345/aph.17423
27. Velligan DI, Wang M, Diamond P, et al. Relationships among subjective and objective measures of adherence to oral antipsychotic medications. *Psychiatr Serv*. 2007;58(9):1187–1192. doi:10.1176/ps.2007.58.9.1187
28. Vik SA, Maxwell CJ, Hogan DB. Measurement, correlates, and health outcomes of medication adherence among seniors. *Ann Pharmacother*. 2004;38(2):303–312. doi:10.1345/aph.1D252