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Factors associated with false-positive self-reported adherence to antihypertensive drugs.

Yacob G. Tedla, PhD, MSc[a] and **Leonelo E. Bautista, MD, MPH, DrPH**[b]

[a]Department of Preventive Medicine, Northwestern University, 680 N Lake Shore Drive Suit 1400, Chicago, IL 60611, United States.

[b]Department of Population Health Sciences, University of Wisconsin at Madison, 610 Walnut Street, WARF 703, Madison, WI 53726 WI, United States.

Abstract

Self-reported medication adherence is known to overestimate true adherence. However, little is known about patient factors that may contribute to the upward bias in self-reported medication adherence. The Objective of this study is to examine whether demographic, behavioral, medication, and mood factors are associated with being a false positive self-reported adherer (FPA) to antihypertensive drug treatment. We studied 175 patients (mean age: 50 years; 57% men) from primary care clinics starting antihypertensive drug treatment. Self-reported adherence was measured with the medication adherence report scale (MARS) and by the number of drug doses missed in the previous week/month and compared to pill count adherence (PCAR) as gold standard. Data on adherence, demographic, behavioral, medication, and mood factors were collected at baseline and every three months up to 1 year. FPA was defined as being non-adherer by PCAR and adherer by self-report. Mixed effect logistic regression was used for the analysis. Twenty percent of participants were FPA. Anxiety increased (odds ratio -OR: 3.00; *P*=0.01), while smoking (OR: 0.40; *P*=0.03), and drug side effects (OR: 0.46, *P*=0.03) decreased the probability for FPA by MARS. An educational below completed high school increased the probability of being a FPA as measured by missing doses in the last month (OR: 1.66; *P*=0.04) and last week (OR: 1.88; *P*=0.02). The validity of self-reported adherence varies significantly according to drug side effects, behavioral factors, and patient's mood. Careful consideration should be given to the use of self-reported measures of adherence among patients likely to be false-positive adherers.

Keywords

Medication adherence; Patient compliance; Self-reported adherence; False-positive adherers; Hypertension

Address correspondence to: Yacob G. Tedla, PhD, MSc, Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, 680 N Lake Shore Drive Suite 1400, Office # 14-030, Chicago, IL 60611, Phone: (608) 395- 9696, yacob.tedla@northwestern.edu.

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INTRODUCTION

Accurate assessment of medication adherence is essential to understand the impact of treatment on disease outcomes and to make decisions about when to change treatment regimens.[1] Self-reported adherence consistently overestimates adherence when compared to objectively measured.[2, 3] Consequently, being a false positive self-reported adherer (i.e. being classified as adherent based on self-report and as non-adherent based on a more objective measurement) is a common occurrence.[2, 3] For instance, in a study among hypertensive patients on a single-drug therapy, the frequency of non-adherence was 21% when measured by self-report and 42% when measured with electronic cap bottles (i.e. missed ≥1 doses in >1 day/week).[4] In spite of its low accuracy, patient self-report is commonly used to measure medication adherence, particularly in clinical settings, because it is easy to implement and has a low cost.[5, 6]

Little is known about patient factors that may contribute to the upward bias in self-reported medication adherence. Social desirability bias (responding in a culturally appropriate and acceptable manner[7]) is considered as a main contributor to false positive self-report of good adherence.[5, 8] Indeed, self-reported adherence has been found to be lower and a better predictor of treatment outcomes (HIV RNA copies/ml) among HIV infected patients with a low tendency than in those with a high tendency towards socially desirable responses.[8] Social desirability bias is more frequent among the elderly, women, minority, less educated individuals,[9, 10] and among those with low socio-economic status.[11, 12] In contrast, social desirability bias is less frequent among individuals with symptoms of anxiety and depression[12, 13] and among alcohol and illicit drugs users.[11, 12] Therefore, it is reasonable to postulate that these factors may be associated with a higher likelihood of a false positive self-report of good adherence.

In this study, we explored whether demographics factors (age, sex, race, education, marital status, income), behavioral factors (smoking, alcohol intake), medication factors (number of BP pills prescribed to be taken per day, number and severity of side-effects, drug copayment, and medication for other conditions), and mood factors (symptoms of anxiety and depression) were associated with a false positive self-report of good adherence using three commonly used self-reported measurements of adherence among hypertensive patients who have started or restarted treatment after stopping for ≥2 months. In addition, we assessed the validity of three self-reported measurements of adherence using pill count adherence as a gold-standard test.

METHODS

Study Design

We used data from a longitudinal study of the role of symptoms of depression and anxiety on adherence to antihypertensive medication among individuals starting or re-starting treatment for essential hypertension.[14] The original study was approved by the University of Wisconsin Madison Institutional Review Board and informed consent was obtained from all participants.

Participants

Individuals were eligible if they had essential hypertension (systolic blood pressure ≥140 or diastolic BP ≥90 mm Hg, based on the mean from two or more clinic visits)[15] and started receiving antihypertensive treatment for the first time (within one week before enrollment into the study) or re-started treatment after stopping for more than 2 months. Individuals <20 or ≥70 years old, those with secondary hypertension, self-reported history of chronic kidney disease, hepatitis, cancer, diabetes, rheumatoid arthritis, psychiatric disease requiring drug treatment, coronary heart disease, congestive heart failure, taking mood-modifying medications, and pregnant women were not eligible.

Cohort recruitment and follow-up

Participants were recruited (visit 0) from clinics in the Department of Family Medicine at the University of Wisconsin Madison and the Wisconsin Research and Education Network. Follow-up visits were conducted at 3 (visit 1), 6 (visit 2), 9 (visit 3), and 12 (visit 4) months after enrollment. Individuals who did not come to a follow-up visits after three invitations were considered missing. No further follow-up visits were scheduled for participants who completely stopped taking their antihypertensive drug for two consecutive follow-up visits. Time-fixed variables, such as gender, were measured only at baseline. All other time-depending variables were measured both at baseline and at each follow-up visit.

Measurements

Predictor variables—Demographics and economic factors (age, sex, race, education, marital status, and annual family income) were ascertained using a questionnaire at the time of enrolment. Also, at baseline and at each follow-up evaluation, participants were asked about smoking (current smoking and number of cigarettes smoked per day), alcohol intake (current drinking and number of drinks per week), and if they were taking medication for other condition and had any copayment for prescription medications.

Severity of depression and anxiety symptoms were evaluated at enrollment and follow-up visits using the Beck Depression Inventory-II (BDI-II)[13] and the anxiety sub-scale of the Psychological General Well-Being Index (PGWB),[16] respectively. The BDI-II has 21 items and the response for each item ranged from 0 (not experiencing the symptom) to 3 (extremely experiencing the symptom). The anxiety sub-scale of the PGWB includes 5 questions and response to the questions ranged from a scale of 0 (not at all experiencing the symptom) to 5 (extremely experiencing the symptom). Higher scores on BDI-II indicates higher risk of depression. PGWB scores were reverse coded so that high scores corresponded to higher risk of anxiety. Reliability and validity of the BDI-II and PGWB have been demonstrated in previous studies.[17, 18]

Twenty four side effect symptoms related to the use of antihypertensive medications were ascertained at each visit using a subset of questions from the Physical Symptoms Distress Index (PSDI).[19] The PSDI has been successfully used to evaluate medication side effects in hypertensive patients.[20] Participant were asked if they had a symptom in the past month (yes or no). Those who had the symptoms, rated the frequent from 1 (1–2 times per month) to 4 (almost daily) and the severity from 0 (not at all bothered) to 4 (extremely bothered). Scores

for presence, severity and frequency of each symptom was multiplied and the resulting values were summed up to create an overall symptom distress (OSD) score. This scoring approach has been successfully used in previous studies among hypertensive patients.[20, 21]

Medication adherence—Participants were asked to bring their antihypertensive medication bottles to each study visit. Data on the name, number of remaining pills in the bottle, and number of prescribed pills of each antihypertensive medication were collected at enrollment and follow-up visits. Pill count adherence ratio (PCAR) was calculated as the proportion of pills taken out of the total number of pills prescribed between two consecutive visits, i.e., (pills taken ÷ pills prescribed)×100.[21] Following current practice, participants were considered adherent if they took ≥80% of the prescribed number of pills (PCAR≥80%). This cut-point has been shown to correlate well with urinary levels of diuretics and changes in blood pressure.[22]

Self-reported medication adherence was ascertained using three different tools during each follow-up visit. We used the Medication Adherence Report Scale (MARS)[10] - a five-item scale that ask patients whether they regularly stop or forget taking their medication, alter the dose, purposely miss a dose, or take less medication than prescribed. The response for each item is rated on a five-point scale (5=never, 4=rarely, 3=sometimes, 2=often, and 1=very often). The total score for the five items ranges from 5 to 25 and following previous studies, participants were considered adherent if their MARS total score was ≥23.[23, 24] A sensitivity analysis was made with a MARS cut points of ≥22 and ≥24. Our findings were consistent across these cut-points (Supplemental Table 1). MARS has been found to have acceptable reliability with a Cronbach's alpha value of 0.75 and a test-retest correlation of 0.72.[25] However, MARS had a sensitivity of only 57.1% when adherence was defined as a total score of >23 on MARS and compared to a PCAR≥80% from an electronic cap pill bottle.[24]

Self-reported adherence during the last month (SRA-1M) was measured by asking participants to score how often they missed a dose of their antihypertensive medication during the last month: 0=never, 1=rarely, 2=sometimes, 3=often and 4=almost daily. Participants who reported never or rarely missing a dose in the previous month were considered adherers for that month. Self-reported adherence during the last week (SRA-1W) was ascertained by asking patients how many times (0 to 7) they missed a dose of their blood pressure lowering drug during the last week. Patients who missed a dose ≤41 during the last week were considered adherers. These cut-off points to identify adherers and non-adherers were chosen because they had the highest agreement with MARS score in our data (87.9% agreement and 0.4 Cohen's kappa for SRA-1M and 88.5% agreement and 0.4 Cohen's kappa for SRA-1W).

False positive self-reported adherers—For each follow-up visit, participants were grouped into: (i) those who were classified into the same adherence category based on PCAR and each of the self-reported measurements (*concordant*); (ii) those who were identified as adherent on self-reported measurements and as non-adherent based on PCAR (*false positive self-reported adherer*); and (iii) those who were classified as non-adherer based on the self-reported measurements and as adherent based on PCAR (*false negative self-reported adherers*). Adherence based on self-report is known to be consistently higher

than objectively measured adherence, and the measurement error is systematically unidirectional toward over-reporting.[4, 5] Consequently, false negative self-reported adherers would be few if they exist at all.[4, 5] In our study, MARS had a higher proportion of false negative adherers than SRA-1M and SRA-1W, but the average number of false negative adherers for MARS was only eight and ranged from fourteen at visit 1 to five at visit 3.

Analysis

We used the actuarial (life table) method to estimate the cumulative risk of becoming non-adherent through the whole period of follow-up.[26] First, we estimated the risk of remaining adherent separately within each period, multiplied these period-specific risks to obtain a cumulative risk of adherence over the whole period of follow-up, and we estimated the cumulative risk of non-adherence as 1 minus the cumulative risk of adherence.

Validity of MARS and reported adherence in the previous month and week in identifying non-adherers was evaluated by calculating sensitivity, specificity, predictive value, Cohen's kappa coefficient, and area under the curve (AUC) using PCAR as the reference test.

We used stepwise random effects logistic regression to obtain population-averaged estimates of the association between the risk factors and being a false positive self-reported adherer. A stepwise approach for variable selection is appropriate in this case because our main goal was to obtain predictors of an outcome. Variables that had a p-value of ≤ 0.3 in univariate (crude) models were chosen to enter into the multivariate model. A rejection criterion of p-value > 0.1 was then used to remove variables from the model, one at a time, starting with the one that had the largest p-value. Thus, all variables in the final model had a p-value ≤0.1. Three separate analyses were made for the outcome (being a false positive adherer), in correspondence to the three self-reported adherence: MARS, SRA-1M or SRA-1W. We obtained robust estimates of the standard errors of the regression coefficients in all models to account for the repeated measures of the outcome.[27] The predictive capacity of the final models were assessed by plotting receiver operating characteristic (ROC) curves based on the model predictions and calculating corresponding area under the (AUC).[28] All analyses were performed using Stata 13 (StataCorp LP. 2013, TX).[29]

RESULTS

Participant characteristics.

A total of 214 patients were recruited in the original study.[14] The number of individuals who had complete data on *both* PCAR and MARS, and were classified as either false positive self-reported adherers, false negative self-reported adherers or concordant were 157 at 3 months, 116 at 6 months, 96 at 9 months, and 80 at 12 months. Those with complete data on *both* PCAR and SRA-1M/SRA-1W were 156 at 3 months, 115 at 6 months 96 at 9 months, and 79 at 12 months. Overall, compared to those who were correctly classified (concordant), false positive adherers were more likely to have less than high school education, to be heavy drinkers (>14 drinks/week for men and >7 drinks/week for women), to have a high anxiety score, lower blood pressure, to take more than one antihypertensive pills, and to report poor or fair health status (Table 1).

Among the 156 participants with complete data on both PCAR and MARS at visit 1, 72% (n=112) were taking 1 antihypertensive pill per day and among those 13 patients were taking a two-drugs pill and two patients were taking a three-drug pill. Another group of 29 participants (18.5%) were taking two pills per day that included a single-drug treatment in 14 patients, two-drugs treatment in 12 patients, and three-drugs treatment in three patients. The remaining 15 participants were taking three or more pills per day that included one-, two- and three drugs-treatment in four, eight and three patients, respectively. The distribution was similar among participants with complete data on both PCAR and SRA-1M/SRA-1W.

Over the study period, average PCAR was 93% (95% confidence interval (CI): 89.5, 96.5) and mean MARS score was 23.7 (95% CI: 23.2, 24.1). The risk of becoming non-adherent based on PCAR was 29.9% at visit 1, 19.8% at visit 2, 17.7% at visit 3, and 18.7% at visit 4. MARS non-adherence (total score <23) risk was 15.4% at visit 1, 11.3% at visit 2, 11.9% at visit 3, and 14.3% at visit 4; SRA-1M non-adherence risk (never or rarely missing a dose) was 6.9% at visit 1, 8.3% at visit 2, 11.0% at visit 3, and 14.4% at visit 4; while SRA-1W non-adherence risk (missed >1 dose/week) was 8.1% at visit 1, 6.1% at visit 2, 6.4% at visit 3, and 14.4% at visit 4. The cumulative risk of non-adherence calculated using the actuarial method[26] was 62.4% (95% CI: 45.2%, 75.3%) for PCAR, 43.4% (95% CI: 25.7%, 57.7%) for MARS, 35.1% (95% CI: 17.5%, 49.7%) for SRA-1M, and 30.8% (95% CI: 14.0%, 45.2%) for SRA-1EW.

Validity indices of self-reported adherence compared to pill count adherence.

The sensitivity to detect non-adherent participants was 19.6% for MARS, 16.8% for SRA-1M, and 15.8% for SRA-1W, while specificity was 89.9% for MARS, 92.8% for SRA-1M, and 94.2% for SRA-1W across all the visits. Positive predictive value was 34.6%, 40.5%, and 44.5% for MARS, SRA-1M and SRA-1W, respectively, during the whole study period. The proportion of false positive adherers was 19.9% (range: 14.3%−27.3%) for MARS, 20.0% (range: 12.3%−27.0%) for SRA-1M, and 20.0% (range: 10.8%−28.2%) for SRA-1W for the whole study period. The observed percent agreement and the chance-adjusted percent agreement (Cohen's kappa) with PCAR were 73.9% and 11.4% for MARS, 75.5% and 12.1% for SRA-1M, and 76.5% and 13.0% for SRA-1W (Table 2). Moreover, the overall ability of MARS, SRA-1M and SRA-1W to discriminate between adherent and non-adherent patients, was only slightly better than chance for all three measurements (AUC=0.55).

Factors associated with being a false positive self-reported adherer.

This analysis included individuals with data for at least one follow-up visit (n=143 for MARS, n=152 for reported adherence in the previous month, and n=149 for reported adherence in the previous week), who were identified either as false positive self-reported adherers (cases) or classified in to the same adherence category by both MARS and PCAR (non-cases). False negative self-reported adherers were excluded from this analysis.

In crude analysis, most of the potential predictors were not significantly associated with the risk of being a false-positive adherer (Table 3). Individuals in the 3rd tertile of anxiety score (3rd tertile) were about 2 times more likely to be false positive self-reported adherers than

those in 1st tertile (odds ratios -OR of 2.10 for MARS 2.04 for SRA-1M, and 2.18 for SRA-1W. Also, for SRA-1W the crude risk of being a false positive self-reported adherer was 2 times higher among individuals with self-reported poor or fair health status as compared to those with good health. Furthermore, for SRA-1M, the risk of being a false-positive adherer tended to be higher among those in the 2nd tertile as compared to in the 1st tertile of depression score (OR=1.63, *P-value*=0.08), and in those who did not complete high school (OR=1.53, *P-value*=0.09). Finally, for SRA-1W, the proportion of false positive self-reported adherer was higher among those who did not completed high school (OR=1.68, *P-value*=0.06) and those who were not employed (OR=1.86, *P-value*=0.08).

Variables retained in the final step-wise regression model (i.e. had *P*-value ≤ 0.1) were: anxiety (*P-value*=0.003), annual income (*P-value*=0.10), current smoking status (*P-value*=0.04), and antihypertensive drug side effects (*P-value*=0.04) for MARS; depression (*P-value*=0.03) and current smoking status (*P-value*=0.06) for SRA-1M; and anxiety (*P-value*=0.01) and high school incomplete (*P-value*=0.02) for SRA-1W. All these variables were simultaneously included in three separate models corresponding to MARS, SRA-1M, and SRA-1W.

Individuals with higher anxiety score consistently showed higher risk of being a false positive adherer in all self-reported measurements of adherence. The multivariate adjusted probability of being a false positive self-reported adherer was 3.0 times higher (95% CI: 1.36, 6.61) in patients in the 3rd as compared to the 1st tertile of anxiety score when MARS was used; 2.96 times higher (95% CI: 1.33, 6.61) when SRA-1M was used; and 3.48 times (95% CI: 1.5, 8.09) when SRA-1W was used (Table 4). Patient without a completed high school education were 1.66 times (95% CI: 1.03, 2.66) and 1.88 times (95% CI: 1.11, 3.20) more likely to be false positive adherers when SRA-1M and SRA-1W were used, respectively. Furthermore, there was a borderline higher risk for being a false positive adherer (OR=2.5, *P-value*=0.08) among individuals with annual family income of <$16,000 when adherence was measured with MARS.

On the other hand, the probability of being a false positive adherer was consistently lower among smokers and individuals who experienced antihypertensive drug side effects on all the three self-reported measurements of adherence (Table 4). For MARS, SRA-1M, and SRA-1W current smokers had a 60% (95% CI: 7%, 73%), 63% (95% CI: 17%, 83%) and 59% (95% CI: 6%, 82%) lower probability of being a false positive adherer than non-smokers, respectively. Participants who experienced antihypertensive drug side effects also had 55% (95% CI: 7%, 77%) lower probability of being a false positive adherer than those who did not experience side effects when MARS was used to measure adherence. There were similar associations when SRA-1M and SRA-1W were used to measure adherence, but they were of borderline statistical significance (OR=0.50, *P-value*=0.06; and OR=0.52, *P-value*=0.07, respectively). When all variables that had *P*-value ≤0.1 were simultaneously included in the models, area under the curve (AUC) was 0.66 when self-reported adherence measure was MARS and 0.67 when SRA-1M and SRA-1W were measures of reported adherence.

DISCUSSION

We assessed the performance of three commonly used approaches to measure self-reported adherence to antihypertensive medication as compared to pill count adherence, a more objective measurement of adherence. The three self-reported measurements of adherence had poor agreement with pill count. Classification of patients as adherers and non-adherers based on self-report was barely better than a random test, such as flipping a coin to decide whether a patients was adherent or not. These findings are consistent with those from previous studies showing that self-report is a poor method to measure adherence to treatment.[2–4] Furthermore, we found that the probability of being a false positive adherer in self-reported measurements was significantly higher among individuals with symptoms of anxiety and those with less than completed high school education, but lower among current smokers and those who experienced antihypertensive drug side effects.

Some but not all of our findings are consistent with those from the only published study of this issue among hypertensive patients, as far as we know. Choo et al.[4] investigated risk factors for over-reporting adherence, as compared to adherence measured using electronic pharmacy records, and found the risk to be 2.6 times higher among participants with annual income of <$15,000 and 1.4 times higher among those with lower perceived health risk. We found a significant increase of risks among individuals with self-reported poor or fair health status (OR=2.1, *P-value*=0.04) and among those with annual income <$16,000 (OR=2.50, *P-value*=0.08). Similar to our study, age, sex, and race were not predictors of being a false positive adherer in Choo et al's study.[4] On the contrary, the number of antihypertensive pills taken per day was associated with a false positive self-reported adherence in their study,[4] but not in ours. Also, in contrast to their study, less than completed high school increased the probability of a false positive self-report in our study. Choo et al.[4] used electronic pill bottle as objective measure among patients on a single blood pressure (BP) drug therapy. In our study, we used pill count among patients were taking one or more antihypertensive drugs. These differences may have contributed for some of the difference in the findings between ours' and Choo et al.'s study.

Our findings give support to the hypothesis of social desirability bias being a main contributor for false positive self-reported good adherence.[5, 30] In fact, individuals with low educational level and low income have a higher tendency to give socially desirable responses,[9, 10] and this could explain the higher risk of being a false positive adherer among patients who had not completed high school and those with an annual income below $16,000. Also, acknowledging alcohol and illicit drugs use has been negatively associated with social desirability bias.[11, 12] Thus, the lower risk of being a false positive adherer among current smokers in our study could be explained by their lower propensity to give a socially desirable response. In fact, individuals who admit being a smoker, a socially undesirable behaviour, may be also more likely to admit not taking their medications in the way it was prescribed.

We found a lower probability of being a false positive self-reported adherer among participants with at least one hypertension drug related side effect. Previously, we have shown that hypertensive patients who experienced ≥4 drug-related side effect symptoms

were more likely to become non-adherers (PCAR<80%).[21] Also, it has been found that a high percentage of patients (85%) who experience drug related side effects share their concerns about side effects with their physicians.[31] This suggests that patients with side effects may be also more open to admit not taking medication as prescibed, since they may not perceive a lack of adherence as their personal failure.

Even though anxiety is negatively associated with social desirability bias,[12, 13] we found an increased probability of being a false positive self-reported adherer among individuals with high anxiety score. Cognitive impairments and memory decline were shown to be common among young and older adults with anxiety disorders.[32, 33] Therefore, it is possible that anxious individuals may have been less likely to correctly remember and report missed doses of their antihypertensive medication due to declines in memory and cognitive functioning.

A higher tendency toward socially desirable responses is more likely among older individuals, women, and minorities.[9, 10] However, these variables were not associated with being a false positive self-reported adherer in our study. This lack of association could be explained by weak effects of these socio-demographic factors on social desirability bias. In addition, the impact of social desirability bias on over-reporting adherence by self-report could have been limited in this study because information on adherence was gathered through a questionnaire instead of being directly reported to a health care provider.

To the best of our knowledge, our study is only the second study that examined predictors of being a false positive self-reported adherer among hypertensive patients, and the first one to use multiple self-reported measurements of adherence commonly used in the clinical and research settings. The use of multiple self-reported measurements improves the generalizability of our findings. In addition, the repeated measurements of PCAR (every 3 months for up to a year) decreases the likelihood of misclassification errors, and increases the chance of capturing the patients' true level of adherence. Our study included newly treated and those who re-started treatment after stopping for ≥2 months. This should induce no bias, since previous treatment may exert its effect on being a false positive self-reported adherer through some of the predictors included in our regression models, such as drug side effects and smoking. In contrast, including previously treated patients likely enhanced the generalizability of our results.

One limitation of our study is the lack of validation of our stepwise regression model. Although we could have conducted a split sample analysis for validation,[34] our sample sizes for each aim were small to warrant the success of this approach. On the other hand, we fitted our stepwise regression model using continuous versions of variables that are naturally continuous (age, income, depression score, and anxiety score) and found the results were similar to those from the analysis with categorical versions of these variables. This indicates that the way these variables were coded did not influenced how significant they were in our final model.

In view of the selection criteria used in the parent study,[14] our findings may not be generalizable to hypertensive patients with chronic diseases and those taking mood-

modifying drugs. Although, elderly and minorities individuals are more likely to respond in a socially desirable way,[9, 10] our findings cannot be extrapolated to those groups because patients ≥70 years old were excluded and only 12% of the participants in the parent study were non-Whites. Pill count adherence is known to overestimate adherence compared to electronic pill bottles.[35] As a result, the proportion of false positive self-reported adherers could have been underestimated in our study. This error is probably non-differential and may have weakened some of the associations examined in our study.[36] Finally, there may be other factors, not measured in our study that may predict being a false positive self-reported adherer. For example, poor patient-physician relationship may force non-adherent patients to over-report their adherence because of fear of judgment from the health care providers. Future studies on this topic should ideally use larger sample sizes, use strategies for internal validation of regression models used in their analyses, and include novel potential predictors of false positive adherence.

In conclusion, self-reported measurements showed poor agreement with an objective measurement of adherence and performed poorly at identifying non-adherent patients. Among newly treated hypertensive patients, individuals who had symptoms of anxiety and those who had not completed high school were more likely, while current smokers and those who had at least one antihypertensive drug side effect were less likely to falsely report good medication adherence. Identifying factors likely to contribute to over-reporting of medication adherence is essential to reduce errors in the measurement of medication adherence. These factors may potentially be used as markers to screen out patients who are at high risk of falsely over-reporting adherence. Considering that the factors associated with a false positive self-reported good adherence are associated with social desirability bias, careful consideration should be given to the use of self-reported measures of adherence among patients who are prone to this type of bias.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is known about this topic

- Self-reported medication adherence is known to overestimate true adherence. Social desirability bias is considered as a main contributor to false positive self-report of good adherence.
- Social desirability bias is more frequent among the elderly, women, minority, less educated individuals, and those with low socio-economic status and less frequent among individuals with symptoms of anxiety and depression and among alcohol and illicit drugs users.

What this study adds

- We examined whether demographic, behavioral, medication, and mood factors are associated with being a false positive self-reported adherer to antihypertensive drug treatment. We found that falsely over-reporting adherence is more likely in patients with anxiety and low educational level and less likely among smokers and those who had BP drug side effects.
- Careful consideration should be given to the use of self-reported measures of medication adherence among patients who are likely to be false-positive adherers.

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Table 1.

Baseline characteristics of newly treated hypertensive patients by status of being a false positive self-reported adherer to prescribed drug treatment.

	Type of self-reported measurement of adherence								
	MARS			Previous Month Adherence			Previous Week Adherence		
	Concordant[a] (n=104)	False positive adherer[b] (n=39)		Concordant[a] n=111)	False positive[b] adherer (n=41)		Concordant[a] (n=107)	False positive adherer[b] (n=42)	
Participant characteristics	**Mean (SD)**	**Mean (SD)**	***P-value***	**Mean (SD)**	**Mean (SD)**	***P-value***	**Mean (SD)**	**Mean (SD)**	***P-value***
Age (years)	49.8 (9.9)	49.4 (11.9)	0.81	50.1 (9.8)	49.8 (11.7)	0.84	50.1 (10.1)	50 (11.1)	0.95
Male (%)	57.7	53.8	0.68	59.5	53.7	0.52	60.7	52.4	0.35
Whites (%)	86.5	92.3	0.35	88.3	87.8	0.93	87.9	88.1	0.97
Education (<high school) (%)	20.2	30.8	0.18	22.5	29.3	0.39	20.6	33.3	0.1
Married (%)	75.7	79.5	0.64	76.6	77.5	0.91	78.5	73.2	0.91
Income (≤$16,000) (%)	5.8	2.6	0.43	6.3	4.9	0.74	6.5	4.8	0.68
Heavy Drinker[c] (%)	29.8	41	0.21	28.8	43.9	0.08	29	42.9	0.11
Current Smoker (%)	12.5	7.7	0.42	13.5	7.3	0.3	13.1	9.5	0.55
Poor/fair general health status (%)	6.7	10.3	0.48	3.6	14.6	0.01	3.7	14.3	0.02
BP drug copayment (%)	88.9	83.8	0.43	90.4	82.1	0.17	90	82.5	0.22
More than 1 BP pill (%)	23.1	33.3	0.22	27	31.7	0.57	27.1	31	0.64
Number of BP drug side effects	5.5 (5.1)	4.5(4.0)	0.32	5.0 (4.8)	5.0 (4.9)	0.94	5.1 (4.8)	5.1 (4.9)	0.99
At least 1 BP drug side effects (%)	88.5	82.1	0.32	86.5	82.9	0.58	86.9	83.3	0.57
Over all symptom distress score[d]	15.0 (22.8)	13.7(32.9)	0.78	13.8 (22.2)	13.9 (32.5)	0.97	14.1 (22.5)	14.1 (32.1)	0.99
Medication for other diseases (%)	12.5	10.3	0.71	11.7	9.8	0.74	12.2	9.5	0.65
Anxiety score (PGWB)	5.9 (3.6)	6.9(4.3)	0.15	5.7 (3.5)	7.0 (4.2)	0.06	5.7 (3.5)	7.1 (4.3)	0.03
Depression score (BDI-II)	4.6 (6.6)	4.5(5.5)	0.93	4.1 (6.3)	5.0 (6.0)	0.4	4.3 (6.5)	5.1 (6.0)	0.46
Systolic BP (mm Hg)	135.3 (15.0)	132.3(15.2)	0.29	135 (15.1)	133.2 (15.3)	0.51	135.4 (15.0)	133.1 (15.2)	0.39
Diastolic BP (mm Hg)	85.7 (10.4)	82.1(10.7)	0.07	85.4 (9.8)	82.5 (10.6)	0.12	85.5 (10.3)	82.6 (10.5)	0.14

Abbreviations: BP, blood pressure; BDI-II, Beck Depression Inventory-II; MARS, Medication adherence report scale; PGWB, Psychological General Well- Being Index; SD, Standard Deviation.

[a]Concordants are individuals who were classified into the same adherence category by both pill count adherence ratio (PCAR) and the self-reported measurement of medication adherence.

[b]False positive adherers are individuals who were non-adherers based on PCAR (<80%) but adherers based on self-reported measurement of adherence.

[c] Heavy drinkers were participants who had >14 drinks/week for males and >7 drinks/week for females.

[d] Overall symptom distress scores was calculated by multiplying the presence, severity and frequency of each side effect symptom and summing the resulting values for all side effect symptoms.

Table 2.

Validity indices and proportion of false-positive adherers for self-reported measurements of adherence using pill count adherence as the reference test.

	Type of self-reported measurement of adherence		
	Non-adherence on MARS	**Non-adherence on Previous Month Adherence**	**Non-adherence on Previous Week Adherence**
Sensitivity	19.60	16.80	15.80
Specificity	89.90	92.80	94.20
Positive Predictive Value	36.40	40.50	44.40
Negative Predictive Value	79.20	79.20	79.30
Percent Agreement	73.90	75.50	76.50
Cohen's kappa (%)	11.4	12.1	13.0
Area under the curve (AUC)	0.55	0.55	0.55
False Positive Adherers (%)[a]	19.80	20.00	20.00

Abbreviations: AUC, Area under the curve, MARS, Medication adherence report scale.

[a]Proportion of false positive adherers was calculated as the ratio of the number of participants who were non-adherers based on pill count adherence ratio (PCAR<80%) but adherers based on self-reported measurements to the total number of participants.

Table 3.

Crude odds ratios for being a false positive adherer by self-reported measurements of medication adherence in newly treated hypertensive patients.

	Type of self-reported measurement of adherence					
	MARS		Previous Month Reported Adherence		Previous Week Reported Adherence	
Predictors	**OR (95% CI)**	***P-value***	**OR (95% CI)**	***P-value***	**OR (95% CI)**	***P-value***
Age (>50 years)	1.12 (0.64, 1.93)	0.69	1.16 (0.70, 1.93)	0.57	1.14 (0.65, 1.99)	0.66
Female	0.92 (0.53, 1.60)	0.77	1.06 (0.64, 1.76)	0.82	1.09 (0.63, 1.89)	0.76
Non-Whites	0.92 (0.32, 2.63)	0.88	1.04 (0.43, 2.51)	0.92	1.22 (0.48, 3.10)	0.67
Less than high school	1.37 (0.78, 2.38)	0.27	1.53 (0.93, 2.51)	0.09	1.68 (0.98, 2.90)	0.06
Unmarried	0.92 (0.46, 1.81)	0.80	0.92 (0.49, 1.75)	0.81	1.03 (0.51, 2.06)	0.94
Annual income (<$16,000)	1.76 (0.64, 4.81)	0.27	1.54 (0.64, 3.70)	0.34	1.46 (0.51, 4.19)	0.48
Heavy drinkers[a]	1.27 (0.72, 2.24)	0.41	1.23 (0.73, 2.09)	0.44	1.15 (0.64, 2.05)	0.64
Current Smokers	0.64 (0.28, 1.49)	0.30	0.61 (0.30, 1.26)	0.18	0.67 (0.30, 1.52)	0.34
More than 1 BP Pills (%)	1.45 (0.78, 2.71)	0.24	1.46 (0.81, 2.63)	0.20	1.57 (0.85, 2.87)	0.15
At least 1 BP drug side effect	0.64 (0.34, 1.20)	0.16	0.68 (0.37, 1.23)	0.20	0.68 (0.37, 1.29)	0.23
>4 BP drug side effects	1.03 (0.56, 1.89)	0.93	1.18 (0.68, 2.06)	0.55	0.69 (0.37, 1.29)	0.25
OSD (above median)[b]	0.78 (0.42, 1.43)	0.42	0.80 (0.44, 1.42)	0.44	1.19 (0.66, 2.15)	0.55
BP drug copayment	0.61 (0.29, 1.28)	0.19	0.67 (0.36, 1.25)	0.21	0.59 (0.30, 1.15)	0.12
Medication for other diseases	1.05 (0.47, 2.36)	0.90	0.70 (0.35, 1.43)	0.33	0.99 (0.43, 2.26)	0.97
General health (poor/fair)	1.36 (0.60, 3.07)	0.46	2.06 (1.05, 4.06)	0.04	1.68 (0.74, 3.83)	0.22
Anxiety score (PGWB)						
Tertile 1 (ref)						
Tertile 2	0.91 (0.50, 1.64)	0.75	0.85 (0.48, 1.53)	0.60	0.87 (0.48, 1.59)	0.66
Tertile 3	2.10 (1.09, 4.03)	0.03	2.04 (1.12, 3.72)	0.02	2.18 (1.11, 4.28)	0.02
Depression score (BDI-II)						
Tertile 1 (ref)						
Tertile 2	1.62 (0.90, 2.94)	0.11	1.63 (0.95, 2.82)	0.08	1.55 (0.88, 2.75)	0.13
Tertile 3	1.49 (0.79, 2.83)	0.22	1.61 (0.92, 2.82)	0.10	1.41 (0.77, 2.58)	0.26

Abbreviations: BP, blood pressure; BDI-II, Beck Depression Inventory-II; MARS, Medication adherence report scale; OR, odds ratio; OSD, Overall symptom distress score; PGWB, Psychological General Well- Being Index.

[a] Heavy drinkers were participants who had >14 drinks/week for males and >7 drinks/week for females.

[b] Overall symptom distress scores was calculated by multiplying the presence, severity and frequency of each side effect symptom and summing the resulting values for all side effect symptoms. Median score for overall symptom distress score was 7 at visits 1 and 6 at visits 2 and 3, and 5 at visit 4.

Note: False positive adherers are individuals who were identified as non-adherers based on pill count adherence ratio (PCAR<80%) but adherers based on self-reported measurements of adherence.

Table 4.

Adjusted odds ratios for being a false positive adherer on self-reported measurements of medication adherence but non-adherer on pill count adherence ratio among newly treated hypertensive patients.

	Type of self-reported measurement of adherence					
	MARS		Previous Month Reported Adherence		Previous Week Reported Adherence	
Predictors	**OR (95% CI)**	***P-value***	**OR (95% CI)**	***P-value***	**OR (95% CI)**	***P-value***
Less than high school	1.38 (0.83, 2.3)	0.21	1.66 (1.03, 2.66)	0.04	1.88 (1.11, 3.2)	0.02
Annual income (<$16,000)	2.50 (0.91, 6.87)	0.08	1.97 (0.79, 4.95)	0.15	1.84 (0.6, 5.66)	0.29
Current Smokers	0.40 (0.17, 0.93)	0.03	0.37 (0.17, 0.83)	0.02	0.41 (0.18, 0.94)	0.03
At least 1 BP drug side effect	0.46 (0.23, 0.93)	0.03	0.50 (0.24, 1.03)	0.06	0.52 (0.25, 1.07)	0.07
Anxiety score (PGWB)						
Tertile 1 (ref)						
Tertile 2	1.05 (0.56, 1.99)	0.87	0.97 (0.52, 1.83)	0.92	1.03 (0.56, 1.92)	0.91
Tertile 3	3.00 (1.36, 6.61)	0.01	2.96 (1.33, 6.61)	0.01	3.48 (1.5, 8.09)	0.004
Depression (BDI-II)						
Tertile 1 (ref)						
Tertile 2	1.61 (0.85, 3.04)	0.14	1.62 (0.9, 2.92)	0.11	1.44 (0.77, 2.68)	0.25
Tertile 3	1.02 (0.49, 2.11)	0.97	1.12 (0.54, 2.29)	0.76	0.89 (0.42, 1.88)	0.76

Abbreviations: BP, blood pressure; BDI-II, Beck Depression Inventory-II; MARS, Medication adherence report scale; OR, odds, ratio; PGWB, Psychological General Well- Being Index. Note: False positive adherers are individuals who were identified as non-adherers based on pill count adherence ratio (PCAR<80%) but adherers based on self-reported measurements of adherence.