

HHS Public Access

JAm Soc Hypertens. Author manuscript; available in PMC 2017 November 01.

Published in final edited form as:

Author manuscript

J Am Soc Hypertens. 2016 November ; 10(11): 857–864.e2. doi:10.1016/j.jash.2016.08.009.

The Association between Self-Reported Medication Adherence Scores and Systolic Blood Pressure Control: A SPRINT Baseline Data Study

William E. Haley, MD¹, Olivia N. Gilbert, MD², Robert F. Riley, MD, MS³, Jill C. Newman, MS⁴, Christianne L. Roumie, MD, MPH⁵, Jeffrey Whittle, MD, MPH⁶, Ian M. Kronish, MD, MPH⁷, Leonardo Tamariz, MD, MPH⁸, Alan Wiggers, DO⁹, Donald E. Morisky, ScD, MSPH, ScM¹⁰, Molly B. Conroy, MD, MPH¹¹, Eugene Kovalik, MD¹⁴, Nancy R. Kressin, PhD¹⁵, Paul Muntner, PhD¹⁶, David C. Goff Jr., MD, PhD¹⁷, and the SPRINT Study Research Group ¹Mayo Clinic, Jacksonville, FL

²Section on Cardiovascular Medicine, Wake Forest University Health Sciences

³University of Washington, Division of Cardiology

⁴Medical University of South Carolina

⁵VA Tennessee Valley Healthcare System Geriatric Research and Education Clinical Center Nashville and Vanderbilt University Medical Center

⁶Milwaukee VA Medical Center

⁷Columbia University Medical Center

⁸Miami Veterans Affairs and University of Miami Health System

⁹University Hospitals, Cleveland, OH

¹⁰UCLA School of Public Health

¹¹Department of Medicine, University of Pittsburgh School of Medicine

¹⁴Duke University Medical Center

¹⁵Boston University School of Medicine, Department of Veterans Affairs

¹⁶University of Alabama School of Public Health

Financial Disclosure Declaration No other relevant disclosures.

Corresponding author: William E. Haley, MD, Division Nephrology and Hypertension, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, Phone: 904-953-7259, Fax: 904-953-6581, haley.william@mayo.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Contributions: Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. WH takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Abstract

We examined baseline data from the Systolic Blood Pressure Intervention Trial (SPRINT) to investigate whether medication adherence, measured by the Morisky Medication Adherence Scale (MMAS-8), was associated with systolic blood pressure (SBP), and whether MMAS-8 score and number of antihypertensive medications interacted in influencing SBP. 8,435 SPRINT participants were included: 21.2% had low adherence (MMAS-8: <6); 40.0% had medium adherence (6 to <8); and 38.8% had high adherence (8). SBP was <140 mmHg in 54.6%; 140 – 160 mmHg in 36.6%; and >160 mmHg in 8.8%. In multivariable regression, medium vs. low adherence weakly associated with lower SBP (OR: 1.17, CI: 1.04, 1.31). SPRINT eligibility criteria should be considered when interpreting results. Efforts to understand and enhance adherence are crucial to improve population health and using self-report instruments might be considered for predicting treatment adherence and response in future efficacy trials and for identifying patients for adherence support in clinical practice.

Keywords

Medication adherence; MMAS-8; systolic blood pressure; hypertension; clinical trial

INTRODUCTION

Medication non-adherence is a common problem and is one of the contributing factors to inadequate blood pressure control.¹⁻⁵ A recent review of non-adherence also underscored the link to complications of hypertension and suggested routine screening.⁶ In addition, low medication adherence has been shown to be associated with adverse safety events.⁷ Several factors can influence patient medication adherence, such as complexity of regimen including number of medications; lack of knowledge about the disease; and medication side effects, including their impact on quality of life.⁸

The 8-item Morisky Medication Adherence Scale (MMAS-8) is an 8 question self-reported instrument that has proven to be a valid and reliable assessment tool for adherence. It provides information about situational factors that may act as barriers to medication adherence. Items on the scale reflect potential etiologies for non-adherent behavior, such as side effects and forgetfulness, with scores indicating low, medium or high adherence.⁹ The Systolic Blood Pressure Intervention Trial (SPRINT) included administration of the MMAS-8 at the baseline visit, and at the 12-month and 48-month followup.¹⁰ We performed a cross-sectional analysis of the SPRINT baseline data to investigate whether participants' baseline MMAS-8 scores are associated with baseline systolic blood pressure (SBP) control prior to intervention, whether there is internal consistency of this association across groups defined by gender, ethnicity, and the SPRINT subgroups [chronic kidney disease (CKD) and Senior (75 year-old)], and whether there is an interaction between MMAS-8 score and number of antihypertensive medications in predicting SBP control.

METHODS

We conducted a cross-sectional examination of the SPRINT baseline data. The trial design has been described previously.¹⁰ In brief, SPRINT is a multicenter, randomized, controlled trial that compared cardiovascular outcomes, including myocardial infarction, acute coronary syndrome, stroke, heart failure, and cardiovascular death between groups with two different systolic blood pressure (SBP) goals: <120 versus <140 mm Hg. All participants were aged 50 years or older with SBP 130 mm Hg and with or at increased risk for cardiovascular disease (CVD). A full list of exclusion criteria has been published¹⁰; major exclusions included diabetes mellitus, 24-hour urine protein 1g/day, previous stroke, and adherence concerns. There were also specific inclusion criteria for SBP linked to the number of anti-hypertensive medications a participant was taking at baseline: 130-150 mmHg on 4 medications, 130-160 mmHg on 3 medications, 130-170 mmHg on 2 medications, and 130-180 mmHg on zero or 1 medication; patients on more than 4 antihypertensives were excluded.

Sample Population

We included in the analysis all participants enrolled in the SPRINT trial with the following available baseline data: demographics, comorbidities, Morisky Medication Adherence Scale (MMAS-8) score, number of medications at start of trial (baseline visit), and SBP. We excluded participants who were not taking any BP medications at baseline and those who had a missing or incomplete baseline MMAS-8.

Predictor Variable: Medication Adherence

Medication adherence was measured using the validated 8-item Morisky Medication Adherence Scale (MMAS-8), which is a self-reported questionnaire intended to measure medication adherence by providing information about behavioral and psychological factors that may act as barriers to medication adherence (Appendix). Items on the scale reflect potential reasons for non-adherent behavior, such as side effects, forgetfulness, and inconvenience. In the present study, participants were asked about medication adherence to anti-hypertensive agents prior to the SPRINT trial randomization. The MMAS-8 is scored as an ordinal measure with scores ranging from 0 to 8. It is categorized with a score of <6 indicating "low adherence", 6 to <8 "medium adherence," and 8 "high adherence" based on previously published definitions.⁹

Primary Outcome: Systolic Blood Pressure Control

The primary outcome of interest was SBP control at baseline. Analyses were performed with SBP control as an ordinal categorical variable: SBP <140 mm Hg (controlled), SBP 140-160 mm Hg, and SBP >160 mm Hg based on current guidelines.¹¹⁻¹³ As outlined in the SPRINT design, all blood pressure data were collected using an OMRON blood pressure cuff (Model 907XL, Omron Healthcare, Lake Forest, IL), by trained research coordinators. Three blood pressures were collected after the participant was sitting quietly <u>alone and unobserved</u> for 5 minutes and were averaged.¹⁰

Covariates

Covariates were selected *a priori* on the basis of clinical significance and included gender, race, ethnicity, age (75 years old versus <75 years old), education level, and comorbidities that might affect either SBP or its management: atrial fibrillation/flutter; heart attack; congestive heart failure; peripheral vascular disease; total number of comorbidities; number of hypertension medications; CVD history; CKD; and tobacco use.

Statistical Analysis

Descriptive statistics for the sample were presented as frequencies and percentages or means and standard deviations. Participant characteristics were reported for the three levels of the MMAS-8: low, medium, and high – using the Chi-square or Fisher's Exact test for categorical variables and analysis of variance for continuous variables. Participant characteristics were similarly reported for the three levels of SBP control, along with their bivariate associations. Unadjusted and adjusted analyses using ordinal logistic regression models were used to produce odds ratios, 95% confidence intervals, and p-values, describing the relationship between MMAS-8 score category and SBP control. The score test for the proportional odds assumption was non-significant, indicating that the ordinal logistic model was appropriate.

In addition, interaction effects between number of medications, senior subgroup (75 years vs <75 years), race/ethnicity, and CKD, each with MMAS-8 score, on SBP control as the outcome were assessed using the Wald Chi-square test. As none of the interaction effects reached a level of statistical significance (p < 0.1), all interaction terms were removed and the final adjusted model included only main effects. All analyses were performed using SAS version 9.4 (Cary, NC), and a 2 sided p-value of <0.05 was considered statistically significant.

RESULTS

There were 8,435 participants who met criteria for inclusion from the SPRINT trial database, from a total 9,361 included in the SPRINT trial. Of the 926 (9.9%) excluded individuals, 861 were not taking any BP medication at baseline and the remainder, 65, had a missing or incomplete baseline MMAS-8.

Low Adherence was observed in 21.2% of participants (N=1788), while 40.0% (N=3372) had Medium Adherence and 38.8% (N=3275) had High Adherence. Participants were predominantly male (63.4%), less than age 75 years (71.1%), Non-Hispanic White (56.8%), and with at least some post high school education (73.9%) (Table 1). Higher adherence was more common among men, participants aged 75 years, and those with higher levels of education, atrial fibrillation, CVD, and CKD. Higher adherence was less common among African Americans and current cigarette smokers. Participants who reported higher adherence reported a greater number of physical comorbidities, and a lower number of mental health comorbidities. The number of blood pressure lowering medications was not associated with adherence (Table 1).

Blood pressure was controlled (baseline SBP < 140 mmHg) in 54.6% of participants (N=4,606); 36.6% (N=3,087) had baseline SBP 140 –160 mmHg; and 8.8% (N=742) had SBP > 160 mmHg (Table 2). Blood pressure control was more common among those reporting higher adherence and those taking more blood pressure lowering medications. Blood pressure control was also more common among men, those with greater education, and with history of heart attack. Participants with controlled blood pressure reported a greater number of mental health comorbidities (Table 2).

Baseline blood pressure lowering medication use in the 8435 participants prescribed at least one antihypertensive medication, overall and by adherence status, may be found in Table S1. The number of other concurrent medications (non-antihypertensive) was also assessed by adherence status: Overall (3.65 ± 2.7), Low (3.25 ± 2.7); Medium (3.74 ± 2.8); High (3.79 ± 2.8) (p<.0001).

In unadjusted analysis, there was a statistically significant association between better adherence and better blood pressure control (Table 2). With multivariable adjustment, this relationship persisted. Compared to participants with Low Adherence, those with Medium but not High Adherence were more likely to have SBP <140 mmHg (OR: 1.17, 95% CI: 1.04, 1.31 and 1.10, CI: 0.98, 1.24, respectively, Table 3). Women, Seniors, and participants with less education or a history of heart failure had less well controlled blood pressure. Participants taking more blood pressure lowering medications, and those with a history of heart attack or more mental health comorbidities had better blood pressure control.

The interaction between the MMAS-8 adherence levels and the number of blood pressure lowering medications on SBP control was assessed and found to be non-significant (p=0.3220). Interaction effects of MMAS levels of adherence with gender, age (Senior subgroup), race/ethnicity, and chronic kidney disease were tested. None reached significance at p<0.05 (interaction p-values ranging from 0.10 to 0.66).

DISCUSSION

The aim of this study was to determine whether medication adherence as measured by MMAS-8 scores <u>at baseline</u> was associated with baseline SBP control and whether there was internal consistency of this association across groups defined by gender, race/ethnicity, and the SPRINT subgroups: CKD and Senior (age 75 years). A second aim was to evaluate whether there was a significant interaction between MMAS-8 scores and number of antihypertensive medications in their associations with SBP control. We hypothesized that there would be a significant association between adherence and SBP control, and that in patients taking a greater number of antihypertensive medications, the MMAS-8 score might be less strongly associated with SBP control. Whereas we observed associations between blood pressure control and both adherence and the number of blood pressure lowering medications, the hypothesized interaction was not observed. This finding is in contrast to studies that have found worse adherence and resultant blood pressure control in those taking greater numbers of medications.⁶, ¹⁴

Assessment of medication adherence is difficult. Direct methods include urine and blood assays of medication metabolites, as well as physical observation. The former method is limited due to availability, cost constraints, and protocol issues making it impractical in long-term studies as well as clinical practice, while the latter may be prohibitively time and cost intensive.¹⁵⁻¹⁷ Indirect methods include self-report, pill counts, prescription refill rates, and electronic monitoring – all of which require time and resources.¹⁸⁻²⁰ Of the aforementioned, self-reporting is the most convenient, and therefore most commonly used method. The MMAS-8 has been deemed valid as an assessment tool which is focused on behavioral determinants of adherence to antihypertensive regimens, and is a commonly utilized instrument.²¹⁻²⁴ It is a parsimonious set of items which measure both unintentional and intentional reasons for non-adherence. In addition, a recent study examining the validity and reliability of antihypertensive adherence questionnaires deemed the MMAS-8 to be the most effective in terms of "sensitivity, specificity, positive predictive value, and negative predictive value, while maintaining acceptable validity and reliability".²¹ The latter was defined with use of Cronbach's alpha, a frequently used estimate of the reliability of questionnaires, with "excellent" results defined by a value of 0.9, "good" $0.9 > \alpha = 0.8$. "acceptable" $0.8 > \alpha$ 0.7, and $0.5 > \alpha$ "unacceptable".²⁵ For the MMAS-8, Cronbach's alpha was calculated to be 0.83.21

We found that better medication adherence as measured by MMAS-8 was weakly associated with better baseline SBP control prior to intervention in SPRINT. Better blood pressure control was more common in the Medium Adherence group but was only marginally more common in the High Adherence group than in the Low Adherence group. There was no significant interaction between MMAS-8 and gender, race/ethnicity, and the SPRINT subgroups: CKD and Senior (age 75 years), in associations with SBP control. In addition, there was no significant interaction between MMAS-8 and the number of antihypertensive medications in their associations with SBP control. Regarding the latter finding, it is important to consider the following factors. Patients selected for participation in SPRINT did not represent a random sample with respect to SBP and anti-hypertensive medications. Whereas the baseline SBP values were not constrained in SPRINT, the eligibility criterion for SBP at screening was 130 to 180. Furthermore, those with higher baseline BP were excluded unless the number of antihypertensive medications being taken at the time of screening was relatively low. Those with SBP between 170 and 180 mm Hg could have been taking only 1 hypertension medication, those between 160-170 mm Hg up to 2 medications, and those between 150-160 mm Hg up to 3 medications; while those with SBP between 130-150 mm Hg could have been taking up to 4 hypertension medications. ¹⁰ Also excluded were those with history of poor adherence with medications or clinic visits, and those with medical, psychiatric or behavioral factors that in the opinion of the principal investigator might interfere with study participation or ability to adhere to the intervention program. Taken together, such conditions could be expected to weaken the ability to observe a relationship between medication adherence, number of antihypertensive medications, and SBP control in SPRINT. Nevertheless, these results add to the understanding of antihypertensive medication adherence and its link to SBP control.

Certain limitations are notable. SPRINT was a randomized, controlled, open-label trial conducted at 102 sites throughout the U.S. and Puerto Rico.¹⁰ This large diverse cohort of

9,361 individuals includes 36% female and 42% non-white, which is enriched with 2636 participants aged 75 years and 2646 with CKD. SPRINT was not designed to test the relationship between medication adherence and BP control. Inclusion and exclusion criteria identified a trial population to ensure adequate event rates for statistical power, provide maximum generalizability, safety, and protocol implementation; these eligibility requirements facilitated a population at high risk for the major trial endpoints. Also excluded were patients with diabetes, polycystic kidney disease, stroke, proteinuria in excess of 1g/ day, eGFR <20 mL/min/1.73m², any organ transplant, those in nursing homes, those with clinical diagnosis of dementia at baseline, those with secondary hypertension, and baseline standing orthostatic hypotension of concern (one minute standing BP <110). Generalizability is compromised with respect to these excluded groups. Another limitation relates to use of survey data. Even though, as noted previously, the MMAS-8 has been judged valid and reliable, nevertheless, relevant factors that may influence the accuracy of the MMAS-8 include individuals' tendencies for recall bias, overestimation of adherence, and pursuit of socially acceptable responses.⁹ It should be noted that the current study reflects baseline data collected prior to the SPRINT trial randomization. Thus, the closer personal attention and motivation that are intrinsic to participation in research would not have influenced these results. Options for monitoring medication adherence, including drug serum and urine metabolite levels, physical observation, electronic monitoring, pill counting, and pharmacy fill rates, are cumbersome and otherwise fraught with their own weaknesses.⁶ We are aware that use of multiple measures of adherence may enhance validity; however, we judged that we did not have the resources required to incorporate other assessments of adherence at baseline in SPRINT. Selection bias must be considered, insofar as those individuals with history of poor adherence with medications or clinic visits, and those with medical, psychiatric or behavioral factors that in the opinion of the principal investigator might interfere with study participation or ability to adhere to the intervention program were excluded from participating in this trial. The latter would tend to constrain our variance in adherence, decreasing the likelihood of detecting associations. Finally, we noted that selection criteria for SPRINT did not allow for a representative population with respect to numbers of antihypertensive medications and SBP, a condition that could be expected to weaken the ability to detect a relationship between SBP control, number of antihypertensive medications, and medication adherence at baseline.

Higher medication adherence, assessed by MMAS-8, was weakly associated with better SBP control in SPRINT. SPRINT eligibility criteria should be considered when interpreting these findings: individuals with SBP <130 were excluded; likewise, the high end of the SBP range was constrained differentially by the number of baseline medications. These trial features restricted the range of SBP observed, reducing variation and hence power to detect an association of adherence with SBP control. Assessment of adherence is challenging in research and practice settings; nevertheless, we believe that efforts to understand and enhance adherence are critical to improve population health; use of parsimonious self-report instruments such as the MMAS-8 might be considered for predicting treatment adherence and response in future efficacy trials and for identifying patients for adherence support in clinical practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Support

The Systolic Blood Pressure Intervention Trial is funded with Federal funds from the National Institutes of Health (NIH), including the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute on Aging (NIA), and the National Institute of Neurological Disorders and Stroke (NINDS), under Contract Numbers HHSN268200900040C, HHSN268200900046C, HHSN268200900046C, HHSN268200900046C, HHSN268200900047C, HHSN268200900048C, HHSN268200900049C, and Inter-Agency Agreement Number A-HL-13-002-001. It was also supported in part with resources and use of facilities through the Department of Veterans Affairs. The SPRINT investigators acknowledge the contribution of study medications (azilsartan and azilsartan combined with chlorthalidone) from Takeda Pharmaceuticals International, Inc. All components of the SPRINT study protocol were designed and implemented by the investigators. The investigative team collected, analyzed, and interpreted the data. All aspects of manuscript writing and revision were carried out by the coauthors. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, the U.S. Department of Veterans Affairs, or the United States Government. For a full list of contributors to SPRINT, please see the supplementary acknowledgement list:

SPRINT Acknowledgment

We also acknowledge the support from the following CTSAs funded by NCATS: CWRU: UL1TR000439, OSU: UL1RR025755, U Penn: UL1RR024134& UL1TR000003, Boston: UL1RR025771, Stanford: UL1TR000093, Tufts: UL1RR025752, UL1TR000073 & UL1TR001064, University of Illinois: UL1TR000050, University of Pittsburgh: UL1TR000005, UT Southwestern: 9U54TR000017-06, University of Utah: UL1TR000105-05, Vanderbilt University: UL1 TR000445, George Washington University: UL1TR000075, University of CA, Davis: UL1TR000002, University of Florida: UL1 TR000064, University of Michigan: UL1TR000433, Tulane University: P30GM103337 COBRE Award NIGMS.

The authors also acknowledge Dr. Jeffrey A. Cutler's role in the initial consideration of this trial concept during 2003-2007, which led to the subsequent sponsorship of SPRINT by NHLBI.

Ian Kronish, MD, MPH; Dr. Kronish was supported by grants K23 HL098359 and R01 HL123368 from NHLBI. Don Morisky receives royalties for use of the copyrighted MMAS scales. Dr. Morisky received no compensation for use of the ©MMAS in the SPRINT Trial. Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA Fielding School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.

Appendix

Appendix 1

Morisky Medication Adherence Scale as Included in the Sprint Trial.

Question	Response Options
1. Do you sometimes forget to take your high blood pressure pills?	Yes
	No
2. Over the past 2 weeks, were there any days when you did not take your high blood pressure	Yes
medicine?	No
3. Have you ever cut back or stopped taking your medication without telling your doctor because	Yes
you felt worse when you took it?	No
4. When you travel or leave home, do you sometimes forget to bring along your medications?	Yes
	No

Question	Response Options
5. Did you take your high blood pressure medicine yesterday?	Yes
	No
6. When you feel like your blood pressure is under control, do you sometimes stop taking your	Yes
medicine?	No
7. Do you ever feel hassled about sticking to your blood pressure treatment plan?	Yes
	No
8. How often do you have difficulty remembering to take all your blood pressure medication?	Never
	Almost Never
	Sometimes
	Quite Often
	Always

REFERENCES

- 1. Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: clinical applications. JAMA. 2002; 288(22):2880–3. [PubMed: 12472330]
- DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care. 2002; 40(9):794–811. [PubMed: 12218770]
- Holland N, Segraves D, Nnadi VO, Belletti DA, Wogen J, Arcona S. Identifying barriers to hypertension care: implications for quality improvement initiatives. Dis Manag. 2008; 11(2):71–7. [PubMed: 18426375]
- McDermott MM, Schmitt B, Wallner E. Impact of medication nonadherence on coronary heart disease outcomes. A critical review. Arch Intern Med. 1997; 157(17):1921–9. [PubMed: 9308504]
- Mendis, S.; Salas, M. Adherence to Long-Term Therapies: A Call to Action. World Health Organization; 2003.
- 6. Gosmanova EO, Kovesdy CP. Adherence to antihypertensive medications: is prescribing the right pill enough? Nephrol Dial Transplant. 2015; 30(10):1649–56. [PubMed: 25335506]
- Hsu KL, Fink JC, Ginsberg JS, Yoffe M, Zhan M, Fink W, et al. Self reported Medication Adherence and Adverse Patient Safety Events in CKD. Am J Kidney Dis. 2015; 66(4):621–629. [PubMed: 25979348]
- Krousel-Wood M, Thomas S, Muntner P, Morisky D. Medication adherence: a key factor in achieving blood pressure control and good clinical outcomes in hypertensive patients. Curr Opin Cardiol. 2004; 19(4):357–62. [PubMed: 15218396]
- Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008; 10(5):348–54. [PubMed: 18453793]
- Ambrosius WT, Sink KM, Foy CG, Berlowitz DR, Cheung AK, Cushman WC, et al. The design and rationale of a multicenter clinical trial comparing two strategies for control of systolic blood pressure: the Systolic Blood Pressure Intervention Trial (SPRINT). Clin Trials. 2014; 11(5):532– 46. [PubMed: 24902920]
- Weber MA, Schiffrin EL, White WB, Mann S, Lindholm LH, Kenerson JG, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. J Clin Hypertens (Greenwich). 2014; 16(1):14–26. [PubMed: 24341872]
- 12. Whitworth JA, Chalmers J. World health organisation-international society of hypertension (WHO/ ISH) hypertension guidelines. Clin Exp Hypertens. 2004; 26(7-8):747–52. [PubMed: 15702630]
- 13. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the

panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014; 311(5): 507–20. [PubMed: 24352797]

- Taylor AA, Shoheiber O. Adherence to antihypertensive therapy with fixed-dose amlodipine besylate/benazepril HCl versus comparable component-based therapy. Congest Heart Fail. 2003; 9(6):324–32. [PubMed: 14688505]
- Jung O, Gechter JL, Wunder C, Paulke A, Bartel C, Geiger H, et al. Resistant hypertension? Assessment of adherence by toxicological urine analysis. J Hypertens. 2013; 31(4):766–74. [PubMed: 23337469]
- 16. Ceral J, Habrdova V, Vorisek V, Bima M, Pelouch R, Solar M. Difficult-to-control arterial hypertension or uncooperative patients? The assessment of serum antihypertensive drug levels to differentiate non-responsiveness from non-adherence to recommended therapy. Hypertens Res. 2011; 34(1):87–90. [PubMed: 20882030]
- De Geest S, Ruppar T, Berben L, Schönfeld S, Hill MN. Medication non-adherence as a critical factor in the management of presumed resistant hypertension: a narrative review. EuroIntervention. 2014; 9(9):1102–9. [PubMed: 24457281]
- De Geest S, Sabaté E. Adherence to long-term therapies: evidence for action. Eur J Cardiovasc Nurs. 2003; 2(4):323. [PubMed: 14667488]
- Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005; 353(5):487–97. [PubMed: 16079372]
- Christensen DB, Williams B, Goldberg HI, Martin DP, Engelberg R, LoGerfo JP. Assessing compliance to antihypertensive medications using computer-based pharmacy records. Med Care. 1997; 35(11):1164–70. [PubMed: 9366895]
- Pérez-Escamilla B, Franco-Trigo L, Moullin JC, Martínez-Martínez F, García-Corpas JP. Identification of validated questionnaires to measure adherence to pharmacological antihypertensive treatments. Patient Prefer Adherence. 2015; 9:569–78. [PubMed: 25926723]
- Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: response to authors. J Clin Epidemiol. 2011; 64(3):255–7. discussion 258-63. [PubMed: 21144706]
- AlGhurair SA, Hughes CA, Simpson SH, Guirguis LM. A systematic review of patient selfreported barriers of adherence to antihypertensive medications using the world health organization multidimensional adherence model. J Clin Hypertens (Greenwich). 2012; 14(12):877–86. [PubMed: 23205755]
- 24. Krousel-Wood MA, Islam T, Webber LS, Re RS, Morisky DE, Muntner P. New Medication Adherence Scale Versus Pharmacy Fill Rates in Seniors With Hypertension. Am J Manag Care. 2009; 15(1):59–66. [PubMed: 19146365]
- 25. Heo M, Kim N, Faith MS. Statistical power as a function of Cronbach alpha of instrument questionnaire items. BMC Med Res Methodol. 2015; 15:86. [PubMed: 26467219]

Highlights					
•	Medication adherence was measured at baseline in SPRINT.				
•	Twenty-one percent had low, 40% had medium, and 39% had high adherence.				
•	Systolic blood pressure was <140 in 55%, 140–160 in 37%, and >160 in 9%.				
•	Baseline adherence and systolic blood pressure were weakly associated.				
•	No interaction between adherence and number of antihypertensive meds on systolic blood pressure control.				

Table 1

Baseline Demographic and Personal Characteristics and their Association with the Morisky Medication Adherence Scale - mean \pm SD or frequency (col %)

Characteristic	Overall n=8435	Low Adherence n=1788 (21.2%)	Medium Adherence n=3372 (40%)	High Adherence n=3275 (38.8%)	p-value*
Gender					0.021
Female	3086	704 (39.4)	1215 (36)	1167 (35.6)	
Male	5349	1084 (60.6)	2157 (64)	2108 (64.4)	
Age					<.0001
75 (Senior)	2430	346 (19.4)	994 (29.5)	1090 (33.3)	
< 75	6005	1442 (80.6)	2378 (70.5)	2185 (66.7)	
Race/Ethnicity					<.0001
Non-Hispanic White	4799	723 (40.4)	1997 (59.2)	2079 (63.5)	
Black/African American	2574	816 (45.6)	988 (29.3)	770 (23.5)	
Hispanic	910	209 (11.7)	325 (9.6)	376 (11.5)	
Other	152	40 (2.2)	62 (1.8)	50 (1.5)	
Education					<.0001
Less than High School	817	214 (12)	327 (9.7)	276 (8.4)	
High School Graduate/GED	1383	317 (17.7)	540 (16)	526 (16.1)	
Post High School	2988	690 (38.6)	1185 (35.1)	1113 (34)	
College Degree	3246	567 (31.7)	1320 (39.1)	1359 (41.5)	
Atrial Fibrillation/Flutter (vs no)	719	117 (6.5)	283 (8.4)	319 (9.7)	0.0005
Heart Attack (vs no)	727	136 (7.6)	313 (9.3)	278 (8.5)	0.12
Congestive Heart Failure (vs no)	316	77 (4.3)	121 (3.6)	118 (3.6)	0.37
Peripheral Vascular Disease (vs no)	463	103 (5.8)	204 (6)	156 (4.8)	0.059
Number of Comorbidities					
Physical (out of 38)	4.5 ± 2.6	4.31 ± 2.6	4.55 ± 2.7	4.56 ± 2.6	0.0042
Mental (out of 6)	0.4 ± 0.8	0.55 ± 1.0	0.38 ± 0.8	0.34 ± 0.7	<.0001
Number of HTN Medications					0.60
1	2673	587 (32.8)	1050 (31.1)	1036 (31.6)	
2	3255	693 (38.8)	1302 (38.6)	1260 (38.5)	
>2	2405	484 (27.1)	979 (29)	942 (28.8)	
CVD History (vs no)	1781	343 (19.2)	753 (22.3)	685 (20.9)	0.029
Chronic Kidney Disease (vs no)	2514	449 (25.1)	1044 (31)	1021 (31.2)	<.0001
Tobacco use					<.0001
Never/Former	7378	1425 (79.7)	2995 (88.8)	2958 (90.3)	1
Current	1050	360 (20.1)	376 (11.2)	314 (9.6)	1

Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA Fielding School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772..

P-value from Chi Square test or Fisher's Exact Test for categorical variables and simple logistic regression for continuous variables

Table 2

Baseline Demographic and Personal Characteristics and their Association with Systolic Blood Pressure - mean \pm SD or frequency (row %)

Characteristic	SBP<140 mmHg n=4604 (54.6%)	SBP 140-160 mmHg n=3087 (36.6%)	SBP>160 mmHg n=742 (8.8%)	p-value*
MMAS				0.015
Low Adherence	949 (53.1)	655 (36.6)	184 (10.3)	
Med Adherence	1894 (56.2)	1187 (35.2)	291 (8.6)	
High Adherence	1763 (53.8)	1245 (38.0)	267 (8.2)	
Gender				<.0001
Female	1522 (49.3)	1196 (38.8)	368 (11.9)	
Male	3084 (57.7)	1891 (35.3)	374 (7.0)	
Age				<.0001
75 (Senior)	1154 (47.5)	1000 (41.2)	276 (11.4)	
< 75	3452 (57.5)	2087 (34.8)	466 (7.8)	
Race/Ethnicity				0.47
Non-Hispanic White	2646 (55.1)	1747 (36.4)	406 (8.5)	
Black/ African American	1408 (54.7)	926 (36.0)	240 (9.3)	
Hispanic	474 (52.1)	356 (39.1)	80 (8.8)	
Other	78 (51.3)	58 (38.2)	16 (10.5)	
Education				0.021
Less than High School	413 (50.6)	311 (38.1)	93 (11.4)	
High School Graduate/GED	754 (54.5)	499 (36.1)	130 (9.4)	
Post High School	1615 (54.1)	1112 (37.2)	261 (8.7)	
College Degree	1824 (56.2)	1164 (35.9)	258 (8.0)	
Atrial Fibrillation/Flutter	386 (53.7)	270 (37.6)	63 (8.8)	0.86
Heart Attack	433 (59.6)	247 (34.0)	47 (6.5)	0.007
Congestive Heart Failure	164 (51.9)	117 (37.0)	35 (11.1)	0.30
Peripheral Vascular Disease	237(51.2)	181 (39.1)	45 (9.7)	0.30
Number of Comorbidities				
Physical (out of 38)	4.48 ± 2.6	4.53 ± 2.7	4.51 ± 2.6	0.54
Mental (out of 6)	0.42 ± 0.9	0.39 ± 0.8	0.31 ± 0.7	0.0002
Number of HTN Medications				0.043
1	1399 (52.3)	1038 (38.9)	236 (8.8)	
2	1826 (56.1)	1146 (35.2)	283 (8.7)	
>2	1326 (55.1)	862 (35.9)	217 (9.0)	1
CVD History	999 (56.1)	639 (35.9)	143 (8.0)	0.25
Chronic Kidney Disease	1378 (54.8)	899 (35.8)	237 (9.4)	0.28
Tobacco use	× *			0.90
Never/Former	4030 (54.6)	2702 (36.6)	646 (8.8)	1

Characteristic	SBP<140 mmHg n=4604 (54.6%)	SBP 140-160 mmHg n=3087 (36.6%)	SBP>160 mmHg n=742 (8.8%)	p-value [*]
Current	574 (54.7)	380 (36.2)	96 (9.1)	

* P-value from Chi Square test or Fisher's Exact Test for categorical variables and simple logistic regression for continuous variables

Page 15

Table 3

The Association between Better Systolic Blood Pressure Control and Medication Adherence While Adjusting for Demographic and Behavioral Risk Factors, Number of Hypertension Medication, and Comorbidities

Characteristic	Adjusted Odds Ratio	95% Confidence Interval	p-value*
MMAS			
Low Adherence			
Med Adherence	1.166	(1.04, 1.31)	0.009
High Adherence	1.100	(0.98, 1.24)	0.11
Gender			
Female	0.702	(0.64, 0.77)	<.0001
Male			
Age			
75 (Senior)	0.644	(0.58, 0.71)	<.0001
< 75			
Race/Ethnicity			
Non-Hispanic White			
Black/African American	1.019	(0.92, 1.13)	0.73
Hispanic	0.926	(0.80, 1.07)	0.31
Other	0.830	(0.60, 1.14)	0.25
Education			
Less than High School	0.816	(0.70, 0.96)	0.012
High School Graduate/GED	0.930	(0.82, 1.06)	0.27
Post High School	0.903	(0.82, 1.00)	0.048
College Degree			
Atrial Fibrillation/Flutter	0.998	(0.85, 1.17)	0.98
Heart Attack	1.244	(1.04, 1.49)	0.019
Congestive Heart Failure	0.779	(0.62, 0.98)	0.036
Peripheral Vascular Disease	0.867	(0.71, 1.05)	0.15
Number of Comorbidities			
Physical	1.007	(0.99, 1.03)	0.47
Mental	1.078	(1.02, 1.14)	0.009
Number of Hypertension Medications			
1			
2	1.150	(1.04, 1.27)	0.007
>2	1.107	(0.99, 1.24)	0.072
CVD History	1.004	(0.89, 1.14)	0.95
Chronic Kidney Disease	1.095	(0.99, 1.21)	0.067
Tobacco use			
Never/Former			

Characteristic	Adjusted Odds Ratio	95% Confidence Interval	p-value*
Current	0.904	(0.79, 1.04)	0.14

* P-value from ordinal logistic regression modeling