New Medication Adherence Scale Versus Pharmacy Fill Rates in Seniors With Hypertension

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Objective: To evaluate the association and concordance of the new 8-item self-report Morisky Medication Adherence Scale (MMAS) with pharmacy fill data in a sample of community-dwelling seniors with hypertension.

Study Design: Cross-sectional study.

Methods: Pharmacy records for antihypertensive medications were abstracted for 87 managed care adult patients with hypertension 65 years and older who completed a survey that included the MMAS. Continuous single-interval medication availability (CSA), medication possession ratio (MPR), and continuous multiple-interval medication gaps (CMG) were calculated using pharmacy data. The MMAS adherence was categorized as high, medium, and low (MMAS scores of 8, 6 to <8, and <6, respectively); pharmacy fill nonpersistence was defined as less than 0.8 for CSA and MPR and as greater than 0.2 for CMG.

Results: Overall, 58%, 33%, and 9% of participants had high, medium, and low medication adherence, respectively, by the MMAS. After adjustment for demographics and in comparison to high adherers on the MMAS, patients with low MMAS adherence were 6.89 (95% confidence interval [CI], 2.48-19.10) times more likely to have nonpersistent pharmacy fill adherence by CSA and were 5.22 (95% CI, 1.88-14.50) times more likely to have nonpersistent pharmacy fill adherence by MPR. Concordance between the MMAS and CSA, MPR, and CMG was 75% or higher.

Conclusions: The MMAS is significantly associated with antihypertensive drug pharmacy refill adherence. Although further validation of the MMAS is needed, it may be useful in identifying low medication adherers in clinical settings.

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For author information and disclosures, see end of text.

Despite the availability of effective medical treatment for hypertension, control of this chronic disease among adults is poor.[1] Low adherence to prescribed antihypertensive medications is potentially a major barrier to adequate blood pressure control[2-4] and has been characterized by the National Council on Patient Information and Education as "America's other drug problem."[5] Low medication adherence is associated with increased healthcare costs and with high rates of cardiovascular disease and hospitalization.[6,7] Identifying nonadherent patients in outpatient settings is important to effectively increase hypertension control rates. Nevertheless, providers often do not ask about medication-taking behavior.[8] This may be in part because they do not have time, do not think of nonadherence as a likely cause for poor blood pressure control, are uncertain about quantifying nonadherent behavior,[9] or are not in the habit of using this information in clinical practice. Approaches used to assess medication adherence include patient self-report, pill counts, pharmacy records, drug levels, biological surrogates, and medication event monitoring system caps.[10] However, the most practical approach to apply in clinical practice is patient self-report. The advantages of assessing medication adherence by self-report include simplicity, speed, and viability of use. Self-report scales to assess antihypertensive medication adherence have been developed.[11-13] However, concordance of patients' responses on previously developed self-report scales with objective measures of medication adherence has been variable.[14,15] The objective of the present analysis was to evaluate the association and concordance of the new 8-item self-report Morisky Medication Adherence Scale (MMAS)[13] with prescription claims in a managed care population of older adults with hypertension.

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METHODS

Study Population

This analysis was part of a study designed to determine patient participation rates and factors associated with antihypertensive medication adherence and to explore methods for analyzing medication adherence in older adults with chronic disease.[16] The study population was drawn from a large southern managed care organization that offered healthcare benefits to persons enrolled in the Medicare

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risk plans. Using a race/ethnicity–stratified sampling approach, 200 study participants (100 white patients and 100 black patients) were randomly selected from an administrative database using the following inclusion criteria: member of the Medicare risk product, at least 2 documented encounters with a primary or secondary diagnosis of essential hypertension (*International Classification of Diseases, Ninth Revision, Clinical Modification,* code 401.XX) as recorded in the managed care organization's administrative database, and continuous enrollment in the managed care organization for at least 1 year at the time of study participation. After excluding 23 patients (2 institutionalized, 8 incapacitated, and 13 with invalid contact information), 177 patients were eligible for the survey. One hundred sixteen surveys were completed, yielding an overall response rate of 66%, with a slightly higher overall participation rate (68% vs 60%) among whites versus blacks.[16] Patients were excluded from the present analysis if they did not complete the MMAS (n = 13), were missing data on age (n = 1), did not have pharmacy fill data available (n = 13), or had fewer than 3 antihypertensive medication pharmacy fills in the study interval (n = 2). After these exclusions, 87 patients were included in the present analysis. The age, sex, and race/ethnicity distributions were similar among those included and those excluded from the analysis ($P > .1$ for all). The study was approved by the institutional review board of the Ochsner Clinic Foundation, New Orleans, Louisiana.

Data Collection

Patient surveys were conducted from December 2002 to March 2003 using a standardized data collection instrument. The survey data (including sociodemographic data and medication adherence) were entered into a Microsoft Access database (Microsoft Corporation, Redmond, WA) and were transferred to SAS version 9.1.3 (SAS Institute, Inc, Cary, NC) for analysis; quality check revealed less than 1% data entry error. All patient identification information was collected and maintained according to Health Insurance Portability and Accountability Act of 1996 regulations and health plan privacy rules.

Self-report MMAS

Self-reported medication adherence was measured using the MMAS,[13] which was developed from a previously validated 4-item scale and supplemented with additional items to better capture barriers surrounding adherence behavior. Each of 8 items measures a specific medication-taking behavior and not a determinant of adherence behavior. The MMAS is provided in **eAppendix A**, available at **www.ajmc.com**. The new scale has been determined to have higher reliability compared with the 4-item scale ($\alpha = .83$ vs $\alpha = .61$).[11,13] The MMAS scores can range from 0 to 8 and have been trichotomized previously into the following 3 levels of adherence to facilitate use in clinical practice: high adherence (score, 8), medium adherence (score, 6 to <8), and low adherence (score, <6).[13] Prior research revealed that the new scale is significantly associated with blood pressure control in patients with hypertension ($P < .05$), with 67.2% of low adherers having uncontrolled blood pressure versus 55.2% and 43.3% of medium and high adherers, respectively, having uncontrolled blood pressure.[13]

Pharmacy Adherence Measures

The managed care organization's data warehouse system was the source of the pharmacy fill data for the present study. The data warehouse (an Oracle relational database [Oracle Corporation, Redwood Shores, CA]) was populated with historic claims data, patient roster data, diagnosis and procedural codes, and code descriptions. Data were extracted by informatics analysts using the Oracle Discoverer tool and were transported into SAS version 9.1.3. The pharmacy data were abstracted on 87 patients and included 42 different antihypertensive medications with 1578 fills captured in the study period.

Pharmacy fill data were extracted for the 2002 calendar year and included a listing of all antihypertensive prescriptions filled, the date filled, generic and brand names of the drugs, and number of pills dispensed. The following 3 measures of adherence were calculated: continuous single-interval medication availability (CSA), medication possession ratio (MPR), and continuous multiple-interval medication gaps (CMG).[17,18] The CSA was calculated by dividing the days' supply obtained at a pharmacy fill by the number of days before the next pharmacy fill for that same medication. The MPR was calculated as the sum of the days' supply obtained between the first pharmacy fill and the last fill (the supply obtained in the last fill was excluded), divided by the total number of days in this period. The CMG was calculated by dividing the total number of days without medications (ie, treatment gaps) between the first and last pharmacy fills by the number of days in this period. A graphical example of how CSA, MPR, and CMG were calculated is provided in **eAppendix B**, available at **www.ajmc.com**.

For every participant, CSA was calculated for each pharmacy fill interval, and MPR and CMG were calculated by class of antihypertensive medication being taken. Values greater than 1 were truncated at the maximum value of 1 for CSA and MPR.[19] Given that self-reported adherence reflects adherence to participants' antihypertensive medication regimen, 1 CSA was assigned to each participant based on the mean of all CSAs calculated from all of his or her antihypertensive

drug pharmacy fill intervals. One MPR and 1 CMG were assigned to each participant. For participants filling more than 1 class of antihypertensive medication, MPR and CMG were calculated for each class and then averaged across all classes to assign a single MPR and CMG to each participant. Given that a cut point of 0.8 has been previously used to define adequate medication adherence using pharmacy data,[19-22] pharmacy fill nonpersistence was defined as less than 0.8 for CSA and MPR and as greater than 0.2 for CMG. The continuous single-interval gap statistic is the inverse of CSA and is not presented.

Statistical Analysis

This study constitutes a test of concordance and concurrent criterion–related validity using pharmacy fill medication adherence as the criterion of interest and its association with self-reported medication taking. Although our comparisons involved the same patients taking antihypertensive medications, the adherence measures were collected independent of each other.

Patient demographic characteristics, education, marital status, smoking status, and number of antihypertensive medications filled were calculated by MMAS category (low, medium, or high). The statistical significance of trends across categories was determined using least squares and maximum likelihood for continuous and categorical variables, respectively.

The distributions of CSA, MPR, and CMG were plotted, and the median, 25th, and 75th percentile minimum and maximum values were determined overall and by MMAS category. Quantile regression analysis was used to determine the statistical significance of trends in median values for these measures across MMAS categories. The prevalences of nonpersistence as determined by CSA, MPR, and CMG were calculated overall and by MMAS category. Log binomial regression models that included adjustment for age, sex, and race/ethnicity were used to determine the prevalence ratio of nonpersistence (CSA, MPR, and CMG separately) associated with MMAS category. Percentage concordance between the MMAS and pharmacy fill adherence was used to describe the agreement between the approaches for assessing adherence. Low adherers are likely to be at greatest risk for uncontrolled blood pressure and subsequent adverse outcomes and could benefit most from tailored interventions to overcome barriers to adherence. Therefore, we assessed the concordance between low adherence on the MMAS with nonpersistence by CSA, MPR, and CMG. All statistical analyses were performed using SAS version 9.1.3.

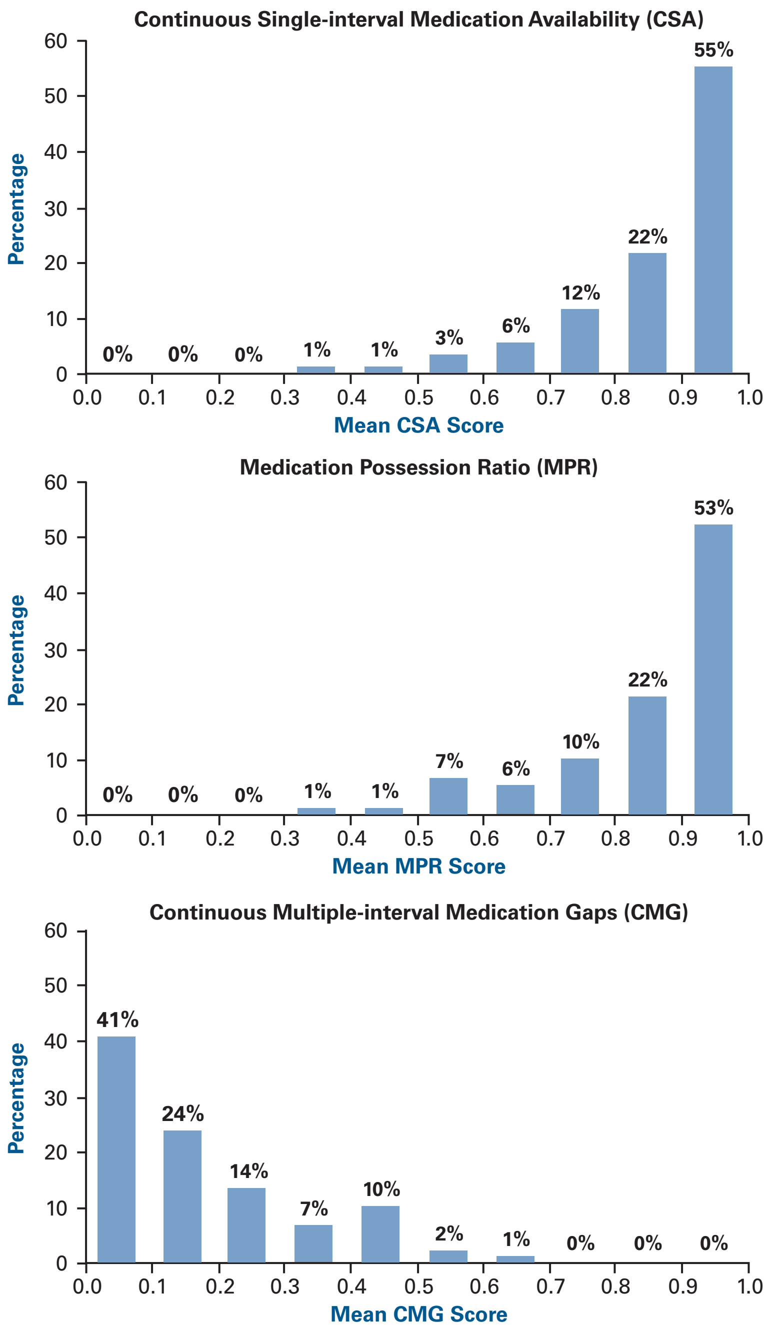
RESULTS

Of 87 patients included in the study, the mean age was 76 years, 31% were men, 48% were black, 47% had graduated from high school, 43% were married, 43% smoked cigarettes, and the mean number of antihypertensive medications being taken was 2.2 (range, 1-4 medications). The mean (SD) MMAS score was 7.4 (0.9). Demographic characteristics of the study participants by MMAS category are given in Table 1. A significantly higher percentage of black versus white patients were low adherers by the MMAS. There were no other significant differences in patient demographics across MMAS categories. By self-report using the MMAS, the distribution of participants' adherence to prescribed medication use in this study population was 58% high adherence, 33% medium adherence, and 9% low adherence. The distributions of the pharmacy fill adherence measures are shown in the Figure. The median CSA, MPR, and CMG were 0.91, 0.91, and 0.12, respectively (Table 2). However, 23% and 25% of patients had nonpersistent CSA and MPR, respectively, and 35% had nonpersistent CMG.

Table 1. Baseline Characteristics of the Study Population by Morisky Medication Adherence Scale (MMAS) Score Category

	MMAS Category (Score Range)			
Characteristic	**Low (<6) (n = 8)**	**Medium (6 to <8) (n = 29)**	**High (8) (n = 50)**	***P***
Age, mean (SE), y	72.8 (1.8)	76.8 (1.6)	76.3 (0.9)	.41
Male sex, %	0	28	38	.03
Black race/ethnicity, %	88	48	42	.04
High school education, %	63	48	44	.61
Currently married, %	25	35	50	.16
Current smoker, %	50	35	47	.51
Antihypertensive medications filled, mean (SE)	2.0 (0.2)	2.1 (0.2)	2.2 (0.2)	.55

Figure. Frequency Distributions of Pharmacy Fill Adherence



Association of the MMAS With Nonpersistence as Determined by Pharmacy Fill

The MMAS was significantly associated with nonpersistence as determined by pharmacy fill adherence (Table 3). After adjustment for age, race/ethnicity, and sex, patients with medium and low adherence by the MMAS were 2.58 (95% CI, 1.08-6.17) and 6.89 (95% CI, 2.48-19.10) times, respectively, more likely to have nonpersistent pharmacy fill adherence by CSA than patients with high adherence by the MMAS (*P* <.001 for trend). Also, patients with medium and low adherence by the MMAS were 2.31 (95% CI, 0.94-5.66) and 5.22 (95% CI, 1.88-14.50) times, respectively, more likely to have nonpersistent pharmacy fill adherence by MPR than patients with high adherence by the MMAS (*P* = .001 for trend). The prevalence of nonpersistent CMG for patients with low adherence on the MMAS was 100%.

Concordance of Low Adherence on the MMAS With Nonpersistence as Determined by Pharmacy Fill

Seven patients with low adherence by the MMAS had nonpersistence by CSA, and 66 patients with medium or high adherence by the MMAS had persistence by CSA, yielding 84% concordance (Table 4). The concordances of low adherence by the MMAS with nonpersistence by MPR and CMG were 79%, and 75%, respectively.

DISCUSSION

Hypertension, a public health challenge in the United States and worldwide, is a modifiable risk factor for cardiovascular events.[23,24]

Table 2. Median, 25th, and 75th Percentile Minimum and Maximum Pharmacy Fill Adherence

Adherence	Median	25th	75th	Minimum	Maximum
CSA	0.91	0.82	0.96	0.35	1.00
MPR	0.91	0.79	0.99	0.35	1.00
CMG	0.12	0.05	0.26	0.00	0.65

CMG indicates continuous multiple-interval medication gaps; CSA, continuous single-interval medication availability; MPR, medication possession ratio.

Table 3. Median, Prevalence, and Adjusted Prevalence Ratio of Nonpersistent Pharmacy Fill Adherence by Morisky Medication Adherence Scale (MMAS) Score Category

	MMAS Category (Score Range)			
Adherence[a]	**Low (<6)**	**Medium (6 to <8)**	**High (8)**	***P* for Trend**
CSA				
Median (95% CI)	0.66 (0.56-0.72)	0.88 (0.76-0.93)	0.94 (0.89-0.97)	<.001
Prevalence, %	88	31	8	<.001
Prevalence ratio (95% CI)	6.89 (2.48-19.10)	2.58 (1.08-6.17)	1 [Reference]	<.001
MPR				
Median (95% CI)	0.65 (0.58-0.79)	0.89 (0.72-0.97)	0.98 (0.86-1.00)	.001
Prevalence, %	75	31	14	.002
Prevalence ratio (95% CI)	5.22 (1.88-14.50)	2.31 (0.94-5.66)	1 [Reference]	.001
CMG				
Median (95% CI)	0.43 (0.29-0.52)	0.13 (0.09-0.31)	0.09 (0.04-0.20)	.002
Prevalence, %	100	35	24	<.001
Prevalence ratio (95% CI)	—[b]	1.14 (0.74-1.77)	1 [Reference]	.08

CI indicates confidence interval; CMG, continuous multiple-interval medication gaps; CSA, continuous single-interval medication availability; MPR, medication possession ratio.
[a]The median is of the 25th to 75th percentiles, and the prevalence ratio is adjusted for age, race/ethnicity, and sex.
[b]Could not be calculated because the prevalence of nonpersistent CMG is 100%.

Table 4. Cross-Tabulation of Antihypertensive Medication Adherence by Morisky Medication Adherence Scale (MMAS) Score Category and by Pharmacy Fill Adherence

	MMAS Category (Score Range), No. (%)		
Adherence	**Low (<6)**	**Medium (6 to <8)**	**High (8)**
CSA			
Persistent (≥0.8)	1 (12.5)	20 (69.0)	46 (92.0)
Nonpersistent (<0.8)	7 (87.5)	9 (31.0)	4 (8.0)
Total	**8** (100.0)	**29** (100.0)	**50** (100.0)
MPR			
Persistent (≥0.8)	2 (25.0)	20 (69.0)	43 (86.0)
Nonpersistent (<0.8)	6 (75.0)	9 (31.0)	7 (14.0)
Total	**8** (100.0)	**29** (100.0)	**50** (100.0)
CMG			
Persistent (≤0.2)	0 (0.0)	19 (65.5)	38 (76.0)
Nonpersistent (>0.2)	8 (100.0)	10 (34.5)	12 (24.0)
Total	**8** (100.0)	**29** (100.0)	**50** (100.0)

CMG indicates continuous multiple-interval medication gaps; CSA, continuous single-interval medication availability; MPR, medication possession ratio.

Clinicians require information on antihypertensive medication adherence to draw proper conclusions about the effectiveness of treatment.[25] The goal is to have access to a quick, reasonably accurate self-report adherence measure for use in outpatient settings to facilitate clinical decision making. We evaluated the accuracy of a new self-report measure by assessing its association and concordance with pharmacy fill rates. To our knowledge, the concordance between the MMAS and pharmacy fill for antihypertensive medications has not been previously evaluated. In this study, the MMAS maintained a strong, graded, statistically significant association with pharmacy fills. Using CSA, MPR, and CMG for

comparison, the MMAS correctly classified at least 75% of patients as being adherent or not. Furthermore, patients classified as low adherers by the MMAS were significantly more likely to be nonpersistent by each measure of pharmacy fill. Therefore, the MMAS may be a practical and valid approach for identifying low adherers to chronic medication regimens in outpatient settings.

Low adherence poses unique challenges for clinicians trying to determine if prescribed treatment is effective. If clinicians are able to accurately identify patients with low adherence, then appropriate and timely interventions can be implemented. Several modifiable factors have been reported to negatively affect adherence to prescribed therapies. These include forgetfulness,[11] depression,[26] lack of knowledge regarding hypertension and its treatment,[27] complexity of medication regimen,[28] healthcare system perceptions by the patient,[29] sexual dysfunction,[30] adverse effects of medication,[31] and poor quality of life.[32] The MMAS provides information on behaviors associated with low adherence that may be unintentional (eg, forgetfulness) or intentional (eg, not taking medications when one feels worse). Identification of these behaviors can facilitate tailoring of interventions to specific patient issues.[33] For example, if a patient is identified as a low adherer by the MMAS and the responses indicate forgetfulness as a major barrier, then the clinician may suggest that the patient use weekly pill boxes and engage a family member or friend to assist with medication reminders. If a patient is identified as a low adherer and responds that she stops taking medications when she feels better or worse, then the clinician can address knowledge barriers and medication adverse effects and educate the patient about the chronic nature of hypertension and the importance of taking medication as prescribed. On the other hand, if patients are found to be high adherers and their blood pressure remains uncontrolled, then the clinician should consider increasing medication dosage or adding a medication to their regimen.[2,34] It may be that the use of a simple tool (eg, the MMAS) in the outpatient setting may allow clinicians to eliminate low adherence as a contributing factor to poor blood pressure control.

Although the concordance between self-report and pharmacy fill was good in this study, it was not perfect. Shortcomings of self-report include reliance on recall and social desirability bias, with a tendency to overestimate adherence.[10] In addition, pharmacy fill rates may not capture some nuances of medication adherence behavior[9] and are not practical to capture in real time among outpatient clinical encounters. It is generally assumed that patients who fill medications also take them unless they have been instructed by their provider otherwise or have adverse effects that limit their medication intake.[19] It is possible that patients' medication adherence varies by drug class. In the present study, 21 patients had 1 or more drug classes with an MPR of less than 0.8 and had an MPR of 0.8 or higher for other drug classes. Even after accounting for this using a generalized estimating equation, a strong and statistically significant association between self-reported medication adherence and MPR and CMG nonpersistence pharmacy fill rates remained present (data not shown). This suggests that averaging the pharmacy measures did not mask any drug class–specific relationships.

Stroupe and colleagues[35] reported that more than 20% oversupply (ie, MPR, $\geq$1.2) is related to a similar risk of future hospitalization as that experienced by patients with an undersupply of medication (ie, MPR, $<$0.8). In the present study, only 5 patients had a mean MPR of 1.2 or higher, none of whom had low adherence on the MMAS. After excluding these 5 patients, the associations between nonpersistence and self-report medication adherence were similar to those of the original analysis. When we reclassified these patients as nonpersistent, the results were also similar (data not shown).

Study Limitations and Strengths

This study was limited to older community-dwelling adults with managed care insurance and may not be representative of patients from other socioeconomic backgrounds. However, the restriction of our sample to older adults in the managed care organization minimized some of the confounding effects of health insurance, access to medical care, and employment status in the elderly. Because hypertension is prevalent among the elderly nationwide, results of this study may be useful in the evaluation and management of a substantial segment of the population. In addition, clinical prescribing considerations (eg, pill splitting, taking medications on alternate days, stopping a medication because of adverse drug reactions or adverse effects, and hospitalization) or changes in patient schedules (eg, stockpiling medications to accommodate a prolonged vacation) may not have been accurately reflected in pharmacy fill data. Further research is warranted to identify approaches for correctly classifying patients based on pharmacy fill with respect to medication adherence that takes into account prescribing nuances. Also, because of a modest sample size, we did not differentiate level of adherence by drug class. Similar to previously reported findings,[9] patients in this study were high adherers, and further research is needed to explore the associations between self-report and pharmacy fill at lower adherence levels. Although we did not measure blood pressure as part of the study protocol and cannot determine the relationship between self-reported medication adherence, pharmacy fill, and blood pressure control, a previous study[13] demonstrated a significant association between the MMAS score and blood pressure control. Strengths

of this study include the use of a standardized data collection instrument by trained staff, inclusion of a racially/ethnically diverse sample, and access to pharmacy records as an objective gold standard for comparison.

CONCLUSIONS

There are several important clinical implications of our findings. Compared with pharmacy fill, the self-report MMAS performed well in identifying patients with low adherence to antihypertensive medication use. These patients are likely at greatest risk for uncontrolled blood pressure and subsequent adverse outcomes and could benefit most from tailored interventions to overcome barriers to adherence. Although pharmacy fill data represent an objective assessment of medication adherence, this is impractical for use in clinical settings and does not provide information on reasons for low adherence. The MMAS tool is simple and economical to use in routine outpatient settings and may provide clinicians with important information (ie, barriers to adherence) to guide treatment decisions for patients with hypertension. Scores on the MMAS maintained a strong graded association with antihypertensive drug pharmacy fill adherence in community-dwelling seniors receiving healthcare through a managed care organization. This association suggests that patients' self-report of adherence behavior is consistent with the rate at which they fill their antihypertensive medications. The present study extends prior work demonstrating the internal reliability and predictive validity of the MMAS with respect to blood pressure control. This 8-item tool is simple and feasible to incorporate into clinical practice and may be useful in identifying patients at risk for medication adherence issues, including low adherence in outpatient settings.

Take-away Points

Compared with pharmacy fill, the self-report Morisky Medication Adherence Scale (MMAS) performed well in identifying patients with low adherence to antihypertensive medication regimens.

- Low adherers are likely at greatest risk for uncontrolled blood pressure and for subsequent adverse outcomes and could benefit most from tailored interventions to overcome barriers to adherence.
- Although pharmacy fill rates represent an objective assessment of medication adherence, they are impractical for real-time use in most clinical settings.
- The MMAS tool is simple and economical to use in routine outpatient settings and may provide clinicians and administrators with important information to guide treatment decisions for patients with hypertension.

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