Journal of Gerontology: MEDICAL SCIENCES
2005, Vol. 60A, No. 2, 217–223

Validation of the Hopkins Medication Schedule To Identify Difficulties in Taking Medications

Michelle C. Carlson,[1,2] Linda P. Fried,[1,3] Qian-Li Xue,[1,3] Carmen Tekwe,[1] and Jason Brandt[4]

[1]Center on Aging and Health;
[2]Department of Mental Health, [3]Department of Medicine, and
[4]Department of Psychiatry, Division of Medical Psychology, The Johns Hopkins University, Baltimore, Maryland.

Background. Medications often represent the first line of defense in preventing or delaying the progression of chronic diseases. The health implications of improper medication compliance, and failure to identify it, are considerable. The authors thus developed and validated the Hopkins Medication Schedule (HMS), a new objective test of one's ability to understand and implement a routine prescription medication.

Methods. The authors gave a hypothetical physician's prescription for two common medications (antibiotics and aspirin) to 360 high-functioning, community-dwelling, older participants in the Women's Health and Aging Study II and asked them to fill in a daily schedule for taking these medications and to fill in the compartments of a daily pillbox. These scored and timed performances were evaluated for their ability to predict concurrent and 3-year participant-reported difficulty in performing instrumental activities of daily living (IADLs) and for their associations with memory and attention.

Results. Although fewer than 2% of participants reported difficulty in taking medications, nearly 22% were completely unable to complete the schedule, fill the pillbox, or both. The 7% of participants who reported difficulty in any IADL also performed poorly on the HMS. In addition, performance on the schedule and the pillbox predicted concurrent difficulty. In adjusted regression analyses, the schedule was most highly associated with memory and the pillbox with learning and executive function.

Conclusions. The HMS had concurrent validity for participant-reported IADL difficulty. Furthermore, in community-dwelling older women who largely reported no difficulty in taking medications, the HMS identified nearly 22% who could not write or implement a routine medication regimen. This standardized measure may identify those at increased risk for poor medication adherence and, more broadly, IADL difficulty.

As adults age, adherence to prescribed medication regimens becomes one of the most complex instrumental activities of daily living (IADLs). Older adults generally use more medications than do younger adults to treat age-related chronic diseases, such as arthritis, heart disease, and diabetes. Research shows that older adults take an average of five medications per day (1), and this number may be a conservative estimate given the increasing focus on pharmacologic agents to prevent and treat chronic disease. Medications often represent the first line of defense in preventing or delaying the progression of chronic disease. The health implications of improper medication adherence are significant. Poor adherence to medications may undermine their effectiveness in stemming disease progression, particularly if it remains undetected.

The most common types of nonadherence among older adults during hospital stays include underuse (81%), followed by overuse (17%) and misuse (2%) (2). Among the most commonly stated reasons for such noncompliance are forgetfulness and perceptions that the medication is unnecessary. Other studies have found associations between poor adherence and daily drug dose complexity (3,4), suggesting that problems in adherence stem from difficulties in managing a growing and varied regimen of medications. By comparison, reports of noncompliance resulting from problems in opening or handling medication are more rare (5). Overall, poor adherence among older adults is most often attributed to cognitive problems, although such associations have not been conclusively demonstrated (6).

The risk for poor medication adherence in older adults is underscored by the fact that their increasingly complex regimen of medications is accompanied by a greater likelihood of cognitive impairment. Unfortunately, assessing medication adherence is problematic. First, as with many IADLs, medication-taking behavior is not easily observed or directly assessed. Efforts to monitor daily adherence using pill counts and medication refill rates have met with limited success. Persons motivated to appear compliant have been known to discard excess pills before appointments (7–9). Furthermore, pill counts do not show when and how medications were taken. More tamper-proof assessments of adherence, such as blood assays, are often not practical in clinical and large-scale study settings. Thus, clinicians and researchers alike have relied primarily on more indirect measures in the form of patient reporting. Unfortunately, the accuracy of patient-reported adherence has proven questionable when compared with medication monitoring systems (10). Sacrifices in accuracy associated with participant reports of this and other IADL functions almost uniformly lead to an underestimation of difficulty (11–14).

These challenges highlight the value of assessing older adults' ability to take medications using an objective, practical, and standardized instrument. Factors that frequently vary across medications include dosage, dosing intervals, and

dosing conditions. Understanding how these factors are incorporated into the implementation of medication instructions would extend our knowledge of a critical and difficult-to-observe behavior. An objective versus self-reported measure of this IADL may serve to identify persons at risk for poor adherence before it leads to an exacerbation of medical conditions and increased morbidity. Furthermore, identification of cognitive and other factors associated with noncompliance may provide insights into improved methods for the detection of nonadherence, management of medication use, and the design of preventive interventions.

Methods

Participants

The Women's Health and Aging Study II (WHAS II) is a prospective study of physical functioning among the least disabled two thirds of 70- to 80-year-old, community-dwelling women in eastern Baltimore, Maryland. The sampling and recruitment of this cohort have been described before (15,16). Trained interviewers determined eligibility according to whether the women: 1) were 70 to 79 years old as of the sampling date, 2) had sufficient hearing and proficiency in English to be interviewed, 3) could be contacted by telephone, 4) had a Mini-Mental State Examination (MMSE) (17) score greater than 23, and 5) had no reported difficulty or difficulty in only one of the following four domains: mobility and exercise tolerance, upper extremity function, higher functioning tasks (e.g., shopping), and basic self-care (16,18). Based on these eligibility criteria, 436 of 880 eligible women participated in the baseline examination. Of these, 360 participants were able to return to the clinic for year three testing and were given the Hopkins Medication Schedule (HMS).

Each participant gave informed consent and completed an interview, which included a comprehensive medical history that assessed the presence of 14 chronic conditions or diseases by physician diagnosis (18) and vision or hearing difficulties and a cognitive examination, as part of a 1-day evaluation in the Functional Status Laboratory at The Johns Hopkins Outpatient General Clinical Research Center. Those who were lost to follow-up or who otherwise did not complete the HMS during year 3 were older than those who did and more often were black ($p < .01$). This loss to follow-up likely resulted in an underestimation of difficulty with medication adherence.

Components of the Hopkins Medication Schedule

The HMS is a standardized test of the ability to understand (schedule) and implement (pillbox) a complex IADL critical to health: managing medications.

The schedule.—On the HMS, presented in the Appendix, the participant was read (and read along with) a hypothetical scenario in which her physician gave her 1 prescription for an antibiotic and for aspirin to treat an infection along with directions for taking each. The participant was then asked to plan a schedule for taking these medications and water during the course of a day, following the instructions provided. The participant filled in the schedule with hours of the day marked and standard times for breakfast, lunch, and dinner indicated. The test was completed at the participant's own pace or until 8 minutes had elapsed. The schedule was scored on a standard form according to nine criteria: compliance with timing of doses, method, and daily dosage of antibiotics (3 points) and aspirin (3 points), and proper intake of snacks and water (3 points).

The pillbox.—After completing the schedule, the participant was given an 8-ounce bottle of aspirin and a prescription bottle with a non–child-proof cap containing approximately 10 capsules filled with an inert powder (cornstarch or baking powder). This latter bottle was labeled as ''antibiotics,'' with instructions to take 1 pill three times a day. The participant was then given a common pill dispenser with 4 open compartments labeled *morning, lunch, dinner*, and *bed* and instructed to follow the same instructions for filling as for the schedule (which remained available). Participants received assistance, as needed, to open bottles and then filled the dispenser at their usual pace or until 4 minutes had elapsed. The pillbox was scored on a standard form for proper placement of the proper numbers of antibiotics (1 point) and aspirin (1 point) to obtain a maximum possible score of 2.

Time to complete each component varied widely among the participants who obtained similar scores and was considered a potentially important measure of ability. We evaluated time in the following two ways. The first method accounted for speed and accuracy trade-offs on each component by creating a ratio to represent each score divided by its time (to 0.1 seconds). The second, more clinically suited method incorporated time more simply as a bonus point to be applied to each score if the participant accurately completed the schedule ($\geq$6 of 9 points) within 4 minutes and the pillbox (2 points) within 2 minutes. These cutoffs were chosen during pilot clinical testing because they gave those who were able to do the task sufficient time to complete each component at a usual pace. The resulting time-adjusted scores ranged from 0 to 10 on the schedule and from 0 to 3 on the pillbox.

Prevalent and Incident Participant-Reported Difficulty in Higher-Order Instrumental Activities of Daily Living

Difficulty in performing IADLs is most often obtained by patient report (yes vs no). Previous research in the WHAS I, a complementary cohort to the WHAS II representing the one third most disabled community-dwelling older women, has identified six related IADL tasks that appear to depend critically on cognition (18). These tasks have been categorized as representing the higher functioning domain of physical function and include light housework, using the telephone, preparing meals, shopping, taking medications, and managing finances. Self-reported difficulty in one or more of these higher functioning tasks signaled difficulty and was assessed along with the administration of the HMS.

Cognitive Assessment

Cognitive testing by a trained technician consisted of an initial examination of global cognitive function with the

Table 1. Demographic, Health, Global Cognitive and Functional Characteristics of the WHAS II Participants Administered the Hopkins Medication Schedule ($N = 360$)

Demographics		%
Age (y; mean, *SD*)	77.5 (2.8)	
Race		
White		83.1
Black		16.9
Education (y)		
0–8		12.2
9–11		13.6
12		31.4
>12		42.8
MMSE (mean, *SD*)	28.4 (1.6)	
No. of chronic diseases		
0		2.4
1		13.9
2–4		73.3
≥5		10.6
Self-reported difficulty in HF IADLs		
Composite		6.7
Light housework		0.8
Preparing meals		1.1
Using phone		1.9
Shopping		4.2
Taking medication		1.4
Managing money		0.8

Note: *SD* = standard deviation; HF IADLs = higher functioning instrumental activities of daily living; MMSE = Mini-Mental Status Examination.

MMSE. Standardized neuropsychological tests were also administered to evaluate verbal memory, psychomotor speed, and executive attention. The Hopkins Verbal Learning Test-Revised (19,20) assessed verbal learning of 12 common words from three learning trials and delayed recall of these words after a filled, 15-minute interval.

Pychomotor speed and executive planning and flexibility were assessed in a standard manner using the Trail Making Test (TMT), Parts A and B, respectively (21,22). If participants could not complete either portion of the test for cognitive reasons, they were assigned the maximum time allotted for Parts A (300 seconds) and B (420 seconds). A second measure of executive function, Digit Span Backward (with Digit Span Forward as a control measure of repetition), was administered according to standard criteria (21) and required the participant to repeat sequences of numbers of successively increasing length (forward) and then to repeat similar sequences of increasing length in reverse order (backward).

Results

Table 1 summarizes the demographic and health characteristics and MMSE scores of the sample. Participants were approximately 77 years old. Most received a high-school education and obtained an MMSE score well within normal limits. Only 6.7% ($n = 23$) of participants reported difficulty in any of the six higher functioning IADLs surveyed. Participants most often reported difficulties in shopping (3.8%) and less often in taking medications (1.5%). Table 2 presents the mean performances on cognitive tests, which were within normal limits.

Table 2. Comparisons of Hopkins Medication Schedule Scores and Cognitive Test Performances Between Those Reporting Difficulty in One or More Higher-Order, Instrumental Activities of Daily Living and Those Reporting None

Hopkins Medication Schedule	Overall ($N = 360$)	Difficulty in ≥1 HF IADL ($N = 26$) × (*SD*)	No Difficulty in HF IADLs ($N = 334$) × (*SD*)
Schedule			
Score	5.2 (2.5)	4.3 (2.2)†	5.3 (2.5)
Range	0–9.0	0–8.0	0–9.0
Time-adjusted score	5.6 (2.8)	4.5 (2.5)‡	5.64 (2.8)
Range	0–10.0	0–10.0	0–9.0
Score/time	1.8 (1.2)	1.2 (0.7)*	1.8 (1.2)
Range	0–6.1	0–6.1	0–2.7
Pillbox			
Score	1.4 (0.7)	1.2 (0.9)	1.4 (0.7)
Range	0–2.0	0–2.0	0–2.0
Time-adjusted score	1.9 (1.2)	1.7 (1.3)	1.9 (1.4)
Range	0–3.0	0–3.0	0–3.0
Score/time	1.2 (0.9)	0.8 (0.6)†	1.3 (0.9)
Range	0–4.1	0–2.0	0–4.1
Cognitive tests			
HVLT Learning	23.4 (5.6)	21.4 (6.3)	23.5 (5.5)
HVLT Recall	8.3 (2.7)	7.8 (2.9)	8.3 (2.7)
TMT, Part A (s)	50.9 (33.1)	94.5 (93.8)‡	47.1 (21.0)
TMT, Part B (s)	148.7 (94.6)	209.2 (111.8)‡	144.9 (92.4)
Digit Span, Forward	7.8 (2.0)	7.8 (2.1)	7.8 (2.0)
Digit Span, Backward	5.7 (2.1)	5.7 (2.1)	5.7 (2.1)

Notes: *$p < .0005$.
†$p < .005$.
‡$p < .05$.
SD = standard deviation; HF IADLs = higher functioning instrumental activities of daily living; HVLT = Hopkins Verbal Learning Test; TMT = Trail Making Test.

Participants' Performance on the Hopkins Medication Schedule

Participants' mean performances on the schedule and pillbox varied considerably. Participants completed the schedule in approximately 228 seconds, with an average raw score of 5.2 of 9 possible points. Nineteen participants tried but could not successfully complete any part of the schedule, obtaining a score of 0, and an additional 31 could not attempt the schedule for cognitive reasons. Raw scores on the pillbox averaged 1.4 of 2 possible points, with an average completion time of 106 seconds. Forty-nine participants tried but could not successfully complete any part of the pillbox, and an additional 13 could not attempt the pillbox for cognitive reasons. A total of 82 participants incorrectly completed (0 score) or could not complete one or both components of the HMS. Among those who could not complete the schedule, 42% were nonetheless able to complete the pillbox, whereas 100% of those unable to complete the pillbox also could not complete the schedule. Scores on each component were modestly correlated ($r = .38$; $p < .0001$). When time was incorporated as a bonus point, 35% obtained a bonus point on the schedule and 47% obtained a bonus point on the pillbox.

Table 3. Characteristics of WHAS II Participants Performing in the Lowest and Highest Quartiles on the Schedule and Pillbox Components of the Hopkins Medication Schedule

	Schedule		Pillbox	
Characteristic	Poor	Best	Poor	Best
Age (mean, *SD*)	77.9 ± 2.7	77.1 ± 2.7	78.1 ± 2.8	76.9 ± 2.6‡
Race (%)				
White	59.3	96.5*	67.4	93.5*
Black	39.5	3.5	31.5	6.5
Education (%)				
0–8 years	18.6	3.5*	20.0	2.2*
9–11 years	23.3	5.8	19.1	10.9
12 years	34.9	27.9	23.6	26.1
>12 years	23.3	62.8	37.1	60.9
MMSE (mean, *SD*)	27.5 ± 1.9	29.0 ± 1.1*	27.7 ± 1.9	29.0 ± 1.1*
No. of chronic diseases (%)				
0	1.2	2.3	0	2.2
1	9.3	18.6	11.2	18.5
2–4	77.9	72.1	77.5	73.9
≥5	11.6	7.0	11.2	5.4
Self-reported difficulty in HF IADLs (%)				
Composite	8.1	2.3	9.0	2.2
Light housework	1.2	0	1.1	0
Preparing meals	0	0	1.1	0
Using phone	0	1.2	1.1	2.2
Shopping	3.5	0‡	5.6	0‡
Taking medication	3.5	0	2.4	0
Managing money	0	1.2	1.2	0

Notes: *$p < .0005$.
†$p < .005$.
‡$p < .05$.
SD = standard deviation; MMSE = Mini-Mental State Examination; HF IADLs = higher functioning instrumental activities of daily living.

Hopkins Medication Schedule as a Predictor of Concurrent Difficulty With Instrumental Activities of Daily Living

To evaluate the criterion validity of the HMS, we compared performances on the schedule and pillbox to the standard method for assessing participant-reported IADL difficulty. Table 2 shows HMS performances among participants reporting IADL difficulty ($n = 23$) and compares them with those reporting no such difficulty. The IADL difficulty group was significantly more impaired on raw, time-adjusted, and score:time ratio scores on the schedule and pillbox. In addition, the IADL difficulty group exhibited significantly greater difficulty on cognitive tests of verbal learning (Hopkins Verbal Learning Test-Revised), psychomotor speed (TMT, Part A), and, particularly, mental flexibility (TMT, Part B).

Logistic regressions of IADL difficulty, adjusted for participant age, education, and race, showed that the schedule score:time ratio, but not raw or time-adjusted bonus scores, marginally predicted concurrent difficulty in any IADL, with an odds ratio of 0.61 (95% confidence interval [CI], 0.36 to 1.01; $p = .0563$). In other words, for every unit increase in this ratio, there was a 39% reduced risk of being in the IADL difficulty group. The pillbox score:time ratio also predicted concurrent difficulty with IADLs, with an odds ratio of 0.54 (95% CI, 0.29 to 0.98; $p = .0442$), indicating a 46% reduction of risk for IADL difficulty with every unit increase in this ratio. In summary, participant-reported difficulty in any IADL was very infrequent, and when reported, it occurred along with objective difficulty on the HMS as assessed by a speed-based measure.

Comparison of the Best and Poorest Performers of the Hopkins Medication Schedule

We developed the HMS to identify those who may underreport IADL difficulty as a result of cognitive impairment. To determine whether objective IADL difficulty was associated with cognition, and thus to provide external validation for this instrument, we compared cognitive test performances of the poorest and best HMS performers according to their ratio scores. Table 3 presents demographic, health, and cognitive test comparisons of those in the lowest (i.e., poor) and highest (i.e., best) quartiles on the schedule and pillbox, respectively. We found nearly 51% overlap among participants performing in the lowest quartiles on both the schedule and the pillbox.

On the schedule, only 8% (7 of 86) of poor performers reported any higher functioning IADL difficulty in shopping and taking medications. Fewer than 2% (2 of 86) of the best performers reported any higher functioning IADL difficulty. On the pillbox, approximately 9% (8 of 89) of poor performers reported any higher functioning IADL difficulty, most often in shopping. The two best performers reported higher functioning IADL difficulty in using the telephone, which they attributed to arthritis of the hand.

Associations Between Performance on the Hopkins Medication Schedule and Cognition

In the entire cohort, we conducted separate regression analyses of cognition on the schedule and pillbox score:time ratio and time-adjusted scores, adjusting for previously noted covariates. When each cognitive measure was regressed separately in univariate models (Table 4), most measures were associated with score:time ratio and time-adjusted measures on both components of the HMS, with one exception. Digit Span Forward was not associated with either pillbox score or with score:time on the schedule. When we entered all cognitive measures simultaneously in a competing model, Hopkins Verbal Learning Test-Revised Delayed Recall and Digit Span Backward scores were each independently and positively associated with both measures on the schedule. The selective association between score:time, versus the time-adjusted score, and the TMT, Part A likely reflects the greater emphasis that the former measure places on speed of processing. Competing models for the pillbox also showed that the score:time ratio, but not the time-adjusted score, was most strongly associated with TMT, Part A. The absence of any selective associations for the time-adjusted pillbox score suggests that each measure of cognition is collinear, accounting for common underlying cognitive variability in performance.

Discussion

This study suggests that a new, objective measure of medication adherence, the HMS, may serve as a sensitive

Table 4. Univariate and Competing Regression Models of the Associations Between Speeded Measures on the Schedule and Pillbox and Cognitive Test Performances, Adjusted for Age, Race, and Education

	Univariate Regressions				Competing Regression			
	Schedule		Pillbox		Schedule		Pillbox	
Score/Time	Beta	*SE*	Beta	*SE*	Beta	*SE*	Beta	*SE*
HVLT Learning	0.06*	0.01	0.04*	0.01	0.01	0.02	0.02	0.01
HVLT Delayed Recall	0.16*	0.03	0.07*	0.02	0.13*	0.04	0.02	0.03
Trail Making Test, Part A	−0.01*	0.003	−0.01*	0.002	−0.01‡	0.004	−0.01†	0.003
Trail Making Test, Part B	−0.004*	0.001	−0.002*	0.001	−0.001	0.001	−0.001	0.001
Digit Span, Forward	0.06	0.03	0.02	0.02	0.003	0.03	0.004	0.03
Digit Span, Backward	0.13*	0.03	0.05‡	0.02	0.10*	0.03	0.01	0.03
	Comp.		Pillbox		Comp.		Pillbox	
Time-adjusted Bonus	Beta	*SE*	Beta	*SE*	Beta	*SE*	Beta	*SE*
HVLT Learning	0.14*	0.03	0.04*	0.01	−0.05	0.04	0.01	0.02
HVLT Delayed Recall	0.37*	0.06	0.09†	0.03	0.39*	0.08	0.05	0.04
Trail Making Test, Part A	−0.02†	0.007	−0.006‡	0.003	−0.01	0.01	−0.001	0.004
Trail Making Test, Part B	−0.01*	0.002	−0.002‡	0.001	−0.002	0.002	−0.001	0.001
Digit Span, Forward	0.19‡	0.07	0.01	0.03	0.04	0.07	−.02	0.04
Digit Span, Backward	0.35*	0.07	0.06‡	0.03	0.27*	0.07	0.04	0.04

Notes: *$p < .0005$.
†$p < .005$.
‡$p < .05$.
SE = standard error; HVLT = Hopkins Verbal Learning Test.

clinical tool in assessing an older adult's ability to understand and implement a routine medication schedule. Fewer than 7% of older, community-dwelling women reported any difficulty in most IADLs, with only 2% reporting difficulty in taking medications. These participant-reported IADL difficulties occurred along with difficulties with both components of the HMS, particularly the pillbox. In addition, this subset of participants exhibited cognitive impairment relative to the larger group on measures of memory, psychomotor speed, and mental flexibility.

In contrast to participant-reported data, nearly 22% of older women could not complete either component of the HMS. Their substantial difficulties in understanding and implementing instructions for 2 standard medications (antibiotics and aspirin) suggest that the HMS may identify a significant number at risk for IADL difficulty in the absence of perceived or acknowledged impairment. Given the proportion of persons who report ''forgetfulness'' in taking medications, and the inaccuracies associated with self-reported IADL difficulties in cognitively impaired persons in this and other cohorts, the HMS may more closely approximate the true proportion of persons at risk for current or future difficulties in medication adherence. Certainly, the proportion of participants exhibiting (versus reporting) difficulties on the HMS conforms to reported rates of medication nonadherence in older patient groups (23–25), which range from 25% to 60%. These findings indicate that this test may have utility as a sensitive screening tool in otherwise high-functioning older women.

When we developed scoring methods for the HMS, we hypothesized that the time required for a participant to complete each component at her usual pace would provide useful information regarding current and future risk for IADL difficulty. In other words, all other things being equal (e.g., environment, score), a person who requires more time to achieve the same result as another may be having more trouble. To test this hypothesis, we developed two speed-based measures, one that weights time and score information equally in a score:time ratio, and one that more simply incorporates time as a bonus point if a participant completes the test within a specified period. Comparisons of each of these speeded measures initially suggest that the ratio increases sensitivity in predicting concurrent difficulty. Nevertheless, both measures were comparably associated with specific domains of cognition, which will be discussed here. We must still determine whether the more clinically amenable time-adjusted score will be equivalent to the less clinically intuitive ratio (score:time) in predicting future risk for difficulty.

In validation analyses, the schedule and pillbox were associated with most cognitive functions and with executive function, in particular. Specifically, performance on the schedule was most strongly associated with Digit Span Backward, an index of executive function, and with memory recall, the cognitive domain implicated in the earliest stages of Alzheimer's disease. Performance on the pillbox was comparably associated with all domains of cognition measured. The associations we observed on the schedule are consistent with other research findings that show that executive ability is particularly important to organizing new information to initiate and complete a course of action (26).

Medication adherence is thought to be among the most complex of the higher functioning IADLs. As such, decline in this function may signal a cascade or hierarchy of changes in other functions critical to safe and independent living. Indeed, the HMS schedule was able to predict subsequent IADL difficulty by participant report. Early detection of difficulty with medication adherence may also offer a window for the introduction of remedial strategies and behavioral interventions. In addition, those persons at risk for IADL difficulty in the absence of self-reported difficulty may rep-

resent a group in the early stages of progressive neurologic diseases, such as Alzheimer's disease. A hallmark of this disease in its prodromal and early clinical stages is a progressive loss of memory and function in complex IADLs. The multiple cognitive demands required on the HMS to remember and organize information may expose vulnerabilities not yet evident on global cognitive screening tools or on an individual cognitive test. As such, it may provide an important supplement to current, more fallible detection methods by identifying vulnerable persons who require follow-up and who may benefit from targeted interventions.

We designed the HMS to present a realistic scenario of a physician prescribing medications and factors associated with the ability to manage medications. The schedule evaluated explicit comprehension and ability to integrate information on daily dosing for each medication. The pillbox simulated a typical method for implementing a physician's instructions and optimized performance by approximating what a participant may routinely do in her home. Eighteen participants who could not complete the schedule were nonetheless able to complete the pillbox. The inability to fill the pillbox for this simple regimen raises the real possibility of significant impairment in performing what is likely to be a more complex regimen at home. What this task by itself cannot show is how the context in which an older adult takes medications may affect adherence. Important contextual factors include a person's level of exposure to and experience with managing medications (e.g., number of medications, access to medications, or assistance from a spouse), and use of environmental and home aids to reduce forgetfulness (e.g., a clock, placing pills in a prominent location). These and other factors must be evaluated in conjunction with HMS test performance to better identify those at true risk for poor medication compliance as well as those compensations or strategies that may be developed to facilitate adherence.

Finally, use of this instrument need not be restricted to older populations. For example, psychiatric patient populations often suffer a recurrence or exacerbation of symptoms as a result of poor medication adherence. Although poor adherence can occur in response to the remission of symptoms, the HMS may be used in selected patient populations (e.g., those with head injuries) to identify those with compromised ability to either comprehend or organize their medications.

Acknowledgments

Supported in part by National Institute on Aging grants R01-AG11703 and R01 AG19825-01.

The authors thank Laura Fishpaw and Ora White for their supervision and assistance in data collection, and Marcia Omondi for assistance in manuscript preparation.

Address correspondence to Michelle C. Carlson, PhD, Center on Aging and Health, The Johns Hopkins University, 2024 E. Monument Street, Suite 2-700, Baltimore, MD 21205. E-mail: mcarlson@jhsph.edu

References

1. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone Survey. *JAMA.* 2002;287:337–344.
2. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med.* 1990;150:841–845.
3. Greenberg RN. Overview of patient compliance with medication dosing: a literature review. *Clin Ther.* 1984;6:592–599.
4. Hulka BS, Cassel JC, Kupper LL, Burdette JA. Communication, compliance, and concordance between physicians and patients with prescribed medications. *Am J Publ Health.* 1976;66:847–853.
5. McElnay JC, McCallion CR, al-Deagi F, Scott M. Self-reported medication non-compliance in the elderly. *Eur J Clin Pharmacol.* 1997;53:171–78.
6. Wong BS, Norman DC. Evaluation of a novel medication aid, the calendar blister-pak, and its effect on drug compliance in a geriatric outpatient clinic. *J Am Geriatr Soc.* 1987;35:21–26.
7. Rand C, Wise R, Nides M, et al. Metered-dose inhaler adherence in a clinical trail. *Am Rev Respir Dis.* 1992;146:1559–1564.
8. Rudd P, Byyny R, Zachary V, et al. The natural history of medication compliance in a drug trial: limitations of pill counts. *Clin Pharmacol Ther.* 1989;46:2309–2327.
9. Rudd P, Ahmed S, Zachary V, Barton C, Bonduelle D. Compliance with medication timing: implications from a medication trial for drug development and clinical practice. *J Clin Res Pharmacoepidemiol.* 1992;6:627–628.
10. Waterhouse D, Calzone K, Mele C, Brenna D. Adherence to oral tamoxifen: a comparison of patient self-report, pill counts, and microelectronic monitoring. *J Clin Oncol.* 2001;11:1189–1197.
11. DeBettignies BH, Mahurin RK, Pirozzolo FJ. Insight for impairment in independent living skills in Alzheimer's disease and multi-infarct dementia. *J Clin Exp Neuropsychol.* 1990;12:335–363.
12. Guralnik J, Branch L, Cummings S, Curb J. Physical performance measures in aging research. *J Gerontol Biol Sci Med Sci.* 1989;44A: M141–M146.
13. Keller D, Kovar M, Jobe J, Branch L. Problems eliciting elders' reports of functional status. *J Aging Health.* 1993;5:306–318.
14. Sager M, Dunham N, Schwantes A, Mecum L, Halverson K, Harlowe D. Measurement of activities of daily living in hospitalized elderly: a comparison of self-report and performance-based methods. *J Am Geriatr Soc.* 1992;40:457–462.
15. Carlson MC, Fried LP, Xue QL, et al. Association between executive attention and physical functional performance in community-dwelling older women. *J Gerontol Soc Sci.* 1999;54B:S262–S270.
16. Fried L. Epidemiology of aging. *Epidemiol Rev.* 2000;22:95–106.
17. Folstein M, Folstein S, McHugh PR. Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:189–198.
18. Fried L, Bandeen-Roche K, Kasper J, Guralnik J. Association of comorbidity with disability in older women: the Women's Health and Aging Study. *J Clin Epidemiol.* 1999;52:27–37.
19. Benedict R, Schretlen D, Groninger L, Brandt J. Hopkins Verbal Learning Test–Revised: normative data and analysis of inter-form and test-retest reliability. *Clin Neuropsychol.* 1998;12:43–55.
20. Brandt J. The Hopkins Verbal Learning Test: development of a new memory test with six equivalent forms. *Clinical Neuropsychol.* 1991;5: 125–142.
21. Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Mot Skills.* 1958;8:271–276.
22. Spreen O, Strauss E. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary,* 2nd Ed. New York: Oxford University Press; 1991
23. Stewart R, Cluff L. Commentary: a review of medication errors and compliance in ambulant patients. *Clinical Pharmacol Ther.* 1972;13:463.
24. Blackwell B. The drug defaulter. *Clinical Pharmacol Ther.* 1972;13:841.
25. Schernitski P, Bootman J, Byers J. Demographic characteristics of elderly drug overdose patients admitted to a hospital emergency department. *J Am Geriatr Soc.* 1980;28:544.
26. Grigsby J, Kaye K, Baxter J, et al. Executive cognitive abilities and functional status among community-dwelling older persons in the San Luis Valley Health and Aging Study. *J Am Geriatr Soc.* 1998;46: 590–596.

Received May 27, 2003
Accepted October 3, 2003
Decision Editor: John E. Morley, MB, BCh

Appendix: Medication Schedule

Read the medication instructions below. Assume that you eat breakfast, lunch, and dinner at the following listed times. Please indicate at what times you should take each medication and how many you need to take. Also, indicate when your should drink water and eat any snacks.

Antibiotics:	Take 1 pill three times a day, at least 30 minutes before meals.		
Aspirin:	Take 2 tablets every 4 hours. May cause stomach upset if taken on an empty stomach. Make sure to eat meals and snacks with tablets.		
Water:	Drink a full glass of water every 2 hours.		
7:00 AM	Wake up	3:00 PM	
7:30 AM		3:30 PM	
8:00 AM	Breakfast	4:00 PM	
8:30 AM		4:30 PM	
9:00 AM		5:00 PM	
9:30 AM		5:30 PM	
10:00 AM		6:00 PM	Dinner
10:30 AM		6:30 PM	
11:00 AM		7:00 PM	
11:30 AM		7:30 PM	
12:00 Noon	Lunch	8:00 PM	
12:30 PM		8:30 PM	
1:00 PM		9:00 PM	
1:30 PM		9:30 PM	
2:00 PM		10:00 PM	
2:30 PM		10:30 PM	
		11:00 PM	Go to bed