ASSESSING MEDICATION ADHERENCE AMONG OLDER PERSONS IN COMMUNITY SETTINGS

Shelly A. Vik,[1] Colleen J. Maxwell,[1,2,3] David B. Hogan,[1,2] Scott B. Patten,[1,3] Jeffrey A. Johnson,[3,4] Lori Romonko-Slack[5]

[1]Departments of Community Health Sciences, [2]Medicine, University of Calgary, Calgary AB
[3]Institute of Health Economics, Edmonton AB, [4]Department of Public Health Sciences, University of Alberta, Edmonton AB, [5]Calgary Health Region

Corresponding Author: maxwell@ucalgary.ca

ABSTRACT

Background
Medication adherence is an important public health issue. To better understand its relevance among vulnerable populations requires the availability of a valid, reliable and practical measurement approach. Researchers have proposed various competing methods, including pill counts and self-report measures.

Objective
To examine the utility of pill counts compared with self-report measures in the assessment of medication adherence among older home care clients.

Methods
The sample included 319 home care clients aged 65+ years randomly selected from urban and rural settings. During in-home assessments, nurses performed a medication review (including a pill count), administered the Morisky self-report scale, obtained supplemental information on medication use and completed the Resident Assessment Instrument for Home Care (RAI-HC). Responses to the Morisky scale and an open-ended question on nonadherence were combined to form a composite self-report measure of adherence.

Results
Pill counts were either not feasible or considered inaccurate for 34.7% of subjects (47.5% of all eligible drugs). For the 205 subjects with available pill counts, estimates derived from the dispense date were found to underestimate adherence when compared with the actual start date reported by clients. The Morisky scale showed low reliability (Cronbach's α=0.42) and subjects' responses to the scale were often in disagreement with their responses to the open-ended question on nonadherence. There was poor agreement between the pill count and self-report measures.

Conclusion
Our findings raise concerns about the feasibility and accuracy of pill counts as well as the validity of the Morisky self-report scale in the assessment of medication adherence among community-dwelling seniors.

Key Words: *Medication adherence, measurement, pill count, self-report, elderly, home care*

Medication nonadherence among older persons is a public health concern and has generated significant research interest. The proportion of hospitalizations attributable to drug nonadherence has been estimated to be as high as 10 percent.[1-3] However, interventions to improve adherence have rarely been linked to better health outcomes.[4] This may be due, in part, to the inherent difficulties in measuring a complex behavioural risk factor such as nonadherence.

At present, there is no 'gold standard' measure of medication adherence. Various objective methods have been employed to assess adherence, including biological assays,[5-9]

prescription claims[10-13] and pill counts.[14-17] All have their limitations. Biological assays are intrusive, costly and may be impractical. Further, results may be influenced by factors other than adherence such as drug or food interactions, physiological variability, dosing schedules and the half-life of the drug.[18-20] Claims data have primarily been used to estimate adherence with medications taken for chronic illnesses.[12,13,21] They provide a direct record of drugs dispensed but at best a proxy measure of drugs consumed. With pill counts, prescriptions may be filled some time before needed and subjects may not accurately recall the date medications were started,[22] drugs may not be stored in their original containers and/or tablets from other bottles may be added to the new container.[14] The Medication Event Monitoring System (MEMS) can provide information on adherence by electronic monitoring of dosing schedules.[23-25] As with biological assays, poor availability and the cost of these devices limit their feasibility in community settings.

An alternative approach involves the use of self-report measures of medication adherence.[26-31] Early studies found self-report to underestimate nonadherence when compared with pill counts or biological assays.[32-34] Subsequent research, however, suggests that self-report may provide a reasonably accurate estimate of adherence.[5,6,22,35]

The objectives of our study were: to document the limitations of pill counts when used to assess medication adherence in a community setting; and, to compare pill counts with two self-report measures: (i) a 4-item scale (Morisky scale)[36] and (ii) a composite self-report assessment combining responses to the Morisky scale items and to a single open-ended question regarding reasons for nonadherence. To our knowledge, this is the first study to systematically document the limitations of using pill counts to assess adherence among older, at-risk persons in a community setting.

METHODS

Subjects

Participants were older home care clients enrolled in a longitudinal study examining medication adherence and health-related outcomes. Between March and June of 2000, 330 subjects were recruited from a computer-generated random sample of all older home care clients in two Alberta health regions. Inclusion criteria were: currently receiving publicly funded home care services; residing within the jurisdiction of their respective health region; age 65 years of age or older; and, written informed consent from either the subject or a legal guardian. To obtain our target sample size, 376 eligible participants were contacted (response rate = 87.8%).[37] Eleven subjects were not taking any prescribed medications and were excluded, leaving 319 subjects for the present analysis. Further details of the study protocol can be found elsewhere.[37] This study received ethical approval from the Health Research Ethics Board of the University of Calgary and the Ethics Review Committee of the Chinook Health Region.

Data Sources

Trained study nurses performed a comprehensive medication review and administered the Resident Assessment Instrument for Home Care (RAI-HC)[38-40] during in-home interviews with the subjects (and caregivers where appropriate). The in-home assessment included supplemental questions regarding medication administration, health service utilization and access, non-prescribed and alternative medicines, reasons for nonadherence and use of tobacco and alcohol.[37] The following information was recorded for all prescribed and over the counter (OTC ~ excluding prescription-related data items) medications consumed during the previous seven days: generic drug name; dose; route of administration; frequency of use; amount administered; date medication dispensed and started; duration of use; name of dispensing pharmacy and prescribing physician; and, quantity of medication dispensed and remaining.

Measures of Adherence

The following three measures of adherence were examined:

(i) Morisky Scale

Subjects were randomly administered one of two response versions of a 4-item self-report scale developed by Morisky et al[36]: 1) the original binary response option (no / yes) OR 2) a 5-point

response version (never / rarely / sometimes / often / always). The two versions were used in order to examine their respective sensitivity and predictive validity. Scores for the scale range from 0-4 (dichotomous version) and 0-16 (5-point version) with higher scores indicative of worse adherence (Tables 1a & 1b).

TABLE 1a Summary of responses to questions from the Morisky scale[a] administered with a dichotomous response option (n=157).

Question	**Percent (number)**	
Response (Coding)	**No (0)**	**Yes (1)**
Do you ever forget to take your medications?	61.2 (96)	38.9 (61)
Are you careless at times about taking your medications?	92.4 (145)	7.6 (12)
When you feel better, do you sometimes stop taking your medications?	91.1 (143)	8.9 (14)
Sometimes if you feel worse when you take your medications, do you stop taking them?	77.1 (121)	22.9 (36)
Distribution of Scores	**Total Sample**	
0	47.1 (74)	
1	34.4 (54)	
2	12.1 (19)	
3	5.7 (9)	
4	0.6 (1)	
Binary estimate of nonadherence (score 2+)	18.5 (29)	

[a]Subjects were asked: "Thinking of the medications PRESCRIBED to you by your doctor(s), please answer the following questions."

TABLE 1b Summary of responses to questions from the Morisky scale[a] administered with a 5-point response option: never=0; rarely=1; sometimes=2; often=3; always=4 (n=161).

Question	**Percent (number)**				
Response (Coding)	**0**	**1**	**2**	**3**	**4**
Do you ever forget to take your medications?	48.8 (78)	37.5 (60)	12.5 (20)	0.6 (1)	0.6 (1)
Are you careless at times about taking your medications?	80.0 (128)	11.3 (18)	8.1 (13)	0.6 (1)	0.0 (0)
When you feel better, do you sometimes stop taking your medications?	83.8 (134)	4.4 (7)	9.4 (15)	1.9 (3)	0.6 (1)
Sometimes if you feel worse when you take your medications, do you stop taking them?	77.5 (124)	6.9 (11)	7.5 (12)	1.9 (3)	6.3 (10)

Distribution of Scores	**Total Sample**
0	35.4 (57)
1	20.5 (33)
2	16.8 (27)
3	7.5 (12)
4	9.3 (15)
5	3.7 (6)
6	3.1 (5)
7	0.6 (1)
8	3.1 (5)
Binary estimate of nonadherence (score 3+)	27.3 (44)

[a]Subjects were asked: "Thinking of the medications PRESCRIBED to you by your doctor(s), please answer the following questions."

Can J Clin Pharmacol Vol 12 (1) Winter 2005: e152-e164; Apr. 2005

ii) Pill Count

Pill counts were attempted on all prescribed medications that were to be taken regularly in discrete dosages. Percent adherence was calculated using the following equation: (number of tablets taken / number of tablets that should have been taken) x 100.

Estimates derived using the dispense date were compared with those obtained using the start date as reported by the client. Overall adherence was estimated by averaging the adherence estimates for each medication the subject was taking. To facilitate analyses, when overuse was observed we subtracted the number of extra tablets from the number of tablets that should have been taken and this figure was used in the numerator. To determine the representativeness of the subject's average adherence estimate, the proportion of all medications counted per subject was calculated.

(iii) Composite Self-Report Measure

A composite estimate of adherence was made utilizing all available recorded self-report data. This measure was derived by cross-referencing subjects' responses to the individual scale items (Morisky) with their responses to an open-ended question regarding reasons for nonadherence (see Table 2).

TABLE 2 Reasons for nonadherence reported by 153 subjects[a] in response to an open-ended question[b].

Reason	**Percent (number)**
Intentional Nonadherence	
Side Effects	28.7 (52)
Alter regimen as see fit	14.9 (27)
Think medications not effective	5.0 (9)
Don't care to take medications	3.9 (7)
Modify diuretics due to increased urination	3.3 (6)
Omit medications if feeling ill	1.1 (2)
Alter dosing schedule for convenience	1.1 (2)
Stop to see if still needed	1.1 (2)
Fasting once/month	0.6 (1)
Total Intentional	**59.7 (108)**
Unintentional Nonadherence	
Forget	33.7 (61)
Confusion/hiding pills	1.7 (3)
Too expensive	0.6 (1)
Trouble swallowing pills	0.6 (1)
Trouble operating dispensers (inhalers)	0.6 (1)
Trouble reading labels	0.6 (1)
If run out (e.g. pharmacy delivers late or makes error)	2.8 (5)
Total Unintentional	**40.3 (73)**
Total Reported Reasons for Nonadherence	**100.0 (181)**

[a] The majority (n=126) of these subjects reported only one reason, 26 reported 2 reasons and one reported 3 reasons for nonadherence.

[b] Many people have trouble taking their medications exactly as prescribed by their doctor, thinking back to the last time you didn't take your medication(s) as prescribed, can you tell me why? *(prompts: side effects/feel healthy and don't need medications/don't think medication is helping/unclear about dosing regimen/etc.)*

Those who responded 'no' or 'never/rarely' to all Morisky items AND provided a negative response to the open-ended question (indicating no problems in taking medications as prescribed) were classified as adherent. Subjects with positive responses for any Morisky item OR to the open-ended question were classified as nonadherent, except in cases of infrequent nonadherence (e.g. rarely, occasionally forget) or where subjects' responses to the open-ended question clarified their Morisky responses. For example, some subjects who indicated that they always forgot medications on the Morisky scale may have clarified their response in the open-ended question by indicating that they no longer had problems since others assisted with the administration of their medications.

Analyses

Descriptive statistics were used to summarize subjects' baseline characteristics and adherence estimates. Percent agreement between adherence estimates and kappa coefficients[41] were calculated. A binary variable was created from the pill count data utilizing a cut-point of <80% vs. ≥80%. This cut-point was chosen based on the distribution of the data and to permit comparisons with previous studies.[9,10,13,14,16,42] For the Morisky scale, binary variables using categorizations of <2 vs. ≥2 (dichotomous response) and <3 vs. ≥3 (5-point response) were employed, based on the distribution of the data and preliminary analyses (although alternative cut-points were also investigated). The analysis of agreement between pill count and composite self-report adherence estimates was stratified by subjects' level of cognitive impairment based on the derived cognitive performance scale (CPS).[43] Subjects were categorized as cognitively intact (score of <2) or impaired (score of ≥2).

We examined the association between self-reported intentional or unintentional nonadherence and nonadherence as estimated by pill count data.[25] Unintentional nonadherence was defined as a positive response (>0) to questions 1 and 2 of the Morisky scale (Table 1b), or any unintentional reasons reported in the open-ended question (Table 2). Intentional nonadherence was defined as a positive response to questions 3 and 4 of the Morisky scale or any intentional reasons recorded in Table 2.

RESULTS

The mean age of subjects was 83 years (sd =7.7, range 65-101). Most were female (79%), not married (70.8%) and had completed less than 13 years of education (57.1%). Approximately 73% had three or more chronic health conditions, 22.9% had a CPS of 2+ and 36.7% were living in a residential facility (e.g., lodge). No significant age or sex differences between non-respondents (where data were available) and respondents were observed.

Subjects were taking a total of 1999 prescribed substances (mean number per subject = 6.2, sd =3.6; median=6; range 1-19). Over half (56.7% of subjects) received some assistance with medication administration. Cognitive impairment (CPS score of 2+) was significantly more common among those receiving assistance (37.6% versus 3.6% in those not receiving assistance).

(i) Morisky Scale

Scores for both response versions were skewed, with the majority of subjects reporting good adherence (Tables 1a & 1b). Both versions demonstrated low internal consistency reliability coefficients (Cronbach's alpha = 0.42). Reliability was not significantly improved with the removal of any one item. When responses to the Morisky scale were cross-referenced with responses to the open-ended question regarding reasons for nonadherence (Table 2), some inconsistencies were observed. Some who scored low on the scale (indicating good adherence) reported nonadherence for reasons not captured by the scale items (e.g., some subjects reported modifying their drug regimens as opposed to stopping their medications for various reasons). Other subjects with relatively high scores reported, in the open-ended question, that others had taken over the administration of their medications (e.g., because of past problems with medication management).

(ii) Pill Count

We could not calculate a pill count in five subjects who were only taking medications in non-discrete

Can J Clin Pharmacol Vol 12 (1) Winter 2005: e152-e164; Apr. 2005

dosage forms (e.g., topical ointments) or prescribed medications on an as-needed basis. The remaining 314 subjects were taking approximately 1654 medications (note: for 2 subjects the exact number was unknown due to unclear/unlabelled storage). A pill count was not feasible for 42 (13.4%) subjects who were taking 473 (28.6%) medications (see reasons in Table 3).

TABLE 3 Availability of pill count data for eligible drugs (n=1654 drugs [a])

Availability of Pill Count Data	**Percent (number)**
Pill count not feasible due to:	
Missing information (labels, original containers)	9.5 (157)
Prescription just filled and not yet started	9.1 (150)
Old prescription combined with new	5.9 (98)
Unclear information[b]	2.0 (33)
Subjects objected to pill count[c]	1.0 (17)
Regimen altered by physician (dates not available)	0.8 (13)
Subject using old prescription	0.2 (4)
Subject reported tablets dispensed different from that indicated on label	0.06 (1)
Subjects unable to estimate date prescription started	18.9 (312)
Available pill counts	**52.5 (869)**
Total medications regularly administered in discrete doses	100.0 (1654)

[a] Actual number is greater as 2 subjects had an undefined number (due to packaging) of medications on hand.
[b] Possibly labelling or data collection errors (e.g., medication started prior to dispense date, extreme overuse).
[c] 3 Subjects.

Pill count estimates were not considered valid for an additional 65 (20.7%) subjects who were taking 312 (18.9%) medications. These subjects could not provide the date they started their medications. For 166 of the medications with an unknown start date, subjects reported that the medications were definitely started at an unspecified date later than the dispense date. Both a dispense date and a start date (reported by the subject) were available for 862 medications taken by 205 (65.3%) subjects. For seven medications there was a start date given but no dispense date available. When adherence estimates calculated using the dispense date were compared to those using the reported start date, the figure obtained using the dispense date underestimated adherence by >20% for 175 (20.3%) of the 862 drugs.

The proportion of the medication regimen counted for the 205 subjects with any counts ranged from 10-100%. Fifty-seven (27.8%) subjects had a pill count estimate of adherence based on less than 75% of their prescribed medications. For 118 (57.6%) subjects, pill count data were available on their total drug regimen. The length of time over which adherence was monitored by pill counts ranged from 0 (medications started on the day of interview) to 559 days. For 148 drugs (17.0%), the start date was either the day before or the day of the interview.

Pill count estimates ranged from 3.6% - 232%, with a median value of 100% (Figure 1).

Figure 1 Distribution of adherence estimates (by drug) from pill count data.

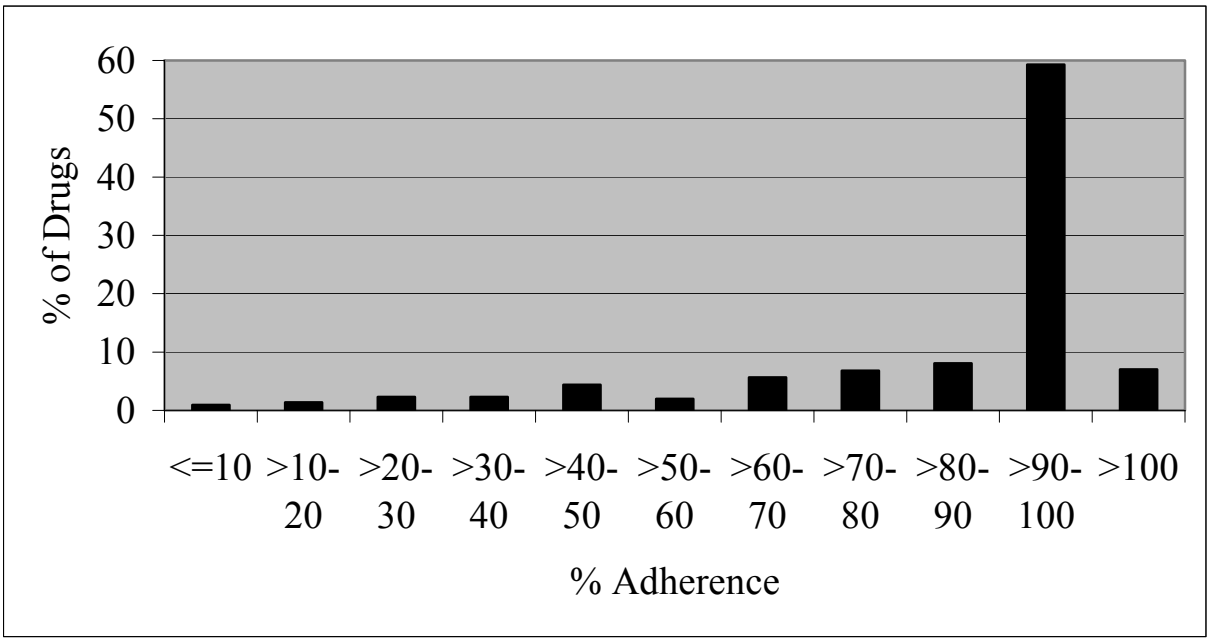
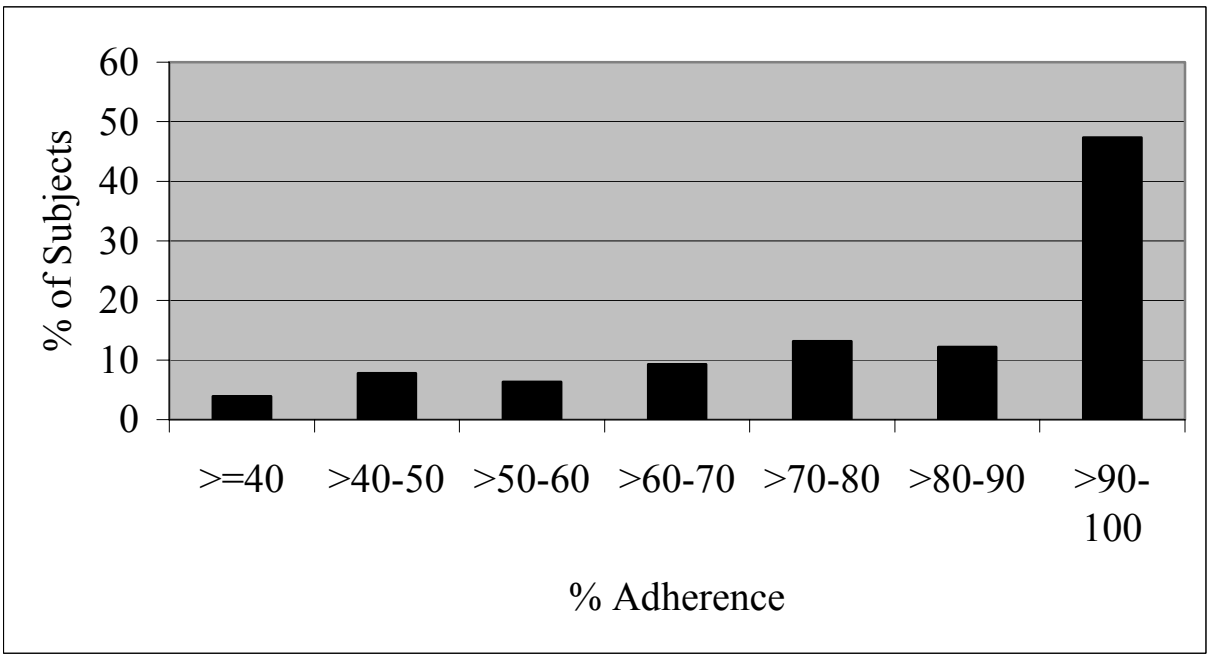


Figure 2 Distribution of adherence estimates (by subject) from pill count data.



Most instances of nonadherence were under use (350 drugs). Overuse was observed for 61 medications. Adherence by subject ranged from 8.1 to 100%, with a median of 88.2% (Figure 2).

(iii) Composite Self-Report Measure

Of 158 subjects administered the dichotomous response version of the Morisky scale, 98 (62.0%) were classified as adherent using the composite

Can J Clin Pharmacol Vol 12 (1) Winter 2005: e152-e164; Apr. 2005

measure. Of 161 subjects administered the 5-point response version, 98 (60.9%) were classified as adherent by our composite measure. Overall, 196 (61.4%) subjects were classified as adherent and 123 (38.6%) as nonadherent using the composite measure.

Agreement Between Measures

Percent agreement with pill count adherence ranged from 58.4% (5-point Morisky form) to 66.3% (composite self-report measure) (Table 4).

TABLE 4 Agreement between medication adherence estimates: Pill Count compared with Self-Reported Measures.

	Pill Count (n=205) Percent (number)			
	≥80%	**<80%**	**% agreement**	**kappa (95%CI)**
Morisky Scale				
Dichotomous response (n=104)				
adherent (score ≤1)	51.9 (54)	27.9 (29)		
nonadherent (score ≥2)	9.6 (10)	10.6 (11)	62.5	0.13 (-0.09-0.35)
5-Point response (n=101)				
adherent (score ≤2)	47.5 (48)	30.7 (31)		
nonadherent (score ≥3)	10.9 (11)	10.9 (11)	58.4	0.08 (-0.13-0.29)
Composite Assessment (n=205)				
adherent	43.9 (90)	17.6 (36)		
nonadherent	16.1 (33)	22.4 (46)	66.3	0.29 (0.16-0.43)

The kappa coefficients showed low agreement between the pill count and both versions of the Morisky scale. Agreement was only slightly improved with the composite measure. Varying the cut-offs for pill count estimates and for the Morisky scores did not improve agreement; nor did a comparison of pill counts with individual scale items. The stratified analyses (by CPS score <2 vs. ≥2) indicated poorer agreement between the pill count and composite self-reported adherence estimates among subjects with cognitive impairment (κ = 0.05; 95%CI: -0.33-0.42) versus those cognitively intact (κ = 0.32; 95%CI: 0.17-0.47).

Approximately twice as many subjects were classified as nonadherent by pill count than by either version of the Morisky scale alone. Fifty-six percent of those classified as nonadherent by pill count were also classified as nonadherent by our composite self-report measure. Subjects reporting intentional nonadherence were more likely (49.4%) than those reporting only unintentional nonadherence (35.6%) to be classified as nonadherent by pill count (data not shown).

DISCUSSION

Despite the known limitations of pill counts,[35] there have been few studies detailing the extent of these problems in observational settings. Although a previous study reported that pill counts "were unavailable" for a similar proportion of patients (~30%), few specifics were provided.[44] We found that pill counts often could not be done or underestimated adherence (when calculations were based on the dispensed rather than start date). This latter point raises concerns about previous studies that calculated adherence using the dispense date.[6,14,16,45] Some researchers have attempted to obtain more accurate pill counts by conducting both a baseline and a follow-up assessment with the date and number of tablets observed at baseline as the starting point.[17] However, the additional costs of this approach and the lack of information regarding reasons for nonadherence would remain important limitations.

The absence of a 'gold standard' measure of adherence limits the interpretation of our findings regarding the agreement among the various measures examined. However, the shortcomings of the specific measures observed in our study may provide useful data for developing more appropriate approaches to assessing adherence in older populations. The inconsistencies between the Morisky scale responses and responses to the open-ended question on nonadherence raise concerns about the construct validity of the scale. We feel the open-ended question regarding possible reasons for nonadherence added to the Morisky scale, dealt with general reasons for nonadherence. The latter approach has been preferred due to the non-judgemental, non-threatening tone of such questions.[22,26,45-47] Yet, we found that some subjects initially denied any difficulties in taking their medications, but then discussed why they had discontinued or modified a certain drug regimen during the open-ended question.

Intentional reasons for nonadherence have been reported more frequently than unintentional.[27] Contrary to other studies,[25] we observed a stronger association between self-reported intentional (vs. unintentional) nonadherence and the pill count estimate. Although this inconsistency may reflect differences in the study populations, further investigations are warranted.

Varying time frames covered by the various adherence measures may also have contributed to their relatively poor agreement. Seventeen percent of the counted medications were started either the day before or the day of the interview. Pill counts based on these data may not capture previous nonadherence, nor provide an accurate estimate of adherence. Supporting this concern is our finding that 16% of subjects classified as adherent by pill counts were classified as nonadherent by the self-report composite measure. The consensus in the literature is that subjects who report nonadherence are in fact nonadherent, but that other methods may be required to detect those who report they are adherent, but in fact are not.[22,33,47,48] Although the pill count may also have detected some cases of nonadherence missed by the self-report measure, the large proportion of missing pill count data undermines the utility of this measure. In our previous report, the self-report composite assessment was found to be correlated with variables expected to be associated with nonadherence (e.g. number of medications, regimen complexity – data not shown)[37] This was not the case for pill count data, lending further support to the validity of the self-report measure.

Given the large proportion of our subjects receiving assistance with their medications, our findings regarding the strengths and limitations of the various approaches to adherence assessment may not be generalizable to other patient populations. Nonetheless, previous authors have also debated the appropriateness of using simple quantitative measures to assess a complex behavioural characteristic such as adherence.[49-51] Observational studies conducted without the monitoring and reinforcement of drug consumption found in clinical trials, are intended to assess actual medication use patterns. Our data indicate that quantitative measures commonly used in clinical trials, such as pill counts, may be either impractical (due to missing data) or result in extensive misclassification of adherence status. Such bias may explain, in part, the relative absence of evidence linking nonadherence to adverse health outcomes. Future research efforts should be directed toward exploring novel approaches to adherence assessment (e.g., semi-

Can J Clin Pharmacol Vol 12 (1) Winter 2005: e152-e164; Apr. 2005

structured clinical interviews, use of multiple methods) and performing prospective studies of associations between adherence measures and subsequent adverse health outcomes.

Acknowledgements

We are most grateful to the four home care nurses (Michelle Copeland and Sue Couchman from the Calgary Health Region and Bonnie Matson and Trudy Harbidge from the Chinook Health Region) for their data collection efforts and clinical input on the RAI-HC home care study. We wish to also acknowledge Chad Mitchell for his clinical input and assistance with drug coding. Special thanks is also given to the 330 home care clients and their caregivers (formal and informal) who graciously gave of their time to participate in this important study. The RAI-HC study/initiative was supported by an unrestricted grant from The Merck Company Foundation, the philanthropic arm of Merck & Co. Inc. Whitehouse Station, New Jersey, USA to the Institute of Health Economics.

Shelly Vik is currently a PhD candidate, funded by the Canadian Institutes of Health Research - Skeletal Health, and Alberta Bone and Joint Training Programs. Dr. Maxwell is funded by a New Investigator Award from the Canadian Institutes of Health Research – Institute on Aging and a Population Health Investigator Award from the Alberta Heritage Foundation for Medical Research (AHFMR). Dr. Hogan is the holder of the Brenda Strafford Foundation Chair in Geriatric Medicine, University of Calgary. The Chair provides financial support to Drs. Maxwell and Hogan. Dr. Johnson holds a Government of Canada Research Chair in Diabetes Health Outcomes and an AHFMR Health Scholar Award. Dr. Patten also holds an AHFMR Health Scholar Award.

There is no conflict of interest reported by any of the authors.

REFERENCES

1. 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(4):841-5.
2. Grymonpre RE, Mitenko PA, Sitar DS, Aoki FY, Montgomery PR. Drug-associated hospital admissions in older medical patients. J Am Geriatr Soc 1988;36(12):1092-8.
3. McKenney JM, Harrison WL. Drug-related hospital admissions. Am J Hosp Pharm 1976;33(8):792-5.
4. Haynes RB, McKibbon KA, Kanani R. Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications. [erratum appears in Lancet 1997 Apr 19;349(9059):1180.]. Lancet 1996;348(9024):383-6.
5. Craig HM. Accuracy of indirect measures of medication compliance in hypertension. Res Nurs Health 1985;8(1):61-6.
6. Fletcher SW, Pappius EM, Harper SJ. Measurement of medication compliance in a clinical setting. Comparison of three methods in patients prescribed digoxin. Arch Intern Med 1979;139(6):635-8.
7. Pullar T, Kumar S, Tindall H, Feely M. Time to stop counting the tablets? [see comments.]. Clin Pharmacol Ther 1989;46(2):163-8.
8. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records. Description and validation. Med Care 1988;26(8):814-23.
9. Gilmore JE, Temple DJ, Taggart HM. A study of drug compliance, including the effect of a treatment card, in elderly patients following discharge home from hospital. Aging (Milano) 1989;1(2):153-8.
10. Blenkiron P. The elderly and their medication: understanding and compliance in a family practice. Postgrad Med J 1996;72(853):671-6.
11. Gurwitz JH, Glynn RJ, Monane M, et al. Treatment for glaucoma: adherence by the elderly. Am J Public Health 1993;83(5):711-6.
12. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Avorn J. Noncompliance with congestive heart failure therapy in the elderly. [see comments.]. Arch Intern Med 1994;154(4):433-7.
13. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effects of initial drug choice and comorbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. Am J Hypertens 1997;10(7 Pt 1):697-704.
14. Botelho RJ, Dudrak R, 2nd. Home assessment of adherence to long-term medication in the elderly. J Fam Pract 1992;35(1):61-5.
15. Kendrick R, Bayne JR. Compliance with prescribed medication by elderly patients. CMAJ 1982;127(10):961-2.
16. Okuno J, Yanagi H, Tomura S, et al. Compliance and medication knowledge among elderly Japanese home-care recipients. Eur J Clin Pharmacol 1999;55(2):145-9.
17. Gray SL, Mahoney JE, Blough DK. Medication adherence in elderly patients receiving home

health services following hospital discharge. Ann Pharmacother 2001;35(5):539-45.
18. Roberts J, Tumer N. Pharmacodynamic basis for altered drug action in the elderly. Clin Geriatr Med 1988;4(1):127-49.
19. Smith NL, Psaty BM, Heckbert SR, Tracy RP, Cornell ES. The reliability of medication inventory methods compared to serum levels of cardiovascular drugs in the elderly. J Clin Epidemiol 1999;52(2):143-6.
20. Rang HP DM, Ritter JM, Gardner P. Pharmacology. New York: Churchill Livingstone Inc., 1995.
21. Maronde RF, Chan LS, Larsen FJ, Strandberg LR, Laventurier MF, Sullivan SR. Underutilization of antihypertensive drugs and associated hospitalization. Med Care 1989;27(12):1159-66.
22. Haynes RB, Taylor DW, Sackett DL, Gibson ES, Bernholz CD, Mukherjee J. Can simple clinical measurements detect patient noncompliance? Hypertension 1980;2(6):757-64.
23. Guerrero D, Rudd P, Bryant-Kosling C, Middleton B, Middleton BF. Antihypertensive medication-taking. Investigation of a simple regimen. [erratum appears in Am J Hypertens 1993 Nov;6(11 Pt 1):982.]. Am J Hypertens 1993;6(7 Pt 1):586-92.
24. Cramer JA. Microelectronic systems for monitoring and enhancing patient compliance with medication regimens. Drugs 1995;49(3):321-7.
25. Choo PW, Rand CS, Inui TS, et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. Med Care 1999;37(9):846-57.
26. Coons SJ, Sheahan SL, Martin SS, Hendricks J, Robbins CA, Johnson JA. Predictors of medication noncompliance in a sample of older adults. Clin Ther 1994;16(1):110-7.
27. Cooper JK, Love DW, Raffoul PR. Intentional prescription nonadherence (noncompliance) by the elderly. J Am Geriatr Soc 1982;30(5):329-33.
28. Hemminki E, Heikkila. Elderly people's compliance with prescriptions, and quality of medication. Scand J Soc Med 1975;3(2):87-92.
29. McElnay JC, McCallion CR, al-Deagi F, Scott M. Self-reported medication non-compliance in the elderly. Eur J Clin Pharmacol 1997;53(3-4):171-8.
30. McLane CG, Zyzanski SJ, Flocke SA. Factors associated with medication noncompliance in rural elderly hypertensive patients. Am J Hypertens 1995;8(2):206-9.
31. Spagnoli A, Ostino G, Borga AD, et al. Drug compliance and unreported drugs in the elderly. J Am Geriatr Soc 1989;37(7):619-24.
32. Gordis L, Markowitz M, Lilienfeld AM. The inaccuracy in using interviews to estimate patient reliability in taking medications at home. Med Care 1969;7(1):49-54.
33. Park LC, Lipman RS. A comparison of patient dosage deviation reports with pill counts. Psychopharmacology 1964;6(4):299-302.
34. Rickels K, Briscoe E. Assessment of dosage deviation in outpatient drug research. J Clin Pharm New Drugs 1970;10(3):153-60.
35. Grymonpre RE, Didur CD, Montgomery PR, Sitar DS. Pill count, self-report, and pharmacy claims data to measure medication adherence in the elderly. Ann Pharmacother 1998;32(7-8):749-54.
36. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care 1986;24(1):67-74.
37. Vik SA, Maxwell CJ, Hogan DB, et al. Determinants and health related outcomes associated with nonadherence to prescribed drug regimens: a comparison of rural and urban home care clients (Working Paper #03-02) http://www.ihe.ca/publications/papers/index.cfm?year=2003. Edmonton: Institute of Health Economics, 2003.
38. RAI-Home Care (RAI-HC) Assessment Manual for Version 2.0. Marblehead, MA: Opus Communications, 2001.
39. Hirdes JP, Carpenter GI. Health outcomes among the frail elderly in communities and institutions: Use of the Minimum Data Set (MDS) to create effective linkages between research and policy. Canadian Journal of Aging 1997;S:53-69.
40. Morris JN, Fries BE, Steel K, et al. Comprehensive clinical assessment in community setting: applicability of the MDS-HC. J Am Geriatr Soc 1997;45(8):1017-24.
41. Streiner DL, Norman GR. Health Measurement Scales: A Practical Guide to Their Development and Use. 2nd Edition ed. Oxford: Oxford University Press, 2001.
42. Rich MW, Gray DB, Beckham V, Wittenberg C, Luther P. Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure. Am J Med 1996;101(3):270-6.
43. Morris JN, Fries BE, Mehr DR, et al. MDS Cognitive Performance Scale. J Gerontol 1994;49(4):M174-82.
44. Conn VS, Taylor SG, Kelley S. Medication regimen complexity and adherence among older adults. Image - J Nurs Scholarship 1991;23(4):231-5.
45. Gilbert JR, Evans CE, Haynes RB, Tugwell P. Predicting compliance with a regimen of digoxin therapy in family practice. CMAJ 1980;123(2):119-22.

46. Bender B, Wamboldt FS, O'Connor SL, et al. Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. Ann Allergy Asthma Immunol 2000;85(5):416-21.
47. Inui TS, Carter WB, Pecoraro RE. Screening for noncompliance among patients with hypertension: is self-report the best available measure? Med Care 1981;19(10):1061-4.
48. Roth HP, Caron HS. Accuracy of doctors' estimates and patients' statements on adherence to a drug regimen. Clin Pharmacol Ther 1978;23(3):361-70.
49. Conrad P. The meaning of medications: another look at compliance. Soc Sci Med 1985;20(1):29-37.
50. Trostle JA. Medical compliance as an ideology. Soc Sci Med 1988;27(12):1299-308.
51. Weintraub M. Compliance in the elderly. Clin Geriatric Med 1990;6(2):445-52.