

Research article

A cohort study of possible risk factors for over-reporting of antihypertensive adherence

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Abstract

Background: The identification of poor medicinal adherence is difficult because direct observation of medication use is usually impractical. Up to 50% of individuals on chronic therapies may not be taking their medication as prescribed. This study is one of the first to explore possible risk factors for over-reporting of antihypertensive adherence using electronic medication monitoring.

Methods: The adherence of 286 individuals on single-drug antihypertensive therapy in a large managed care organization was electronically monitored for approximately three months. Questionnaires on socioeconomic background, adherence to therapy, health beliefs, and social support before and after adherence monitoring were completed. Over-reporting of antihypertensive adherence was assessed by comparing the self-reported frequency of noncompliance with that determined from electronic dosing records. Risk factors for over-reporting were identified by contingency table analysis and step-wise logistic regression.

Results: Although only 21% of participants acknowledged missing doses on one or more days per week, electronic monitoring documented nonadherence at this or a higher level in 42% of participants. The following variables were associated with over-reporting: >1 versus 1 daily dose (OR = 2.58; 95% CI = 1.50–4.41; $p = .0006$), lower perceived health risk from nonadherence (OR = 1.35; 95% CI = 1.10–1.64; $p = .0035$), and annual household income of <\$15,000 versus >\$30,000 (OR = 2.64; 95% CI = 1.13–6.18; $p = .025$).

Conclusions: Over-reporting of adherence may be affected by factors related to dosing frequency, health beliefs and socioeconomic status. This topic deserves further investigation in other patient populations to elucidate possible underlying behavioral explanations.

Background

Nonadherence to drug therapy can undermine the attainment of therapeutic goals and contribute to the occurrence of medication side effects. Numerous adverse clinical outcomes have been linked to nonadherence including loss of blood pressure control [1,2], acute cardiac events [3], renal transplant rejection [4], seizures [5], and elevated Human Immunodeficiency Virus RNA levels [6]. Efforts to enhance medicinal adherence have met with varying levels of success [7–9].

The detection of nonadherence to recommended treatment can be problematic. In the clinical setting asking patients about their medication use is the most practical means of ascertainment, but it is prone to inaccuracy [10,11]. Strategies to increase the accuracy of screening for nonadherence such as considering as nonadherent all those who do not respond to therapy can augment sensitivity. However, this unfairly mislabels some adherent patients as nonadherent [10]. In general, patients tend to overestimate their adherence [8,12] and unless a patient is not responding to therapy, it may be extremely difficult to identify under-adherence. In research settings, pill counts, drug levels, pharmacy dispensing records and electronic medication monitors are available to measure medicinal adherence but even some of these methods such as pill counts may be susceptible to overestimating adherence [8,13–15]. In many non-research situations these approaches may be difficult to implement due to their obtrusiveness, cost, or complexity.

Although studies have been conducted to identify risk factors for nonadherence itself [16], to the best of our knowledge, only one previous study has examined possible risk factors for *over-reporting* of adherence [17]. None has utilized electronic medication monitors to study this area involving antihypertensive medications. We consequently undertook this present study among several hundred individuals who were receiving antihypertensive therapy in order to explore which demographic, behavioral, and clinical characteristics might be associated with over-reporting of adherence. The investigation was exploratory in nature and was meant to identify possible leads for future research. Electronic medication monitors were used to track actual medication use against which the accuracy of patient-reported adherence was determined.

Methods

Study population

The study design of this investigation has been described previously in detail [15]. Briefly, the study was conducted at Harvard Pilgrim Health Care (HPHC), a managed care organization located in New England, among members who were receiving antihypertensive medication from 1992 to 1994. Automated medical, pharmacy, and claims

records of the study population were screened to identify potential study subjects and retrieve their outpatient blood pressure data. Patients were eligible if they had been HPHC members for at least three months, were at least 18 years of age, and carried a diagnosis of hypertension. Only individuals on single-drug therapy for high blood pressure were selected to simplify electronic adherence monitoring.

Of 1,285 potentially eligible individuals, 330 consented to participate and completed all phases of the study. The majority of those who did not enroll in the study (71%) declined mailed or telephone invitations to participate. In addition, 42 subjects dropped out midway through the study, and 44 individuals were later excluded because of indications of improper use of their electronic medication monitor such as removal of multiple doses at an opening or incomplete closure of the medication vial. The remaining 286 patients constituted the study population for this investigation. Individuals who were eligible but did not complete this investigation had a similar age, gender, and blood pressure distribution as our study population. However, calcium antagonists were prescribed slightly more frequently (37% versus 24%) and angiotensin-converting inhibitors less frequently (37% versus 49%) to individuals excluded from the final study population [15].

Collection of electronic and patient-reported adherence data

Individuals who consented to participate were mailed a baseline questionnaire that covered their socioeconomic background, medications (antihypertensive and other drugs), adherence, health beliefs, health status (Medical Outcomes Study, Short Form [SF-36]) [18], and social support. Responses to the questionnaire were obtained by telephone interview conducted by a research assistant.

Self-reported adherence during the monitoring period was obtained using the following question, which was adapted from the Brief Medication Questionnaire (Svartstad B., personal communication): *While you were using the special medication bottle, on how many days in an AVERAGE WEEK did you forget to take a pill? 0, 1, 2, 3, 4, or 5+ days.* Our previous study [15] had indicated that responses to this item (compared with 4 other adherence items) correlated most closely with adherence as measured by electronic medication monitoring.

Social support was assessed using a 9-item inventory. The inventory inquired about how often the participant could rely on having someone to (1) listen to them, (2) accompany them to the physician, (3) show affection to them, (4) give them information, (5) provide them with advice that they would want, (6) do things with them to turn their minds to other things, (7) help with chores, (8)

share worries and fears with, and (9) do enjoyable things with. Responses to each question were recorded on a Likert scale (1=none, 2=a little, 3=some, 4=most, or 5=all of the time).

Electronic monitoring vials were dispensed with a fresh supply of antihypertensive medication upon enrollment in the study. Participants were instructed by pharmacists to keep all their medication in the monitoring vial, use no other source of antihypertensive medication, and to remove only one dose at a time from the monitoring vial. Participants were informed of the purpose of the electronic medication monitor.

Dosing events were recorded for approximately three months using the Medication Event Monitoring System-4 (MEMS-4), manufactured by APREX Corporation, Union City, CA. MEMS-4 is a microelectronic device housed within a medication bottle cap that records the date and time of each opening. The device blocks repeated openings that occur within 15 minutes of each other to prevent artifactual inflation of the number of dosing events. Data were downloaded from the cap to a personal computer using a manufacturer-supplied communicator and software.

Two to three weeks after completion of electronic monitoring, a followup questionnaire was sent to participants to update information on their socioeconomic status, prescribed antihypertensive therapy, self-reported adherence during the monitoring period, and health beliefs. Responses were once again obtained by telephone. All aspects of the study protocol were reviewed and approved by the Human Studies Committee of Harvard Pilgrim Health Care.

Data analysis

Due to the highly skewed distribution of questionnaire responses (only 4.5% of participants reported missing doses 2 or more days per week), the average number of days in a week when participants missed a dose of antihypertensive medication was dichotomized at 0 versus ≥ 1 day per week. Setting the breakpoint between adherent and non-adherent days at one day per week represents a frequency of missed-dose days of 14.3% (1/7). MEMS-4 records were used to derive the actual frequency of days when 1 or more doses of antihypertensive medication were omitted. Adherence was defined to be over-estimated by the patient if they reported an average frequency of nonadherence of < 1 day per week (i.e. $< 14.3\%$) while electronic monitoring indicated a higher frequency of days with missed doses (i.e. $\geq 14.3\%$).

Data analysis proceeded from an assessment of crude (unadjusted) associations with over-reporting of adherence to step-wise logistic regression to identify which associations

remained after adjustment for other potential risk factors. Six categories of variables were considered: (1) socioeconomic and demographic background (age, gender, education, marital status, employment, income); (2) clinical features (blood pressure, duration of treatment, number of doses per day); (3) clinician communication (previous inquiry by clinician regarding medicinal adherence) (4) health beliefs (perceived effectiveness of treatment and susceptibility to adverse health outcomes); (5) health status (SF-36 indices); and (6) social support (a summary score derived from the 9-item support inventory). These variables were chosen either because their information might be obtainable or inferred by practicing clinicians, or they had been evaluated in previous studies of adherence behavior [8,9,19,20]. Chi-square or likelihood ratio tests from logistic regression models were used to evaluate crude associations between over-reporting and possible predictor variables. In executing the stepwise logistic regression procedure, a selection criterion of $p \leq .2$ was selected to allow for the evaluation of the joint effect of multiple variables. The rejection criterion was also set relatively high at $p \geq .1$ to permit identification of all potential associations with over-reporting of adherence. As described later in this paper, all variables that were ultimately retained in the final logistic regression model amply met these retention criteria. All data manipulations and statistical analyses were conducted using SAS, release 6.12 (SAS Institute, Carey, NC).

Results

The study population was composed of 286 individuals whose mean age was 55 years (range: 18–84 years). As listed in the Table 1, approximately half were female, one third Black, and two thirds had some college or graduate level education. The mean (\pm standard deviation) systolic and diastolic blood pressures in the previous year were 140.0(\pm 16.1)/86.3(\pm 10.4). Angiotensin converting enzyme inhibitors were the most commonly prescribed antihypertensive agents (48%) followed by calcium antagonists (22%), diuretics (16%), beta blockers (13%), and other agents (1%). The median duration of antihypertensive therapy prior to involvement in the study was slightly greater than four years.

Average nonadherence was 16% among individuals who reported that they were nonadherent < 1 day a week compared with 40% among individuals who reported more frequent nonadherence. The Spearman correlation between reported and electronically measured adherence was 0.34 (p -value = .0001). While only 21% of participants acknowledged missing doses one or more days per week, electronic medication monitoring documented nonadherence at this or greater levels in 42% of participants. Seventy-eight (27%) of the 286 participants over-reported their actual adherence. As shown in Table 1, be-

Table 1: Distribution and crude odds ratios of possible risk factors for over-reporting of antihypertensive adherence

Variable	Distribution	Crude OR (95% CI); p-value
<i>Demographic/Socioeconomic</i>		
Mean age in years (range)	55 (18–84)	1.01 (0.99–1.03) p = .23
Female	53%	1.29 (0.76–2.18) p = .26
<i>Race</i>		
White	58%	reference
Black	35%	1.35 (0.79–2.32) p = .28
Other	7%	1.56 (0.55–4.48) p = .41
<i>Marital status</i>		
Unmarried	51%	reference
Married	49%	0.56 (0.33–0.95) p = .03
Mean years of education (range)	16 (9–23)	0.96 (0.89–1.03) p = .24
<i>Employment</i>		
Working	71%	reference
Retired	18%	1.46 (0.76–2.80) p = .25
Unemployed or other	11%	0.69 (0.27–1.78) p = .44
<i>Income</i>		
>29,000	9%	reference
\$15,000–29,000	24%	1.55 (0.85–2.85) p = .16
<\$15,000	61%	2.66 (1.16–6.09) p = .02
Mean (Standard Deviation) Social Support Score (Range-9–45)	34.9 (8.6)	1.01 (0.98–1.04) p = .48
<i>Clinical Parameters</i>		
Median years of treatment (interquartile range)	4.5 (2–10)	1.00 (1.00–1.00) p = .76
Mean (± s.d) systolic BP in previous year	140.0 (± 16.1)	0.98 (0.96–1.01) p = .15
Mean (± s.d) diastolic BP in previous year	86.3 (± 10.4)	0.97 (0.93–1.01) p = .10
Number of doses of antihypertensive medication per day ≤ 1	85%	reference
>1	15%	2.66 (1.57–4.51) p = .0003
Doctor did ask how well patient was taking medication	46%	0.71 (0.42–1.19) p = .20
<i>Mean (± s.d) Health Status Indices (Short Form-36)</i>		
Physical Function	82.5 (± 21.2)	1.00 (0.98–1.01) p = .39
Energy-Vitality	59.6 (± 19.8)	1.00 (0.98–1.01) p = .56
Social Function	85.4 (± 19.4)	1.00 (0.99–1.01) p = .98
Mental Health	76.5 (± 17.1)	1.00 (0.98–1.01) p = .80
General Health Perception	68.4 (± 19.2)	1.01 (0.99–1.02) p = .46
Role Physical	80.9 (± 33.9)	1.00 (0.99–1.01) p = .73
Role Emotion	82.1 (± 32.4)	1.00 (0.99–1.00) p = .27
Pain	71.8 (± 22.6)	1.01 (0.996–1.02) p = .22
<i>Health Beliefs</i>		
Confidence in medication to control blood pressure		
Very confident	66%	reference
Not very confident	34%	0.89 (0.51–1.55) p = .68
Chance that something bad will happen if not taking medication		
very unlikely	18%	
fairly unlikely	14%	0.78 (0.65–0.94) p = .01
as likely to happen as not to happen	27%	(for each change in level)
fairly likely	23%	
very likely	16%	

ing unmarried (which included being widowed, separated, divorced, or never married; OR = 1.80; 95% CI = 1.06–3.06; p = .03), annual income of <\$15,000 relative to >\$30,000 (OR = 2.66; 95% CI = 1.16–6.09; p = .02), prescription of >1 dose per day (OR = 2.66 95% CI = 1.57–4.51; p = .0003), and diminished perceived risk from non-

adherence (OR = 1.28 for a 1-level difference; 95% CI = 1.06–1.55; p = .01) were associated with over-reporting of adherence in unadjusted analyses.

Step-wise logistic regression selected and retained being prescribed >1 dose per day (OR = 2.58; 95% CI = 1.50–

Table 2: Cross-tabulation of self-reported versus actual adherence¹

Self-Reported Adherence	Cell counts (%)	Actual Adherence ²		Row Totals (%)
		<1 Day/Week	≥ 1 Day /Week	
<1 Day/Week		147 (51.4)	78 (27.3)	225 (78.7)
≥ 1 Day/Week		18 (6.3)	43 (15.0)	61 (21.3)
Column Totals (%)		165 (57.7)	121 (42.3)	286 (100.0)

¹Adherence defined as number of days when 1 or more doses were missed ²Electronically measured using MEMS-4

4.41; $p = .0006$), diminished health risk perception (OR = 1.35; 95% CI = 1.10–1.64; $p = .0035$), and annual income of <\$15,000 (OR = 2.64; 95% CI = 1.13–6.18; $p = .025$) in that order. Lower mean systolic blood pressure in the year prior to participation in the study was initially selected ($p = .12$) but not retained in the final regression model. Marital status was not chosen by the step-wise procedure. Age, gender, and race/ethnicity also were not associated ($p > .05$) with over-reporting in both the crude and step-wise logistic regression analyses. Including all variables with crude associations ($p \leq .1$) with over-reporting of adherence (marital status, income, mean diastolic blood pressure in the previous year, number of daily doses, and perceived risk) in a single logistic regression model did not materially affect our findings (results not shown). The link between >1 daily dose and over-reporting of adherence was blocked (OR = 1.38; 95% CI = 0.73–2.64; $p = .33$) by adjusting for actual adherence as measured by MEMS-4 in the final, selected model indicating that the association between dosing frequency and over-reporting was most likely mediated by actual adherence.

Discussion

The main purpose of this exploratory analysis was to identify potential risk factors for over-reporting of adherence. We observed that frequent daily dosing, reduced risk perception from nonadherence, and lower annual income were associated with over-reporting in our study population. Not surprisingly, less adherent individuals were also more likely to over-report their adherence than other more adherent individuals, a pattern that has been reported by other investigators [8,12].

The exploratory nature of this investigation makes cautious interpretation of our findings necessary. Multiple comparisons were made in this study and consequently the results may have been chance findings. Use of a very conservative standard of significance based on the Bonferroni adjustment would require a p-value of $\leq .002$ (.05/23 where .05 represents the traditional standard of signifi-

cance and 23 the number of comparisons made). By these criteria, only dosing frequency would still be considered statistically significant.

The association between dosing frequency and over-reporting of adherence was apparently mediated by actual adherence behavior because adjusting statistically for electronically measured adherence blocked this relationship. This is not surprising because frequent dosing usually predicts lower adherence [5,21] and lower adherence is associated with over-reporting. As a consequence, frequent dosing would be expected to correlate with over-reporting via its connection with actual adherence.

On a more conjectural level, the observed connection between decreased perception of health risk from nonadherence and over-reporting of adherence may indicate that health belief models that posit a direct relationship between perceived risk and adherence may also apply to the accurate recollection of past medication use [22–25]. In addition, the association with lower household income in our study population may indicate that a more stressful if not disorganized life situation, as suggested by lower socioeconomic status, may increase the likelihood of inaccurately believing that missed doses were taken. Furthermore, some individuals may report what they believe that clinicians or researchers want to hear. This behavior might be more likely when the perceived difference in power (as measured by wealth and income) is maximal.

Several factors that may contribute to the inaccurate re-counting of adherence by patients were not evaluated in this study. The research instruments did not cover participants' attitudes towards the healthcare system, their healthcare providers, or the research staff involved in this study. The quality of the patient-physician (and by extension the participant-researcher) relationship may have a significant impact on what patients will discuss with their healthcare provider [26]. Furthermore, formal psycholog-

ical and cognitive testing were not performed on study participants to permit evaluation of the effect of memory, judgement, mood, and personality on adherence and the accurate reporting of noncompliance.

Conclusions

This investigation is one of the first to evaluate possible risk factors for over-reporting of adherence by patients. The findings suggest that factors related to socioeconomic status, the dosing regimen, and perceived risk from non-adherence may influence how accurately patients recall and report their adherence. Additional investigation will be needed to confirm and extend these findings as well as elucidate the possible underlying behavioral mechanisms that are involved.

Competing interests

None declared.

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