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Author Manuscript

AIDS. Author manuscript; available in PMC 2013 November 28.

Published in final edited form as:

AIDS. 2012 November 28; 26(18): 2399–2403. doi:10.1097/QAD.0b013e328359aa68.

Differences between self-reported and electronically monitored adherence among patients receiving antiretroviral therapy in a resource-limited setting

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Abstract

Background—Measurement of adherence to antiretroviral therapy (ART) by patient self-report is common in resource-limited settings but widely believed to overstate actual adherence. The extent to which these measures overstate adherence has not been examined among a large patient population.

Methods—HIV-infected adult patients in Kenya who initiated ART within the past 3 months were followed for 6 months. Adherence was measured by participants' self-reports of doses missed in the past 7 days during monthly clinic visits and by continuous Medication Event Monitoring System (MEMS) in participants' pill bottles. Seven-day self-reported adherence was compared to 7-day MEMS adherence, 30-day MEMS adherence, and adherence more than 90% during each of the first 6 months.

Results—Self-reported and MEMS adherence measures were linked for 669 participants. Mean 7-day self-reported adherence was 98.7% and mean 7-day MEMS adherence was 86.0%, a difference of 12.7% ($P < 0.01$). The difference between the two adherence measures increased over time due to a decline in 7-day MEMS adherence. However, patients with lower MEMS adherence were in fact more likely to self-report missed doses and the difference between self-reported and MEMS adherence was similar for each number of self-reported missed doses. When analysis was

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Conflicts of interest

There are no conflicts of interest.

limited to patients who reported rarely or never removing multiple doses at the same time, mean difference was 10.5% ($P < 0.01$).

Conclusion—There is a sizable and significant difference between self-reported and MEMS adherence. However, a strong relationship between the measures suggests that self-reported adherence is informative for clinical monitoring and program evaluation.

Keywords

adherence; adherence measurement; antiretroviral therapy; electronic monitoring

Introduction

Consistent adherence to HIV antiretroviral therapy (ART) is necessary for viral suppression, prevention of drug resistance, and delaying disease progression [1-3]. Although adherence in resource-limited settings (RLSs) is generally sufficient to achieve viral suppression, various structural and behavioral factors can lead to low adherence and treatment failure on long-term therapy [4-8]. Adherence monitoring is necessary to identify individuals needing intervention, especially in the absence of virologic monitoring.

Patients' self-reports of missed doses have been used extensively because they are inexpensive, easy to implement, and can identify patient-specific barriers to adherence [8,9]. Self-reported adherence has seldom been compared to more objective methods for measuring adherence such as electronic monitoring with Medication Event Monitoring System (MEMS) bottle caps. Most studies using MEMS caps have been conducted in North America and have generally found that self-reports overestimate adherence and are only modestly associated with MEMS estimates [1,8,10-12].

We compared 7-day self-reported adherence to several MEMS adherence measures among patients receiving ART in Kenya in order to determine the strength of association and difference between the two measures.

Methods

Setting

This study relied on data collected as part of a randomized trial of text messages to improve adherence to ART conducted at the Chulaimbo Rural Health Center (CRHC), a government-run health facility in Nyanza Province, Kenya where the USAID-Academic Model Providing Access to Healthcare (AMPATH) Partnership provides comprehensive HIV care at no cost to patients [13].

Study population and procedures

HIV-infected adults initiating ART at CRHC were recruited from June 2007 until August 2008. Patients were eligible for the study if they were older than 18 years and had initiated ART less than 3 months prior to enrollment. As the primary goal of the study was to evaluate the effect of text messages on adherence, patients were informed that they would receive a mobile phone and that some would be randomly selected to receive daily or weekly text messages encouraging ART adherence. The study was approved by the Institutional Research Ethics Committee of Moi University School of Medicine and the Institutional Review Boards of Georgetown University and the University of North Carolina at Chapel Hill.

Pharmacy staff transferred one of the participants' three antiretroviral medications (lamivudine) to a bottle with a MEMS cap (Aardex Group, Switzerland) that recorded the date and time of each bottle opening. Participants were informed about the function of MEMS caps during the informed consent process, and they were instructed to open the bottles only when ingesting.

Participants returned every month for appointments with AMPATH clinical officers in accordance with standard clinic procedures. Study staff downloaded MEMS data and obtained patients' reports of the number of doses that they missed in the past 7 days.

Adherence measures

Data from the return visit questionnaires were used to calculate 7-day self-reported adherence at each clinic visit $[(1 - \text{number of missed doses}/14) \times 100]$. The MEMS data were used to calculate three adherence measures for each return visit:

1. Seven-day MEMS adherence, defined as the percentage of prescribed doses taken during the past 7 days ($100 \times \text{number of openings in past 7 days}/14$);
2. Thirty-day MEMS adherence, defined as the percentage of prescribed doses taken during the past 30 days ($100 \times \text{number of openings in past 30 days}/60$).
3. Binary indicator of whether 7-day MEMS adherence exceeded 90%, a standard for excellent adherence that uniformly achieves viral suppression on nonnucleoside reverse transcriptase inhibitor therapy [14].

The number of daily bottle openings was truncated to 2 in order to avoid overstating of adherence. Adherence data were analyzed over the first 6 months after recruitment.

Statistical analyses

For each of the first 6 months of the study, a mean comparison *t*-test was performed to determine whether the difference between 7-day self-reported adherence and 7-day or 30-day MEMS adherence was significantly different from zero. This test was also conducted to compare adherence measures during the first 6 months combined.

Some participants reported removing multiple doses at the same time, perhaps to take doses at a later time when they would not have the bottle with them. As this can artificially lower MEMS adherence and is considered a limitation of MEMS measures [15], we also examined MEMS adherence among participants who did not report removing multiple doses at the same time.

Results

A total of 720 patients were enrolled. MEMS data were obtained from 717 participants. Mean duration of follow-up was 6.2 months [interquartile range (IQR) 3–9 months]. During the first 6 months, 2797 return visit questionnaires were completed among 669 participants and matched to MEMS data. Data entry errors were the most common reason for not matching return visit questionnaires to MEMS data. Participants whose self-reported and MEMS data were not matched had similar age, sex, and education as participants whose data were matched.

Among the 669 participants, 69% were women and the mean age was 36 years. Thirty-one percent were married and 40% widowed. More than half the participants (56%) had completed at least primary school and 22% had completed secondary school. The mean one-way travel time from home to clinic was 1.47 h (IQR 0.75–2).

Self-reported number of missed doses and corresponding Medication Event Monitoring System adherence

Table 1 tabulates the number of self-reported missed doses in the first 6 months of the study and the corresponding MEMS adherence. In 2541 (90.8%) return visit interviews, participants reported 0 missed doses during the past 7 days. The mean 7-day MEMS adherence corresponding to each number of self-reported missed doses indicates that participants who reported greater numbers of missed doses also had lower MEMS adherence; and MEMS adherence was found to be 12–14% lower than self-reported adherence. The proportion with 7-day MEMS adherence more than 90% was also associated with self-reported adherence, as this was lower for those who reported greater numbers of missed doses. Among those who reported no missed doses during the past 7 days, mean 7-day MEMS adherence was 87% and the proportion with MEMS adherence more than 90% was 0.73. In comparison, among those who reported one, two, and three missed doses during the past 7 days, mean 7-day MEMS adherence was 79, 74, and 65% respectively, whereas the proportion with MEMS adherence more than 90% was 0.51, 0.28, and 0.39, respectively.

Comparison of self-reported and Medication Event Monitoring System adherence by month of follow-up

Seven-day self-reported adherence was high in each month, with a mean of 98.7% over 6 months. MEMS data indicated significantly lower adherence. Mean 7-day MEMS adherence over 6 months was 86.0%, or 12.7% lower than 7-day self-reported adherence ($P < 0.01$). The mean difference between the 7-day self-reported and MEMS adherence measures was similar in the study's intervention and control groups (12.6 and 12.9%, $P = 0.74$). Thirty-day MEMS adherence was similar to 7-day MEMS adherence and 12.5% lower than 7-day self-reported adherence ($P < 0.01$). The proportion with adherence more than 90% was also lower than what would be expected based on self-reported adherence. Sex, age, school attainment, household size, marital status, alcohol use, and disclosure to somebody in the household were not significantly associated with the difference between self-reported and MEMS adherence.

There was a statistically significant difference between self-reported and MEMS adherence in each month of follow-up ($P < 0.01$) that increased over time due to a decline in MEMS adherence. The difference between 7-day self-reported adherence and 7-day MEMS adherence was 9.8% at the first month of follow-up and rose to 13.4% at 6 months; a linear trend was statistically significant ($P < 0.01$). The proportion with 7-day MEMS adherence more than 90% also declined over time, from 0.76 to 0.68.

Participants reported having removed multiple doses at the same time in 9.9% (2797) of the return visits. In visits during which multiple dose removal was not reported, the discrepancy between 7-day self-reported adherence and 7-day MEMS adherence was smaller than those reported in Table 2 but remained statistically significant (mean difference = 10.5%; $P < 0.01$; results not reported).

Discussion

Our findings show that although patient-reported measures of adherence are consistently higher than MEMS adherence, there is a significant association between the measures. Self-reported adherence exceeded MEMS adherence by 12.7%, but patients with lower MEMS adherence were in fact more likely to self-report missed doses. Importantly, the difference between the two adherence measures was similar across a range of self-reported adherence; this difference did not get larger for patients with low self-reported adherence. Self-reports of having removed multiple doses at the same time were also consistent with the MEMS

data; the difference between self-reported and MEMS adherence was narrowed to 10.5% among participants who did not remove multiple doses. These findings suggest that although self-reports are an imperfect measure of adherence, they can convey useful information.

Three other findings also warrant discussion. First, the finding that self-reported adherence exceeds MEMS adherence is consistent with several other studies in both resource-rich and resource-limited settings [8,9,12,16], but the size of the difference has not previously been estimated among a large cohort of patients in sub-Saharan Africa. The difference between the two measures is significantly smaller than the 25–30% difference reported in resource-rich settings [9,16] and may be related to the high level of adherence observed in this study.

Second, although self-reported adherence showed minimal decline over time, 7-day and 30-day MEMS adherence showed larger declines, from 89.7 to 83.8% between month 1 and 6 in the case of 30-day adherence. The decline in adherence over time has been attributed to factors including pill fatigue, the plateau of health benefits, and accumulating long-term side-effects [4,6,17]. Our findings imply that self-reports may not detect these declines. As declines in adherence in the long-term may contribute to virologic failure, there is a need for greater adherence monitoring and adherence support interventions. Finally, the inability to find predictors of the difference between self-reported adherence and the more objective MEMS measure of adherence suggests that it is not easy to identify which patients are likely to overestimate adherence.

Several limitations of this study merit consideration. First, the findings apply to one study site and may not be generalizable to other patient populations. The large sample, however, may make the findings more comparable to other such sites than existing data. Second, we do not compare MEMS adherence to other adherence measures that may be relatively easier to implement and are also common in RLS, such as pharmacy refill [18]. Nonetheless, quantifying the difference between self-reported and MEMS adherence provides a better sense of how to interpret one of the most widely used adherence measures in RLS. A third limitation is that we lacked clinical characteristics and are, therefore, unable to compare them to the adherence measures.

Conclusion

In conclusion, we find that although self-reported adherence consistently overestimates adherence, it does contain useful adherence information because the overestimation can be quantified over time. Self-reported adherence measures combined with other objective and feasible measures like those based on pharmacy claims data [18] may be a useful strategy for identifying patients in need of additional adherence support.

Acknowledgments

The authors are grateful to the patients who participated in the study, CRHC staff, and the study interviewers and data entry teams.

The World Bank Research Group provided financial support for this project under contracts 7142349 and 7144565 funded by the Bank Netherlands Partnership Program (BNPP). This research was also supported in part by a grant to the USAID-AMPATH Partnership from the United States Agency for International Development as part of the President's Emergency Plan for AIDS Relief (PEPFAR). H.T. received support from the National Institute of Child Health & Human Development (K01HD061605-01A1).

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Table 1
Medication Event Monitoring System adherence corresponding to varying numbers of missed doses.

Self-reported no. of missed doses in past 7 days	Implied 7-day self-reported adherence (%)	Missed doses in past 7 days (MEMS)			Implied 7-day MEMS adherence		Difference between 7-day self-report and MEMS adherence		Proportion with 7-day MEMS adherence >90%
		N	Mean	SD	Mean (%)	SD	Mean (%)	SD	
0	100	2541	1.8	3.4	87.1	24.3	12.9	24.3	0.73
1	93	166	2.9	3.5	79.3	24.9	13.5	24.9	0.51
2	86	50	3.6	3.1	74.0	22.4	11.7	22.4	0.28
3	79	18	4.9	4.6	65.1	32.8	13.5	32.8	0.39
4 or more	<72	14	6.1	5.4	56.1	38.9	-0.5 ^a	41.1	0.21

Data on self-reported missed doses missing for two visit questionnaires.

^aSeven of 14 observations in this category have self-reported adherence that is lower than Medication Event Monitoring System (MEMS) adherence.

Table 2
 Comparison of self-reported and Medication Event Monitoring System adherence by month of clinic attendance.

Month	N	7-day self-report (%)	7-day MEMS (%)	Difference between 7-day self-report and 7-day MEMS (%)	P value of difference between 7-day self-report and 7-day MEMS	30-day MEMS (%)	Difference between 7-day self-report and 30-day MEMS (%)	P value of difference between 7-day self-report and 30-day MEMS	Proportion with 7-day MEMS adherence >90%
1	532	98.6	88.9	9.7	<0.01	89.7	8.9	<0.01	0.76
2	527	98.9	87.1	11.8	<0.01	87.2	11.7	<0.01	0.73
3	490	98.8	84.8	14.0	<0.01	85.9	12.9	<0.01	0.69
4	452	98.7	83.6	15.1	<0.01	84.3	14.4	<0.01	0.66
5	410	98.9	85.7	13.2	<0.01	85.5	13.4	<0.01	0.69
6	386	98.2	84.8	13.4	<0.01	83.8	14.4	<0.01	0.68
Mean ^a		98.7	86.0	12.7	<0.01	86.2	12.5	<0.01	0.71

Linear trend in difference between 7-day self-report and 7-day Medication Event Monitoring System (MEMS) over 6 months was statistically significant ($P<0.01$).

^aAverage across patient-months (N=2797).