BRIEF REPORTS

Adherence to Antiretroviral Therapy Assessed by Unannounced Pill Counts Conducted by Telephone

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BACKGROUND: Unannounced pill counts conducted in patients' homes is a valid objective method for monitoring medication adherence that is unfortunately costly and often impractical. Conducting unannounced pill counts by telephone may be a viable alternative for objectively assessing medication adherence.

PURPOSE: To test an unannounced pill count assessment of adherence conducted by telephone.

METHODS: HIV-positive men and women (*N*=77) in Atlanta GA completed an unannounced telephone-based pill count immediately followed by a pill count conducted in an unannounced home visit.

RESULTS: A high degree of concordance was observed between phone and home-based number of pills counted (Intraclass correlation, ICC=.997, 95% CI .995–.998, *P*<.001) and percent of pills taken (ICC= .990, 95% CI .986–.992, *P*<.001). Concordance between adherence above/below 90% and phone/home counts was 95%, Kappa coefficient = .995. Concordance between pill counts was not influenced by participant education or health literacy and was maintained when the data were censored to remove higher levels of adherence. Analyses of discordant pill counts found the most common source of error resulted from over-counted doses in pillboxes on the telephone.

CONCLUSIONS: Unannounced phone-based pill counts offer an economically and logistically feasible objective method for monitoring medication adherence.

KEY WORDS: HIV//AIDS treatment; medication adherence; pill counts; adherence assessment; medication monitoring.
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INTRODUCTION

Effective suppression of HIV replication requires as much as 90% adherence to combination antiretroviral (ARV) therapy[1–2]. Because patient reports and provider estimates seriously overestimate adherence[3–6], monitoring medication adherence requires objective and valid measures[7–11]. One of the few available objective methods for assessing medication adherence is pill counting. However, pill counts conducted in offices can be biased by patients failing to bring all of their medications and by dumping pills beforehand[12]. Biases in office-based pill counts can be resolved by conducting pill counts in patients' homes[10]. Unannounced home-based pill counts correlate .91 with electronic medication monitoring[13–14] and predict changes in viral load over time[1,15–16]. Unannounced pill counts virtually eliminate the potential problems faced by office pill counts.

A major limitation of the home-based unannounced pill count, however, concerns its logistical demands and cost. Unannounced home visits are often met with unanswered doors, and there are patients who would prefer not to have home visits. In addition, unannounced home visits are infeasible in rural areas and cities characterized by urban sprawl. In an effort to increase the utility and reduce costs of unannounced pill counts, we tested an adaptation of Bangsberg's[13–14] unannounced pill count protocol for administration over the telephone. In this study, we tested an unannounced phone-based pill count protocol by conducting immediate subsequent unannounced home visits to repeat the pill count.

METHODS

Participants

Participants were 51 men and 26 women; median age 44 years; 67 (87%) African American, 7 (9%) white, and 3 (4%) Hispanic. The mean number of years of education was 12.4 (SD=2.4), with 29% not completing high school; 61% had annual incomes below $10,000. The mean years since testing HIV positive was 12.0 (SD=5.5); 39 (51%) diagnosed with an AIDS defining condition, 66 (85%) had an undetectable viral load, and 63 (81%) had CD4 cell counts greater than 200 cells/mm^3.

MEASURES

Demographics, Literacy, and Health Characteristics. Participants reported their age, ethnicity, education, income, health literacy assessed by the Test of Functional Health Literacy for Adults (TOFHLA)[17], the year that they tested HIV positive, an index of 14 HIV symptoms, whether they had ever been diagnosed with an AIDS-defining condition, and their most recent CD4 cell count and viral load.

Medication Adherence. Participants completed unannounced pill counts for all of the ARVs they were currently taking. Using an adaptation of the protocol of Bangsberg et al.[13,14] for unannounced home-based pill counts, we conducted unannounced pill counts performed by telephone. A trained pill counter called participants at an undisclosed time to count their pills. In a face-to-face training session, we instructed participants to count their medications using the following steps: (a) bring all medications that are in the home to a comfortable flat surface near the phone, including closed bottles, pillboxes, and doses kept in their pockets, purses, backpacks, etc.; (b) prepare the flat surface on which to place all of their medications; (c) sort their medications into clusters; (d) select a medication, report the prescription number, refill date, and dispensed quantity; (e) report to the pill counter if they had lost or gained any pills since their previous count and whether they had taken any of the drug that day; (f) count their pills using a pharmacist tray and cup provided by the study; (g) repeating the procedure to double count.

Only after all pills were counted and double counted on the phone, participants were told that the home visit they had consented to would occur within minutes of completing the call. Participants were not aware that the home visit was that day until their phone assessment was completed. The same process was repeated during the home visit, with the home visitor asking that all pills be present and query whether there were additional pills in rooms, cabinets, and other visible places in the participant's home. Home pill counters also confirmed whether participants kept their pills in their bottles, pillboxes, or pockets.

PROCEDURES

Participants were passively recruited from clinical and community services in Atlanta GA and were enrolled in a larger prospective cohort study. Recruitment was by referral and snowball sampling with participants calling the research office. The only inclusion criterium was being HIV positive and currently taking ARVs. Participants provided informed consent and agreed to complete 13 monthly unannounced phone assessments (for the parent study) and one unannounced home visit. Participants were not told the home visit would occur in relation to a phone assessment and were not told that the home visit would verify their phone-based pill counts. At an initial intake assessment, participants brought their medications to the research office and were instructed in how to perform the unannounced phone-based pill counts. Training occurred in our offices by an intake assessor and a phone-based pill counter present on the phone. Training focused on instructing participants in organizing and counting their pills using the steps outlined above. Participants were given a cell phone that restricted all outgoing and incoming calls except to emergency 911 and the research project office. We provided cell phones only as a back up to the participants' own phones to assure that participants would be able to receive the assessment calls. As part of the intake interview, we asked participants about their daily routines to determine acceptable times to attempt assessment calls. Participants were also administered an intake assessment battery using audio computer-assisted structured interviews (ACASI). The assessments in this study represent 1 of the 13 monthly unannounced phone assessments selected at random paired with an unannounced home-based pill count. Thus, 12 participants received their home visit after the 12th or 13th phone assessment, and 15 participants had their home visit after their second or third phone assessment. Among the 77 participants, 18 had home visits after their first phone assessment, not allowing for the calculation of adherence, which requires 2 successive pill counts.

DATA ANALYSES

We primarily performed analyses to assess the concordance between the unannounced phone-based and home-based pill counts. Because the 77 participants were taking a total of 205 medications, we were able to assess concordance at the individual pill count level. For adherence, we calculated the difference between 2 consecutive pill counts for the 153 medications being taken by the 59 participants with 2 consecutive counts. Adherence was calculated as the difference between pills counted at the 2 times divided by the pills prescribed, taking into account the number of pills dispensed, pills lost, gained, and taken that day. We tested agreement using intraclass correlations (ICC) and tested the difference between pill counts using dependant t tests. To remove the potential bias of higher levels of adherence, we repeated the ICCs after censoring the sample for participants with 90% adherence and again for 80% adherence. We also tested concordance using Kappa coefficients of agreement for 2 clinically meaningful classes: (a) adherence defined as 90% and (b) adherence defined as 80%. We compared participants who had perfectly concordant phone and home pill counts with participants who had discrepant pill counts on the number of phone assessments conducted before the home visit (temporal effects), demographics, and health characteristics.

RESULTS

Five (6%) participants were taking a single combination ARV pill, 16 (21%) were taking 2 ARVs, 48 (63%) were taking 3, and 8 (10%) participants were taking 4 ARV medications. Twelve (15%) participants lived in HIV-positive congregant living situations in their own independent apartments, and 7 participants lived in city-subsidized housing for persons with disabilities. Participants resided throughout Atlanta, representing 31 different zip codes that spanned a 25-mile area. The mean number of miles driven between participant locations on the 3 days of the pill counts was 8.7 (SD=6.5, Median=7, range=1 to 23). On average, home visitors spent 22 minutes (SD=15.0, Median=18, range=4 to 60) driving between home visits. Contacting 77 participants on the phone required a total

of 162 call attempts, with 44 (57%) participants contacted on the first attempted call and 18 (23%) contacted on a the second attempted call, and 11 (20%) requiring 3 or more phone attempts to reach them. The time required to complete pill counts on the phone and in the home was 18 minutes (SD= 7.6, Median=17, range=6 to 35). A total of 15 of the 77 participants were reached on their study cell phone.

Among the 59 participants with a prior consecutive pill count, we found that the mean adherence was 86.7% of pills taken as prescribed; 34% had taken less than 90% of their pills, and 19% had taken less than 80% of their pills.

Concordance for Pills Counted

Table 1 shows the descriptive statistics for the pill counts conducted on the phone and in the home. Among the 205 independent pill counts, we found that 163 (80%) were exactly the same and 42 (20%) were discordant. Among the 42 discordant counts, 26 (13%) had a greater number of pills counted by phone than in the home; 21 discordant counts involved 1 or 2 pills counted on the phone that were not counted in the home. The ICC between the phone and home pill counts was .997, 95% CI=.995–.998, $P<.001$. When censored for levels of adherence less than 90% and 80%, the ICCs were .995 and .993, respectively. There was no association between pill count concordance and temporal effects of the phone assessment, X^2 (df=11, N=77)=5.3, $P>.1$.

Concordance for Adherence Rates. We calculated adherence for the 153 pill counts that had phone counts the previous month and found that there were no significant differences for adherence rates resulting from the phone-based and the home-based counts, t (152)=.4, $P>.1$ (see Table 1). The association between the phone and home adherence rates was significant, ICC .990, 95% CI .986–.992, $P<.001$.

Table 1 shows the clinically meaningful classifications of adherence for the phone and home counts. The Kappa coefficient for agreement at 90% adherence was .995, $P<.001$, and for 80% adherence Kappa was .997, $P<001$.

Table 1. Descriptive Statistics for Pill Counts and Adherence Rates Conducted on the Telephone and in Participant's Homes

Pill counts and adherence	Phone-based pill count	Home-based pill count
Pill counts (N=205)		
Mean pills counted	54.3	54.1
Standard deviation	76.7	76.7
Median pills counted	35	35
Minimum pills counted	0	0
Maximum pills counted	697	697
Sum of pills counted	11,133	11,093
Adherence rates (N=153)		
Mean adherence	86.7%	86.7%
Standard deviation	21.8	21.9
Median adherence	95.2%	95.2%
Minimum adherence	1.3%	1.3%
Maximum adherence	100%	100%
N; %<70% adherent	21; 14%	21; 14%
N; %<80% adherent	29; 19%	29; 19%
N; %<85% adherent	36; 24%	36; 24%
N; %<90% adherent	51; 33%	52; 34%
N; %<95% adherent	73; 48%	72; 47%

Table 2. Continuous Demographic and Health Characteristic Variables of Participants with Discordant and Concordant Pill Counts (N=77)

Characteristics	Discordant pill counts (N=29)		Concordant pill counts (N=48)		T
	M	SD	M	SD	
Age	45.6	6.2	44.7	6.1	0.6
Education	12.2	2.5	12.6	2.3	0.8
TOFHLA % correct	88.5	0.1	83.4	0.1	1.7
Years since testing HIV+	12.4	5.8	11.7	5.4	0.5
HIV symptoms	2.9	3.1	2.85	2.9	0.2

Analysis of Discrepant Counts

Comparisons between participants with discordant pill counts (N=29), and those participants who had precisely the same phone and home pill counts (N=48) did not indicate any significant differences in demographics including education and health literacy, or health characteristics (see Tables 2 and 3). Participants with discrepant pill counts were more likely to use pillboxes and pocket dose containers.

Debriefing interviews with home-based and phone-based pill counters revealed 2 major sources of error that accounted for 50% of the discordant counts. Phone assessments most commonly overcounted pills sorted in pillboxes. Home-based pill counters observed participants counting doses in empty container compartments that were most likely counted on the phone without correction. Pills that had been removed from bottles during the phone count and not identified in the home were a second source of error. For 2 cases, a single pill had fallen on the floor, and once, a pill had fallen in a couch. These pills were counted on the phone but were missed during the home visits. Discovery of the pills occurred after the home visit and was not corrected for concordance analyses.

Table 3. Categorical Demographic and Health Characteristic Variables of Participants with Discordant and Concordant Pill Counts (N=77)

Characteristics	Discordant pill counts		Concordant pill counts		X^2
	N	(%)	N	(%)	
Male	18	62	33	69	0.4
African American	26	90	41	85	
White	1	3	6	12	
Hispanic	2	2	1	2	3.4
CD4 < 200	3	11	9	21	1.2
AIDS condition diagnosis	12	41	27	56	1.6
Keeps pills in bottles	25	86	46	96	2.3
Uses pill box/ mediset	18	62	17	35	5.2†
Carries pills in pockets	16	55	16	33	3.6*

*$P<.06$
†$P<.05$

DISCUSSION

To our knowledge, this study is the first to validate an unannounced pill count method of adherence monitoring conducted by telephone. In this study, phone-based pill counts obtained very high levels of concordance across several indexes of raw pill counts and adherence rates. Only slightly, more than half of the participants were contacted on their first phone attempt, and 20% required 3 or more calls to contact them for the pill count. Missed contacts by phone are inexpensive and allow pill counters to contact another patient without delay. Phone-based pill counts can be conducted in urban and rural areas, and pill counters and patients can reside in different cities, states, or even different countries.

A potential limitation of the unannounced phone-based pill count is that it relies on patients to count their own pills and report the values to a phone assessor. We believe, however, that it is implausible that patients will do the mental calculus needed to determine the number of missed doses they may have had since their previous call, consider the number of pills that had been dispensed, multiply the number of missed doses by the number of pills per dose, and adjust the counting, while the pill counter is on the phone. In addition, only rarely did home visitors discover pills that were uncounted on the phone. The only characteristic that differentiated participants with concordant from discordant pill counts was the use of pillboxes. Adjusting the unannounced phone-based pill count protocol to remove the error resulting from pillboxes would further refine the procedure. It is also possible that the phone-based pill counts were biased by participants knowing that at some point, they would receive a home visit. Another limitation was our use of a convenience sample that cannot be considered representative of people living with HIV/AIDS. Additional research is needed to determine the utility of unannounced phone-based pill counts in research and clinical settings.

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Conflict of Interest: *None disclosed.*

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