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ORIGINAL PAPER

Picture Pill Count: An Innovative, Reliable, Valid and Feasible Method to Measure Adherence to ART

Marcia M. Holstad[1] · Melinda Higgins[1] · Maya Bauman[1] · Eugene W. Farber[2] · Drenna Waldrop-Valverde[1] · Oluchi Okwandu[1] · Igho Ofotokun[3]

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Abstract

We report the reliability, validity, and feasibility of self-performed picture pill count (PPC) as an adherence measure that was used in a randomized trial with HIV positive people living in rural Georgia. The first 61 (of 149) participants conducted an additional PPC 1–2 days after baseline. Reliability, measured by a PPC scoring instrument, analyzed participants' ability to reproduce high quality pill count photographs free from artifact or blurring that could hamper accurate visualization of the pills and bottle labels. Except for label blur, baseline photographs (performed with coaching by study staff) and independently performed post-baseline photographs were rated as acceptable quality (> 93%). Label blur significantly worsened between the baseline and post-baseline scoring (93% vs 80%, $p = 0.039$), possibly indicating that participants required more education to ensure readability. Validity was determined by comparing the number of pills entered into the PC survey with the number of pills in the texted PPC; 77.5% of participants had perfectly matched pill counts ($r = 0.690$, $p < 0.001$). We found PCC to be a reliable and valid method of measuring adherence. The high rate of participant satisfaction underscores its feasibility. It provides an innovative alternative to other more invasive and labor intensive methods of measuring adherence using pill counts.

Keywords HIV/AIDS · Adherence · Antiretroviral therapy · Pill counts · Rural health

Introduction

Adherence to antiretroviral therapy (ART) is crucial to maintaining HIV viral suppression and reducing the risk of transmission [1]. By extension, ART adherence improves overall health and prevents HIV-related morbidity and mortality among persons living with HIV/AIDS [1]. In research and clinical practice, adherence has been measured in several ways. Self-report is probably the easiest but subject to bias from social desirability and recall [2]. Electronic monitoring via medication caps that contain chips that register openings (i.e., Medication Event Monitoring caps, MEMS) are often used in research. The caps are bulky, and clients may have difficulty using them when leaving home or traveling. They are also subject to damage from dropping, water, etc. Caps tend to underestimate adherence due to non-use or error from misuse [3]. Real-time electronic measures, such as WisePill, count pill container openings in real time using a cell phone signal and notify staff of non-openings [4]. These devices are also bulky and subject to damage. Moreover, both electronic monitoring devices could induce concerns for stigma if noticed by others [4]. Pill counts, either in person or by phone, have been shown to be reliable and valid measures of adherence that correlate with other objective measures [5]. In-person counts require a significant workforce, which remain a major barrier and limits accessibility in rural settings [6]. Unannounced telephone counts address the limitations related to in-person pill counts due to their logistical feasibility and minimal effort from staff or patients [5], and they do not increase adherence by drawing attention to future pill counts [6]. However unannounced phone calls might occur at inopportune times. For example, participants may elect not to answer these calls when in circumstances where their privacy cannot be ensured. Even when calls are

✉ Marcia M. Holstad
nurmmcd@emory.edu

[1] Nell Hodgson School of Nursing, Emory University, 1520 Clifton Road, Atlanta, GA 30322, USA

[2] School of Medicine, Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA 30322, USA

[3] School of Medicine, Department of Medicine, Emory University, Atlanta, GA 30322, USA

answered, it may not be feasible to complete the pill counts if the pills to be counted are unavailable at the location where participants are reached.

With the ubiquity of smartphones, new technological methods of measuring adherence are emerging. The advantage of technology is that those who live in rural or remote areas can be monitored without increased participant burden. While text messaging has been used in several interventions to promote medication adherence (including to ART) by sending pill count reminders directly to patients, we could find no studies that used text messaging directly by patients to conduct pill counts and report pills taken. One study [7] used SMS text messages to adults and caregivers of children in Uganda to self-report doses missed over a one week period. An innovative method to monitor adherence is video direct observed therapy (VDOT), in which participants record themselves ingesting medications and upload the video to a secure server. Staff then review the video and confirm ingestion. This method was pilot tested as a substitute for in-person daily directly observed therapy with tuberculosis patients on anti-tuberculosis medications [8]. A similar method was also used in a pilot study of a clinical trial monitoring adherence to a study medication that reduces cannabis dependence [9]. Over a period of four weeks, twenty participants were contacted daily (weekdays only) using Skype ® video link on a study-provided smart phone and asked to show their pill bottles to the research staff. Adherence was determined by visualizing real-time pill ingestion via video. Afterward, participants were asked to open their mouths and move their tongues from side-to-side for the research staff. Results from the video calls were compared to weekly in-person pill counts and plasma drug levels. Adherence rates of 95% measured by video-call were corroborated by the pill counts and plasma drug levels. While useful, daily video or Skype ® pill monitoring requires additional patient technical skills, increases participant burden, and may be considered personally invasive for long-term monitoring of daily medications used to treat chronic illnesses such as ART for HIV treatment.

Smartphone still photography has also been adapted as a means of determining medication adherence. In one pilot study of 20 methamphetamine-dependent persons, daily pill photographs were used to measure modafinil adherence in an 8 week-clinical trial [10]. Each participant took pictures of the pill in his/her hand prior to ingestion and then emailed the picture to study staff. Data from photo-counts were compared with weekly MEMS counts and in-person pill counts. Results revealed concurrence among all three measures in over a third of participants. When discordance occurred between pill counts and other measures, MEMS overestimated adherence compared to photographs and photographs tended to underestimate adherence.

Daily pill pictures are time and labor intensive for both patients and staff and may be impractical for long-term monitoring. The technologies, VDOT, Skype ® and daily pill photographs were used with participants on short term medication regimens and would be impractical for long-term monitoring. They would increase both participant and staff burden. Therefore, there is a need to develop alternative methods that streamline medication adherence monitoring procedures and reduce both participant and staff burden. Toward this end, the study reported herein describes a test of the feasibility, acceptability, reliability, and validity of an HIV antiretroviral adherence monitoring method combining the use of pill photographs and text communications to conduct monthly pill counts via smartphone devices. This method has the potential to reduce adherence monitoring burden by leveraging two commonly used smartphone capabilities, camera and text messaging.

Monthly picture pill counts were conducted with participants in a clinical trial to test the efficacy of a smart phone application (app) to promote adherence and symptom self-management in rural HIV positive adults. Apart from presenting visual evidence of ART usage, picture pill counts may provide a deeper understanding of individuals who self-assess medication adherence. Participants reported ART adherence by taking smartphone photographs of the pills remaining in the pill bottles, texting these pictures to the study staff, and completing a web based self-report survey via smartphone app. This survey contained questions about medication habits and a self-reported pill count. We report on the reliability, validity and feasibility of the use of picture pill counts (PPC).

Methods

Setting and Design

This study took place within a larger project, the Music for Health Project (MFH). MFH was a randomized controlled clinical trial to test the efficacy of a smart phone app containing a music-based messaging program and manual [11] that was designed to promote adherence and symptom self-management in HIV positive adults residing in rural Georgia. The intervention was compared to a control app containing music-based messaging songs and manual with a general education focus. MFH took place at seven sites in six rural cities in Georgia. Six of the sites were Ryan White funded specialty clinics within local health departments; one site was a private infectious disease clinic that served HIV positive patients. The health districts where the sites were located collectively contained the largest number of HIV+ persons outside the metropolitan Atlanta area. The study

received institutional review board approval and all participants provided written informed consent.

Recruitment

Recruitment for the larger MFH project occurred between June 2014 and July 2016. Participants for the PPC project were recruited until May 2015. MFH participants were recruited through local providers, clinic staff, and self-referral. Potential participants were asked to have a referral form signed by their provider, nurse, or case manager that confirmed their eligibility for the study and listed their HIV medications. Eligibility criteria were: (1) HIV positive; (2) age 18 years or older; (3) speaks and understands English; (4) One of the following: ART naïve; changing to a new ART regimen due to side effects or viral resistance, currently on ART; (5) mentally stable based on screening assessment for depression, psychosis, cognitive impairment; (6) willing to participate in all study activities (e.g., use the app, conduct monthly PPC, complete study follow-up visits and surveys).

Overall 263 persons were referred and 149 rural dwelling HIV positive men and women were enrolled into the Music for Health Project. Reasons for non-participation included ineligibility and not interested. Seventy-two were randomized to the intervention group and 77 to the control group. To examine reliability and validity of PPC, the first 61 participants conducted a baseline PPC and PC survey and were invited to conduct an additional PPC and PC survey in 1–2 days post baseline.

Procedures

All MFH study participants completed the PPC and pill count (PC) survey at baseline and monthly for 9 months and completed an end of study evaluation survey that contained questions about the PPC. By the end of the study there was one death, two known incarcerations, and seven withdrawals.

During the baseline visit, participants were taught how to use the study-provided smartphone to conduct the PPC and PC survey. They then conducted a supervised PPC with coaching as needed from study staff. To conduct a PPC, participants used the smartphone camera app to take pictures of each prescribed antiretroviral medication's pill bottle label and all remaining pills in the bottle. Prior to conducting the pill count, participants were instructed to wash hands or use hand sanitizer and have a paper towel or napkin on hand. For the label, the picture needed to include the name of the medication, prescription fill date, dose instructions, and number of pills filled. Often it required two pictures to capture all the information. For the pill pictures, the participant was instructed to empty pills on a white napkin or paper towel, separate pills so they were not on top of each other and if possible place pills in groups of five, and photograph the pills. The participant then sent all photographs via text message to the study pill count coordinator. Once received, the pill count coordinator acknowledged receipt with text message, downloaded pictures to a secure study file, counted the pills twice, and recorded the number in the pill count data base. Participants could then delete the photos from their phones. Participants received $10 gift cards for each pill count they conducted.

To determine the reliability and validity of this method, we evaluated the results of the initial supervised PPC with one-on-one coaching by study staff (baseline visit) and an at-home reliability PPC completed by the participant with no outside help about 2 days later. Sixty-one study participants who finished the baseline PPC and PC survey completed an unsupervised reliability PPC and PC survey. For test–retest reliability, the picture quality of PPC photographs from both time points were scored and compared using the Picture Pill Count Scoring Instrument (PPCSI). For validity, the results of the pill counts conducted by the pill count coordinator were compared to those entered by the patient in the PC survey. We decided a priori to enroll 60 participants to complete the test–retest PPC to achieve a 95% confidence interval width no larger than 0.10 given an expected test–retest correlation of $r = 0.9$ [12]. Sixty-one participants actually completed the test–retest PPC.

Instruments

The 17-item *PC Participant Survey,* meant to be completed along with the monthly texted PPCs, was administered through the MFH app using the SurveyGizmo platform [13]. Questions concentrated on all aspects of medication taking behaviors, including current ART regimens, prescription details (e.g., fill dates, number of refills), lost or dropped pills, shared pills, medication storage, and medication organization. In addition, participants were asked to count their pills and record the results in the survey. These self-report pill counts were used for validity calculations by comparing survey responses with texted PPCs.

The *Picture Pill Count Scoring Instrument (PPCSI)* was a 15-item measure developed for MFH study personnel to evaluate each participant's ability to reliably, repeatedly conduct picture pill counts deemed acceptable and usable to determine adherence. This instrument focused on three photographic dimensions of the pill count images: the quality, clarity and sharpness of images to identify and count the pills; the quality, clarity and readability of pill bottle prescription labels; and whether label pictures contained necessary content (e.g., fill dates, number of refills, special instructions) to complete the pill counts.

We evaluated PPCSI reliability by calculating inter-rater reliability using intraclass correlations (ICC) between two

research staff raters who independently completed the PPCSI for 15 texted pill counts. The overall instrument (i.e., total score) demonstrated a high degree of reliability (Cronbach's alpha of 0.960 with a 95% confidence interval from 0.707 to 0.969, $p < 0.000$). Broken down by section, the picture quality portion of the survey (both pill and label pictures) had a Cronbach's alpha of 0.954 with a 95% confidence interval from 0.772 to 0.971 ($p < 0.000$). The label information section of the PPCSI also demonstrated excellent reliability, with a Cronbach's alpha of 1.000. Based on these results, we concluded that the PPCSI could provide a reliable assessment of each participant's ability to conduct picture pill counts.

Finally, the *End of Study Survey* (EOS) was administered on the final participant visit using audio computer assisted self-interview. This 84-question survey assessed user satisfaction with various aspects of the study. Participants were asked to provide ratings of their experience in interactions with the research staff, the ease of using smart phone technology to complete study-related tasks, how well they liked the individual components of the app content, and use of PPC. To encourage a frank assessment of the program, all EOS surveys were anonymous such that no responses could be traced back to individual study participants.

Analyses

To determine how well the PPC could be completed by participants independent of supervision, we evaluated test–retest reliability by comparing the quality (PPCSI score) of the supervised baseline PPC with the quality of a second unsupervised pill count conducted about 2 days post-baseline. To assess validity of the PPC, we compared the texted PPC results counted by the pill count coordinator with the self-reported pill counts entered by the participant in the Pill Count Survey at both baseline and 2 days post-baseline. Pearson correlations were calculated for both of these counts. Paired t-tests were also performed to compare the PPCSI picture quality scores between the baseline and 2 day post-baseline reliability PPC. Paired differences on the individual PPCSI items were compared based on acceptable versus unacceptable quality using McNemar's test. Participant demographic information was also described. SPSS version 24 was used for all analyses [14].

Results

Characteristics for the 61 participants are presented in Table 1. Ages ranged from 18 to 56 years, with an average of 36 years. Most identified as African American, male, gay/bisexual, unemployed, and unpartnered (e.g., never been married, separated, not in a committed relationship, divorced, or widowed). The highest educational attainment for the majority was high school or less.

Table 1 Demographic characteristics (n = 61)

	Mean (SD)	Range
Age	35.9 (9.9) years	18–56 years
	Median [IQR]	Range
Income/mo (n = 59)	$700 [$190, $1200]	$0–$5317
Gender	N (%)	
Male	42 (68.9%)	
Female	19 (31.1%)	
Consider yourself to be		
Straight/heterosexual	26 (42.6%)	
Gay/lesbian	29 (47.5%)	
Bisexual	3 (4.9%)	
None of above	3 (4.9%)	
Race		
African American	45 (73.8%)	
Caucasian	11 (18.0%)	
Hispanic/Latino	3 (4.9%)	
Other	2 (3.3%)	
Education (n = 60)		
Primary/elementary	1 (1.6%)	
Junior high/middle	3 (4.9%)	
High school/GED	34 (55.7%)	
College/technical school	19 (31.1%)	
Grad/prof school	4 (6.6%)	
Marital status		
Married	5 (8.2%)	
Separated	3 (4.9%)	
Divorced	8 (13.1%)	
Widowed	1 (1.6%)	
Never been married	32 (52.5%)	
Committed relationship	12 (19.7%)	
Work outside home		
No	44 (72.1%)	

Test–Retest Reliability

Fifty-seven of the 61 (93%) participants texted PPCs at both time points. Photograph quality was analyzed by computing PPCSI subscores (pill picture quality, label picture quality, and label content) and total scores. Table 2 presents an overview of the changes in mean PPCSI scores between the baseline and post-baseline PPCs. Overall, there were significant differences in the pill picture scores, label picture scores, and total PPCSI scores. There was no significant difference in the quality of the medication label content.

Because we were most interested in each participant's ability to take readable quality pill and bottle label photographs, we dichotomized the scores of each PPCSI subscale

Table 2 Changes in PPCSI scores from baseline to 2-days post-baseline (n = 57)

	Baseline mean (SD)	Post-baseline mean (SD)	Difference (SD)[a]	t-score	*p* value
Pill picture quality	20.70 (1.48)	20.22 (1.62)	0.47 (1.63)	2.198	0.032
Label picture quality	15.21 (0.92)	14.35 (1.22)	0.86 (1.34)	4.836	0.000
Label picture content	14.72 (1.08)	14.56 (1.15)	0.16 (.82)	1.455	0.151
PPCSI total	50.63 (2.17)	49.14 (2.93)	1.49 (2.68)	4.201	0.000

[a]Difference between baseline and post-baseline mean scores

item to unacceptable (poor quality; difficult to read information and count and identify pills) and acceptable (adequate quality; able to read information and count and identify pills). In this context, it was possible to have an acceptable overall picture quality in the presence of unacceptable blur. For the PPCSI, "blur" refers to the degree to which the images of the pills (picture blur) and the print on the pharmacy label (label blur) soften to the point where they become hard to distinguish from the background. Because few, if any, of the pictures submitted by the participants were blurred to the point of indecipherability and most of the images possessed at least some readable content, the dichotomized results reflected unacceptable blur with somewhat decipherable images versus acceptable blur with easily decipherable images. (See Fig. 1 for examples of blurred PPC.) PPCSI results are displayed in Table 3. With the exception of picture blur and label blur, all items at both baseline and post-baseline had high rates of acceptable quality (> 93%). Acceptability of the label blur quality was significantly lower at post-baseline, 79.7%, than at baseline, 93.1% ($p = 0.039$). Picture blur had the lowest acceptable rates; all were < 45% (44.8% at baseline and 40.7% post-baseline); however, these were not significantly different between the two time points—both were low.

When considering the changes from unacceptable to acceptable label blur and visa-versa: 10/57 (17.5%) participants who had acceptable label blur at baseline got worse (unacceptable label blur) compared to only 2/57 (3.5%) participants who had unacceptable label blur at baseline who got better. Significantly more participants (17.5%) with acceptable label blur at baseline got worse at the post-baseline PPC (McNemar's test, $p = 0.039$).

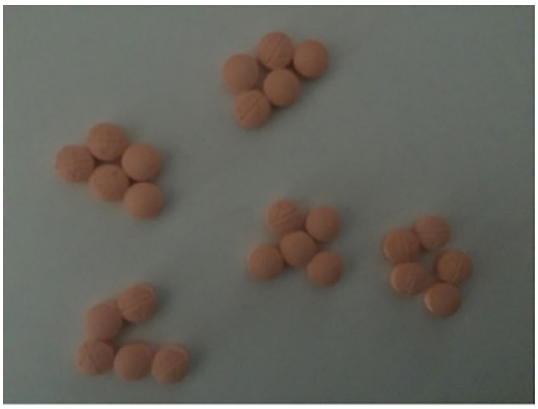
Validity

We compared the number of pills the participant reported in the PC survey at baseline and post baseline with the number of pills in the texted PPC that were counted by the pill count coordinator at these time points (Fig. 2). At baseline, 54 participants had both PC survey and PPC data with differences ranging from 0 to 1 pill, $r = 1.00$ ($p < 0.001$). These were all completed on the same day. Only 2 participants had counts that did not match and differed by only 1 pill. The other 52 participants (96.3%) had perfectly matched pill counts. At post-baseline, 40 participants had both PC survey and PPC data. Differences between the texted PPC and the PC survey counts ranged from −27 to 49. Upon review, these outliers were believed to be typographical errors when participants entered numbers into the survey (for example, one participant entered 55 which was most likely supposed to be a five, given that the texted pill count was six). When these typographical outliers were removed, differences ranged from −2 to 2 pills. Thirty-one of the 40 (77.5%) had perfectly matched pill counts, $r = 0.690$ ($p < 0.001$). The range of days from baseline to post-baseline PPC was from one to 15 days with a median of 2 days.

Satisfaction with PPC

Because the End of Study (EOS) evaluation was anonymous, we were unable to link results to the 61 participants for this analysis. Therefore, results from the 101 participants who completed the survey at the final study visit are reported in this section. Ninety-seven percent of participants agreed/strongly agreed that the PPC instructions were easy to understand, 95% felt PPC were easy to perform, and 80% agreed/strongly agreed that they liked doing them. However, 26% felt PPC were too complicated, 28% would prefer a telephone pill count, and 24% would prefer to come into the office and have a staff member count their pills. With respect to the pill count survey, 95% agreed/strongly agreed that the survey instructions were easy to understand, 94% felt it was easy to use, 83% liked it, and 87% agreed/strongly agreed that they used it monthly.

An open ended item asked for suggestions for changes to the PPC. The majority (70%) of 102 responses received were "none/nothing"; however, two people wanted to be able to send more than one picture at a time, three wanted in-person counts, one responded to connectivity issues, and one wanted a better phone. Other comments included: "Eliminate;" "I think I can learn to like them;" "Everything was easy to understand;" "Would not change a thing, the easier the better;" "I've enjoyed taking the pictures myself;" and "It's perfect and easy and holds you accountable."



The above photograph would be scored as follows: *Stamps are blurred; none/mostly none are readable (Option 1).* None of the stamps can be read.

The above photograph would be scored as follows: *None of the stamps are blurred (Option 4).* (NOTE: Not all of the stamps are facing up in the picture, but the ones that are can be easily identified.)

The above photograph would be scored as follows: *Label is blurred; some print is readable (Option 2).* The print on this label can be read, but with scrutiny.

The above photograph would be scored as follows: *Label is not blurred (Option 4).*

Fig. 1 Examples of unacceptable and acceptable pill and label blur in the PPCSI ▶

Discussion

PPCs provide a technological alternative to in-person or telephone pill counts and avoid common barriers, such as transportation issues and additional time commitments from both patients and staff. It is less intrusive and minimizes privacy or stigma-related concerns associated with real-time monitoring, VDOT, Skype®, and unannounced pill counts. Using standard measurement procedures, we demonstrated that participants could independently take satisfactory, readable pictures of their pills and pill bottles. Blurring of pictures did occur with the post baseline counts, and we believe this is probably due to participants snapping the picture before the phone camera could auto-focus, an issue readily addressed by more intensive participant education by study staff. Nonetheless, we believe that even those photographs with unacceptable picture/label blur scores could still be considered usable because the images were *readable*, albeit with some difficulty (e.g., Fig. 1). We also found that participants' self-reported pill counts entered into the PC survey correlated strongly and repeatedly with staff counts of the pills within the PPC. Overall, though PPCs were not for everyone, the majority of participants felt they were easy and liked doing them.

There were some methodological limitations to this project. First, because the EOS was anonymous, we were unable to analyze how demographic characteristics such as age, a known variable affecting technology acceptance/adoption, influenced EOS responses. Second, periodic connectivity issues in the rural study areas may have contributed to delays receiving texted PPCs in a timely manner due to sluggish or nonexistent data transfer rates. This issue persisted throughout the duration of the Music for Health study. To avoid data loss, participants were instructed to save pictures on their phones until they received confirmation of receipt from the PPC coordinator. This procedure should be incorporated in future use. Third, the app-based pill count survey could not accommodate interruptions. If the connection was lost during the survey, the participant had to re-start from the beginning. This was a common source of frustration for the participants and for the study personnel. Fourth, the few open-ended questions in the pill count survey that involved typing, such as recording the number of pills, allowed for potential typographical errors and decreased data accuracy. Finally, the reliability and validity surveys and pill counts were not always completed within the designated time frame. Several post-baseline PPCs were conducted outside the 2-day window and on some occasions were not conducted at all. However, for the duration of the Music

Table 3 Dichotomized PPCSI scores from baseline to post-baseline (n = 57)

	Baseline acceptable[a]	Post-baseline acceptable[a]	McNemar's test p-value
Pill picture quality			
Lighting	58/58 (100%)	59/59 (100%)	na
Glare	58/58 (100%)	57/59 (96.6%)	na
Background	58/58 (100%)	59/59 (100%)	na
Blur	26/58 (44.8%)	24/59 (40.7%)	0.629
Angle	58/58 (100%)	59/59 (100%)	na
Pill position	58/58 (100%)	58/59 (98.3%)	na
Label picture quality			
Lighting	56/58 (96.6%)	56/59 (94.9%)	1.000
Glare	58/58 (100%)	59/59 (100%)	na
Blur	54/58 (93.1%)	47/59 (79.7%)	0.039
Angle	58/58 (100%)	59/59 (100%)	na
Label picture content			
Medication name	60/60 (100%)	60/60 (100%)	na
Fill date	56/57 (98.2%)	55/58 (94.8%)	0.500
Dispense	57/57 (100%)	58/58 (100%)	na
Refills	53/57 (93.0%)	53/57 (93.0%)	1.000
Instructions	56/58 (96.6%)	57/59 (96.6%)	1.000

[a]Actual points/total possible points (%)

for Health project, receipt of the text message announcing that it is time for a PPC was "unannounced," and the participant was given a 2-day period to conduct and send his/her count. After that, additional reminders were sent. Completion of unannounced telephone counts may provide at least as much urgency as a text message and participants do have potential for delaying with excuses of a bad time, not answering the call, or hanging up on the caller, which could extend the time for completing the pill count.

Guided by psychometric theory as described by Nunally and Bernstein [15], we applied standard measurement procedures to evaluate the PPC. Kalichman and colleagues [5, 6] reported similar methods to ascertain reliability and validity of unannounced telephone pill counts. In addition, they provided data to support that unannounced telephone counts were not subject to assessment reactivity. PPCs may have the potential to induce bias related to assessment reactivity. The procedure is more complicated for the participant than telephone or in-person pill counts, and actively taking pictures of ones' leftover pills may induce personal accountability or the potential for social desirability bias (i.e., pill dumping to "look good" or please the investigators). Though not as intrusive as video monitoring, PPCs could be considered by some as an intervention. Similar to reports by Kalichman et al. [6], the low levels of average monthly PPC adherence (range 56–66%) we saw among the Music for Health study participants over the 9-month course of the study tends to reduce concern for this possibility. Yet, we must consider one participant's comment that the PPC "holds you accountable." Conscientious individuals will most likely feel this way using any method to monitor adherence.

Costs of conducting PPC could be a limiting factor for research, if study phones are provided. We provided smartphones with unlimited data, picture texting, and camera due to the nature of our project (examining efficacy of an app). If phones were needed for only PPC, participant phones with incentives to defray data/texting costs could be employed. Password protections would be needed for security and privacy.

Conclusion

Based on the findings of this analysis, we conclude that PPC is a reliable and valid method of monitoring adherence. It was well received by the majority of participants in the Music for Health Project. It is advantageous for rural projects due to its ease and efficient use of technology, and may provide an innovative alternative to traditional methods in the armamentarium of how to measure adherence using pill counts. Inconsistent reliability of internet and data connections as well as technology acceptance by some patients and participants could place a practical limit on PPC use.

Future recommendations include using the participant's own phone whenever possible to take PPC (password protection will be needed to save pictures); providing intensive education on how to use the camera, including autofocus, to take pill pictures to avoid blur; simplifying the pill count survey using drop down menus, incorporating auto-save, and

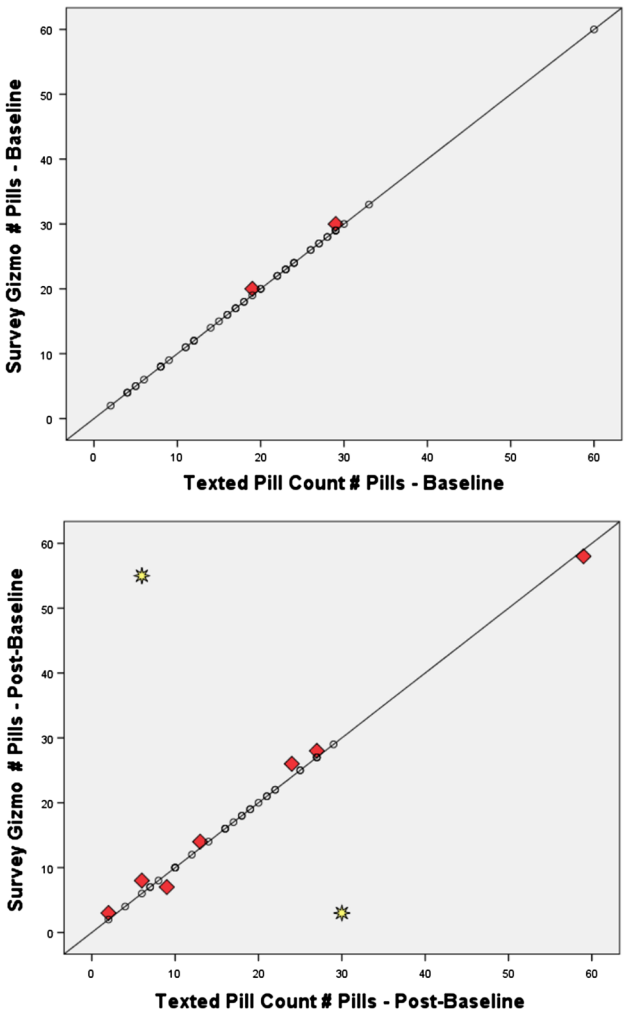


Fig. 2 Self-report pill counts versus texted pill counts at baseline and 2 days post-baseline

educating participants on need for stable internet connection. Future studies that employ and continue to validate this method are encouraged.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV 2018. http://www.aidsinfo.nih.gov/ContentFiles/.
2. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. Clin Ther. 1999;21(6):1074–90 **(discussion 3)**.
3. Choo PW, Rand CS, Inui TS, Lee ML, Cain E, Cordeiro-Breault M, 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.
4. Haberer JE, Kahane J, Kigozi I, Emenyonu N, Hunt P, Martin J, et al. Real-time adherence monitoring for HIV antiretroviral therapy. AIDS Behav. 2010;14(6):1340–6.
5. Kalichman SC, Amaral CM, Cherry C, Flanagan J, Pope H, Eaton L, et al. Monitoring medication adherence by unannounced pill counts conducted by telephone: reliability and criterion-related validity. HIV Clin Trials. 2008;9(5):298–308.
6. Kalichman SC, Amaral C, Swetsze C, Eaton L, Kalichman MO, Cherry C, et al. Monthly unannounced pill counts for monitoring HIV treatment adherence: tests for self-monitoring and reactivity effects. HIV Clin Trials. 2010;11(6):325–31.
7. Haberer JE, Kiwanuka J, Nansera D, Muzoora C, Hunt PW, So J, O'Donnell M, Siedner M, Martin JN, Bangsberg DR. Real-time adherence monitoring of antiretroviral therapy among HIV-infected Adults and children in rural Uganda. AIDS. 2013;27(13):1–5.
8. Garfein RS, Collins K, Munoz F, Moser K, Cerecer-Callu P, Raab F, Rios P, Flick A, Zuniga ML, Cuevas-Mota J, Liang K, Rangel G, Burgos JL, Rodwell TC, Patrick K. Feasibility of tuberculosis treatment monitoring by video directly observed therapy: a binational pilot study. Int J Tuberc Lung Dis. 2015;19(2):1057–64.
9. DeWorsop D, Creatura G, Bluez G, Thurnauer H, Forselius-Bielen K, Ranganathan M, Deaso E, Bhat JA, d'Souza DC. Feasibility and success of cell-phone assisted remote observation of medication adherence (CAROMA) in clinical trials. Drug Alcohol Depend. 2016;163:24–30.
10. Galloway GP, Coyle JR, Guillen JE, Flower K, Mendelson JE. A simple, novel method for assessing medication adherence: capsule photographs taken with cellular telephones. J Addict Med. 2011;5(3):170–4.
11. Holstad M, Ofotokun I, Higgins M, Logwood S. The LIVE network: a music-based messaging program to promote ART adherence self-management. AIDS Behav. 2013;17(9):2954–62.
12. PASS. PASS 15 Power Analysis and Sample Size Software. Kaysville, Utah, USA: NCSS, LLC.; 2017.
13. SurveyGizmo. Boulder, CO: SurveyGizmo.
14. IBM Corporation. IBM SPSS Statistics for Windows, Version 24.0. 2016.
15. Nunally JC, Bernstein IH. Psychometric theory. 3rd ed. New York: McGraw-Hill; 1994.