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Patient-Level Moderators of the Efficacy of Peer Support and Pager Reminder Interventions to Promote Antiretroviral Adherence

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Abstract

Antiretroviral therapy (ART) greatly reduces morbidity and mortality for people with HIV/AIDS. However, for optimal effectiveness patients must achieve strict adherence to dosing regimens, which is difficult to maintain over the long term. Interventions to improve adherence have shown promising results, but with small effects. One explanation for small overall effects is that some patient subgroups are less able to benefit from current interventions; however, this explanation lacks empirical support. This study used multilevel modeling of data from a randomized controlled trial in an exploratory analysis to assess whether patient factors moderated the impact of peer support and pager reminders on ART adherence and biological markers of HIV. According to 272 interaction models using an alpha-corrected significance criteria, none of 34 patient characteristics significantly moderated either intervention. Findings suggest that intervention research might more profitably focus on other ways of improving effects, like individual patient needs, rather than target subgroups.

Keywords

Medication adherence; HIV/AIDS; HAART; Peers; Pager

Introduction

Antiretroviral therapy (ART) greatly reduces morbidity and mortality for people with HIV/AIDS [1, 2]. However, to benefit fully, patients must maintain strict adherence [3]. Actual adherence rates (i.e., percentage of doses taken) generally range from 60 to 70% [4], and often decrease over time [5]. Sub-optimal adherence can produce multidrug resistant strains of HIV, which makes the disease harder to treat in the individual, and results in longer-term public health implications if the virus is transmitted to others [6]. Indeed, as many as 50% of people treated with ART now have strains of HIV that are resistant to at least one of the available antiretroviral drugs [7].

Researchers have tested a number of behavioral health interventions to address low rates of adherence, but, according to a handful of recent meta-analyses, only a small proportion of

intervention studies meet acceptable levels of scientific rigor (e.g., comparison to a control group, multiple outcome measures, and power to detect effects) [8, 9], and generally have small effects on adherence [10–14]. Nonetheless, a wide variety of intervention techniques, including couples counseling [15], modified directly observed therapy [16], nurse-delivered counseling [17], cell phone messages [18], and counseling informed by electronic monitoring data [19], do appear to improve adherence, if only for a limited duration [10].

A growing literature also suggests that certain patient characteristics are related to antiretroviral non-adherence. In a 2002 meta-analysis of 20 studies, Ammassari and colleagues [20] identified several patient factors associated with non-adherence: patient-reported symptoms and medication side effects, perceived negative or stressful life events, lower social support, and lower self-efficacy [20]. In two recent and methodologically rigorous studies, hazardous drinking predicted 2-week adherence [21], and alcohol use was the most significant predictor of adherence among ART patients with a history of alcohol problems [22]. Furthermore, in a meta-analysis of 12 studies within the general adherence literature, DiMatteo [23] found that depressed patients were three times more likely to be non-adherent to treatment for a variety of medical conditions, and that every study reported a negative association between depression and adherence. Depression and alcohol use were also cited as adherence correlates by the World Health Organization in 2003 [24]. In a recent systematic review, Lovejoy and Suhr [25] found that executive functioning and problem solving, learning and memory, attention and working memory, and global cognitive functioning were correlated with lower antiretroviral adherence across 11 empirical studies. Finally, Mills and colleagues [3] identified a broad range of factors related to adherence. The patient characteristics reported by more than a third of the pooled samples in developed countries were: social isolation, transportation problems, uncertainty of long-term effects, treatment as a reminder of having HIV, and simple forgetting. Within developing countries, patient characteristics were somewhat different: financial constraints were reported by about half of pooled samples, and simple forgetting was reported by just over a third of pooled samples [3].

Given modest intervention research outcomes, evidence of many patient correlates of non-adherence, and the need to make interventions more efficient and cost-effective [26], there is a debate in the field as to whether certain patient subgroups should be targeted separately [11, 26,27]. In other words, it may be that current interventions work well for some patients, but not for others. If this were the case, there would be important implications for the implementation of evidence-based interventions. For example, interventions could be matched to patients according to the likelihood of benefit and some patients could be referred for alternative care that was designed for their particular needs. Future intervention research would need to focus on improving outcomes for more difficult-to-reach subgroups so that such alternatives were available. Some researchers have already begun designing interventions that are targeted to subgroups, including alcoholics [28], sex workers [29], IDU [30], and mothers [31].

However, there is insufficient evidence to show that patient characteristics, which appear to be correlated with non-adherence, actually moderate the efficacy of adherence interventions. Two separate meta-analyses of antiretroviral adherence interventions, together covering 43

studies and 3,838 participants, have failed to find evidence of moderation. For example, Simoni and colleagues [10], assessed several patient-level stratification variables, including gender, prior use of HAART, and MSM status, none of which were found to significantly moderate study effect sizes. Similarly, Amico and colleagues [11] failed to find evidence in their meta-analysis of 24 studies suggesting that any demographic or psychosocial factors besides known problems with adherence moderated study effect sizes.

Although not specific to medication adherence, one HIV treatment study suggested that case management had a stronger effect on number of primary care visits among Hispanics, those with unstable housing, and those without depressive symptoms. However, findings with regard to depressive symptoms were based on analysis using a dichotomized continuous variable, a practice which has been found to lead to spurious significant effects [32]; and the authors noted that the higher efficacy of the intervention with Hispanics could have resulted from the fact that the primary care clinic was located in the neighborhood where many Hispanic participants lived, possibly making it easier for them to keep their appointments. None of the other 12 variables tested produced significant moderator effects.

Within the general (non-HIV) treatment adherence literature, there is limited research on patient-level intervention moderators. In one meta-analysis of 71 adherence interventions with pediatric patients, there was a significant negative correlation between proportion of males in the sample and effect size of the intervention, however, this finding was no longer significant in follow-up data [33]. None of the other patient characteristics evaluated—mean age, minority race/ethnicity, length of treatment and time since diagnosis—were significant moderators of effect size. Similarly, in a meta-analysis of medication adherence interventions for older adults, studies with more women in their sample had larger intervention effects [34]. The other characteristics tested—mean age, income, cognitive status, literacy, and whether they had a chronic illness—did not correlate with effect sizes. The authors cautioned, however, that findings were not conclusive given they had moderate to large correlations between moderator variables and their analyses were exploratory [34]. In an additional study, depression did not significantly impact effectiveness of a pharmacy-based intervention to improve adherence to heart failure medication in geriatric patients [35].

We could locate no intervention study that directly examined moderators of an intervention to improve adherence to antiretroviral medication. Thus, despite substantial data supporting a host of adherence correlates, there remains little evidence to suggest that specific subgroups are more or less able to benefit from adherence interventions.

To address this, the current study examined patient level characteristics, including mental health, sociodemographic, and interpersonal factors, as moderators of two ART adherence intervention strategies (peer support and pager reminders) [27].

Methods

Procedures

The current exploratory study involved secondary analyses of data collected in a previously conducted randomized controlled trial (RCT) called Project PAL. As described in the prior publication [27], the 3-month intervention aimed to improve ART adherence through peer support and pager reminders. It was conducted between 2003 and 2006 at a hospital-based HIV/AIDS clinic in Seattle, WA. All procedures were approved by the Institutional Review Board of the University of Washington.

The pager and peer interventions in Project PAL were evaluated in a 2×2 factorial design with participants randomized to one of 4 conditions: peer only, pager only, peer and pager, and control. Participants receiving peer support were assigned to an HIV-positive peer trained to provide medication-related social support in the context of weekly phone calls and biweekly support meetings. Peers were treatment-experienced individuals who had been successful maintaining high ART adherence themselves. Patients who were in the pager messaging condition were provided with a two-way pager (i.e., a pager that can both receive and send messages) that had a customized message schedule based on the patient's daily medication regimen. All participants received standard of care services, which included prescription medication-related counseling from various providers, toxicity monitoring, ongoing adjustments to their ART regimen as needed, and monitoring of medication side effects. Study staff collected psychosocial data through computer-assisted self-interviews or telephone interviews at baseline and four post-baseline time-points: 2 weeks, 3, 6, and 9 months. Participants were compensated \$20–\$30 for completing each interview.

Participants

Eligibility requirements for Project PAL were: at least 18 years of age, proficient in English, starting a new regimen of ART (i.e., naïve to ART, off ART for at least 6 months and restarting, or switching to a new regimen), and not experiencing symptoms of dementia or psychosis.

Two hundred and twenty-six eligible patients were randomized and completed the baseline assessment. Two participants dropped out of the study at the 2-week assessment, leaving a final sample of 224 participants for analysis. The total completed assessments at each time point were: 210 (2-week), 205 (3-month), 195 (6-month), and 202 (9-month). Participants were mainly low-income, with about half reporting less than \$552 per month in income; 80.4% were unemployed. There were more men than women ($n = 169$ and 53 , respectively), and the mean age was 40.0 years ($SD = 8.16$). Complete demographic information can be found in Table 1.

Outcome Measures

Self-Reported (SR) Adherence—Participants were asked to report how often they did not take their medication over the past week on a 0–4 ordinal scale (none of the time, 1–2 times, 3–5 times, 6–10 times, or >10 times), as part of the Simplified Medication Adherence Questionnaire [36]. These scores were then reversed to provide a measure of adherence,

with 4 being perfect adherence (no missed doses) and 0 meaning poor adherence (more than 10 doses missed in past week).

Electronic Data Management (EDM) Adherence—Adherence to the recommended dosage schedule was tracked using the Medication Event Monitoring System (<http://www.aardexgroup.com>). All participants were given a plastic pill bottle and cap containing a microprocessor to record the date and time of each bottle opening. Participants were instructed to keep one of their antiretroviral medications—the one with the most frequent dosing schedule—in the pill bottle for the 9-month duration of the study. The past week's worth of data were then downloaded monthly. Adherence was operationalized as percentage of total possible EDM bottle openings taken on time (± 3 h), with monthly percentages averaged into 4 time points (i.e., 2-week, 3-, 6-, and 9-month).

HIV Biological Markers—HIV-1 RNA viral load in copies per milliliter (VL) and CD4 lymphocyte counts in cells per cubic millimeter were taken from patient medical records when available within 30 days of an assessment time-point. Otherwise, they were obtained from blood draws on the day of the assessment interview. Since VL was not normally distributed, we performed a log transformation and used the transformed data on all analyses. Both biological outcomes were analyzed as continuous variables.

Intervention Moderator Measures—Thirty demographic, mental health, and psychosocial self-report variables collected at baseline were assessed as potential intervention moderators. In addition, four variables only available at 3 months post-baseline were assessed. All measures, with respective item counts, citations for instrument source (when relevant), and reliability coefficients (when applicable) are listed in Table 1.

Intervention Results from the Original Study—Peer support was associated with a greater odds (OR 2.10, $SE = 0.69$, 95% CI 1.10–4.01, $P = 0.02$) of achieving 100% adherence at post-intervention, but this was not maintained at 3 or 6 months post-intervention, and peer support did not significantly effect biological markers. However, greater attendance at peer meetings predicted lower viral load at 9-month follow-up in post-hoc analyses (Est = -0.22 , $SE = 0.08$, 95% CI -0.38 to -0.06 , $P = 0.01$).

The pager intervention showed trend associations with adherence in a priori analyses, and was found in post hoc analyses to predict increased odds of being above biological cut-offs for improvement: VL of less than 1000 copies per milliliter (OR 1.78, $SE = 0.50$, 95% CI 1.03–3.09, $P = 0.04$) and CD4 count above 350 cells per cubic millimeter (OR 2.20, $SE = 0.78$, 95% CI 1.10–4.42, $P = 0.03$) [27]. Because the study had few exclusion criteria, the patients were diverse, providing an opportunity to evaluate whether the interventions were more or less effective for particular subgroups.

Data Analysis for the Current Study—We used growth curve modeling analyses with HLM 6.0 software [37] to model EDM adherence, SR adherence, VL, and CD4 count across four time points. Analysis of longitudinal adherence data is best conducted using multilevel modeling techniques since observations coming from the same individuals are correlated, which must be considered to accurately calculate standard errors. While the mean outcome

trajectories were not perfectly linear, given that we had only four time points, we chose a linear individual growth model, which provides a good approximation for more complex processes [38]. In this study the multilevel models included two levels: Level 1 predicted an individual's adherence at any given time point, and Level 2 modeled how adherence at a given time point might differ across individuals. At Level 1, predictors included the intercept, or the baseline level of adherence, and a linear slope effect that reflected the effects of time on adherence. Both the intercept and slope were estimated as random effects at Level 2, allowing them to vary across individuals. At Level 2, the intercept and slope were predicted by intervention condition and moderator variables and the interaction of the two.

We first tested unconditional growth models to determine whether there was significant variability, or individual differences, in the intercept or slope (or rate of change) in adherence over time. Next, we tested separate models for each of the 34 patient moderators by the two intervention conditions and by each of the four outcomes, a total of 272 models.

Because of the number of comparisons, we evaluated the findings using the Benjamini and Hochberg [5] alpha correction. The Benjamini–Hochberg procedure involves comparing *P* values in descending order to significance criteria that is sequentially calculated, which in this study was conducted separately for each outcome (rather than for all 272 tests together). The Benjamini–Hochberg correction was chosen because its use is appropriate with a very large number of tests aimed at identifying specific items for further research, as is the case in this exploratory study. It has also been shown to provide more power to detect effects than Bonferroni techniques [39]. We used procedures suggested by Thissen et al. [40] for facilitation of the Benjamini–Hochberg technique using Microsoft Excel software.

Missing data were handled in one of two ways. Values missing from specific moderator variables at baseline were replaced with a value of 0. Replacement of missing values is an expedient method, but has the potential to skew the data toward the value selected and decrease standard error. However, since there were no more than 2 data points missing from any one baseline moderator, this was not a problem in these analyses. One common alternative to value replacement is listwise deletions, which entails deleting all values in the dataset for a subject whenever that subject has one missing value. This method was not chosen because it would have reduced the overall sample size and, therefore, the power to detect effects. However, the majority of participants (19 out of 28 individuals) who had data points missing at 3-months post-baseline missed the assessment entirely, so missing data for the four 3-month moderator variables evaluated in these analyses were handled with listwise deletion. As for outcome variables, multilevel analysis of longitudinal data uses restricted maximum likelihood (REML) estimates that are unbiased even with uneven follow-up data [38], so individual outcome trajectories were estimated with as few as two observations.

Results

Unconditional Models

SR Adherence—The average self-reported adherence in the past week collected at 2 weeks after the baseline assessment was 3.6 out of 4.0, which corresponds with between 0

and 1–2 missed doses per week. The slope of adherence was significant and negative, indicating that on average, self-reported adherence declined by 0.14 units every 3 months ($SD = 0.29$). There was also significant variation in this rate of change, $\chi^2(208) = 480.91$, $P < 0.001$. We did not control for number of prescribed doses in moderation analyses as it was unrelated to rate of change, $t(217) = -0.57$, $P > 0.05$.

EDM Adherence—The average percentage of doses recorded as taken on time (± 3 h) by EDM at 2 weeks after the baseline assessment was 47.79% ($SD = 26.38$). On average, EDM adherence decreased by -7.77% every 3 months ($SD = 7.30$); and this rate varied significantly, $\chi^2(214) = 280.96$, $P = 0.001$.

HIV Biological Markers—Average log-transformed VL was 3.85 at baseline, changing on average by -0.53 ($SD = 0.41$) every 3 months. This rate showed significant variability, $\chi^2(209) = 488.46$, $P < 0.001$. The average CD4 count at baseline was 224.52 cells/ m^3 ($SD = 153.90$); average rate of change between time-points was 35.34 cells/ m^3 ($SD = 34.74$); and variation in this rate of change was also significant, $\chi^2(208) = 362.96$, $P < 0.001$.

Reliabilities provide an additional indicator of parameter variance, with those less than 0.05 indicating variance that is close to zero [38]. In our analyses, reliabilities for intercept and slope, respectively, were for SR adherence (0.03, 0.23); EDM adherence (0.56, 0.25); VL (0.19, 0.18); and CD4 count (0.81, 0.43). Given its low reliability and a non-significant chi-square test of its variance component, $\chi^2(207) = 190.86$, $P > 0.05$, the intercept parameter for SR adherence was estimated as a fixed effect. All other parameters were estimated as random effects.

Tests of Moderation—Using the Benjamini–Hochberg procedure for alpha correction with multiple tests, there was no evidence to suggest that any of the 34 patient characteristics tested moderated the effect of peer support or pager reminders on antiretroviral adherence or biological markers of HIV. See Table 2 for the range of values.

Discussion

Exploratory multilevel interaction models of antiretroviral adherence and HIV biomarkers failed to suggest any patient characteristics moderated the effect of peer support or pager reminders. In other words, there was no indication that specific patient subgroups benefitted more or less from the interventions.

As the field moves toward implementation of efficacious adherence interventions within clinical settings [41], there remains little evidence that certain subgroups of patients are less likely to benefit. Moreover, we were unable to locate any other studies that evaluated possible patient-level moderators of an intervention to improve either antiretroviral adherence or HIV biological markers. Despite the expense and time required for an intervention study with these outcomes, there are few studies evaluating patient moderators. Perhaps some studies do not have the amount of variation necessary in the moderator of interest. The field would benefit, then, from future studies that are designed to allow for systematic testing of differential effects based on selected patient characteristics. The lack of

published research in this area may also be attributable to null results like those found in the present study. Whatever the reason, further research in this area appears warranted.

Several limitations of the current analyses must be noted. First, adherence is notoriously challenging to measure. Although EDM adherence data are often considered the gold standard, the technique has drawbacks that include participant resistance and misuse or misunderstanding, which may result in overestimates of low adherence [42]. Some researchers have speculated that using EDM devices may alter adherence behavior, since participants are aware that it is being tracked, and some may already have a pill-taking routine that is disrupted by using a new device [27, 42]. Furthermore, self-reported adherence also is subject to limitations, including general overestimation of adherence, retrospective biases, and inaccuracy, and may be especially inaccurate among participants reporting perfect adherence [43, 44]. Thus, it is possible that our null findings on the adherence outcomes were the result of poor measurement rather than a lack of moderation. Finally, although the current diverse sample (i.e., few exclusion criteria) was useful for assessing a wide variety of individual factors related to intervention effects and strengthening external validity of the findings, it can also reduce power because of smaller cell sizes for group comparisons. Moreover, a hypothesis of “null effects” could be hampered by low power to detect effects; in other words, without sufficient power, analyses could fail to detect meaningful moderation effects. To assess power to detect the effects found in our models, we used Optimal Design v. 2.0 software (<http://www.wtgrantfdn.org>) [45]. Given the sample size for the current study ($N = 224$), and assuming power of 0.80 and alpha of 0.05, the models were powered to detect effects of 0.68 for VL, 0.64 for EDM adherence, 0.60 for SR adherence, and 0.56 for CD4 count, which are considered medium effects according to Cohen’s guidelines [46]. However, the majority of the effect sizes obtained were so trivial (<0.1) as to be virtually undetectable (i.e., requiring sample sizes over 10,000), and none of the effects, even those larger than our minimum level, were significant, suggesting that what moderation effects may exist are either quite small or are captured imprecisely. Nevertheless, replication of these and similar analyses with larger samples would strengthen the results.

Despite these limitations, this study is the first to evaluate moderators of an ART adherence intervention on medication adherence and biological outcomes. Given the need for effective adherence interventions, the costs of implementing interventions in the field, and the small effect sizes of interventions to date, there is an urgent need for information to guide future adherence intervention research and clinical implementation, including further assessment of these and other non-patient factors as potential moderators of intervention efficacy. Perhaps efforts to improve current ART adherence interventions should focus on creating flexibility that allows for adaptation to specific patients and their unique combination of adherence barriers, rather than attempting to adapt current interventions to specific patient subgroups. Such interventions are currently being evaluated in other areas of adherence research (e.g., counseling homework [47] and asthma medication [48]) and this approach holds promise for addressing antiretroviral adherence as well and thus contributing to improved outcomes for those living with HIV.

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Table 1

Initial status of moderator and outcome variables

Moderator variables	<i>n</i>	%	# Items	Cronbach's alpha
Female	53	23.7	1	n/a
Naïve to HAART	86	38.4	1	n/a
White race	105	46.9	1	n/a
Black race	67	29.9	1	n/a
Latino ethnicity	25	11.2	1	n/a
Graduated high school	176	78.6	1	n/a
Monthly income ^a < \$553	114	51.1	1	n/a
Employed part or full-time	43	19.2	1	n/a
Heterosexual orientation	76	33.9	1	n/a
Steady sexual partner	90	40.2	1	n/a
Moderator variables	M	SD	# Items	Cronbach's alpha
Age	40.01	8.16	1	n/a
Years since diagnosis	8.51	6.72	1	n/a
Years of education ^b	3.59	1.37	1	n/a
Social support ^c	61.54	27.78	20	0.47
Medication support ^{d*}	1.55	1.13	8	0.92
Self-control ^{e*}	2.82	0.48	24	0.89
Social network orientation ^f	46.33	8.11	20	0.77
Adherence Self-efficacy ^g	7.14	2.26	14	0.96
Social desirability ^h	5.41	2.08	10	0.57
HAART knowledge ⁱ	3.55	0.31	13	0.63
Depressive symptomatology ^j	25.24	11.55	20	0.92
State anxiety ^k	1.98	0.69	10	0.89
Trait anxiety ^k	2.12	0.67	10	0.89
Perceived stress ^l	1.80	0.61	14	0.86
Alcohol use ^m	5.65	7.58	10	0.88
Drug use ⁿ (<i>N</i> = 223)	5.40	6.71	28	0.89
Communication with provider ^{o*}	69.07	26.22	9	0.84
Engagement with provider ^{p*}	85.57	18.74	13	1.00
Physical health status ^{c,u}	42.33	11.85	20	0.80
Mental health status ^{c,u}	41.41	11.97	24	0.94
Spirituality ^q	26.68	12.94	15	0.97
Spirituality beliefs ^r	19.70	8.88	10	0.95
Spirituality support ^r	7.07	4.87	5	0.96

Moderator variables	<i>n</i>	%	# Items	Cronbach's alpha
Outcome variables	M	SD	# Items	Cronbach's alpha
Self-reported adherence	3.62	0.76	1	n/a
On-time EDM adherence	51.48	38.14	1	n/a
CD4 count ^s	208.23	166.00	1	n/a
HIV-1 RNA viral load ^t	4.36	1.23	1	n/a

Information about variable measures:

^a Monthly income ranges given on a likert scale from 1 (<\$552)–9 (>\$5001)

^b Years of education was assessed on a likert scale from 0 (No formal education) to 8 (Advanced degree [masters or doctorate])

^c Scale originated from the medical outcomes study (MOS)[49]

^d Scale to assess frequency of medication assistance received during the past 3 months (during the intervention phase)

^e Self-control scale [50]

^f Network orientation scale[51]

^g Scale included items from the adult AIDS clinical trials group studies [52]

^h Marlowe-crown social desirability scale [53]

ⁱ Scale included items taken from LifeWindows information motivation behavioral skills ART adherence questionnaire [54] and HIV/AIDS treatment-related knowledge [15]

^j Centers for epidemiological studies depression scale [55]

^k State-trait anxiety inventory [56]

^l Perceived stress scale [57]

^m Alcohol use disorders identification test [58]

ⁿ Drug abuse screening test [59]

^o Physician-patient communication scale [60]

^p Engagement with health care provider scale [61]

^q Systems of belief inventory (SBI)[62]

^r SBI subscales

^s Cells per cubic millimeter

^t log₁₀ copies per milliliter

^u The items used for alpha calculations were based on those identified in the MOS instruments user manual [63]

* Initial assessment of these variables were made at 3 months post-baseline

Note Values were calculated from varying sample sizes due to missingness (*N* = 194–224)

Table 2

Ranges of values for 272 three-way interaction models of hypothesized moderators by intervention condition and time-point for adherence and biological outcomes

Outcome	Intervention	Standardized coefficient	Coefficient	SE	<i>t</i>	<i>p</i> ^c
Self-reported adherence	Pager Reminder	−0.76–0.72	−0.19–0.20	0.002–0.16	−1.57–2.27	0.02–0.96
	Buddy Support	−0.71–1.01	−0.20–0.26	0.002–0.22	−1.59–2.20	0.03–0.95
On-time EDM Adherence	Pager Reminder	−0.93–0.95	−6.86–7.15	0.07–5.29	−2.02–2.20	0.03–0.99
	Buddy Support	−1.69–1.30	−11.60–9.46	0.07–7.70	−3.07–4.85	0.003–0.99
CD4 count ^a	Pager Reminder	−1.43–0.99	−49.84–34.73	0.26–20.50	−2.43–2.44	0.02–0.99
	Buddy Support	−0.92–1.25	−31.21–43.69	0.34–35.79	−2.12–1.39	0.04–0.99
HIV-1 RNA Viral load ^b	Pager Reminder	−0.68–1.17	−0.18–0.31	0.003–0.23	−2.07–1.58	0.04–0.99
	Buddy Support	−1.47–1.12	−0.39–0.29	0.003–0.38	−1.95–1.75	0.05–0.90

^a Cells per cubic millimeter

^b log₁₀ copies per milliliter

^c *P* values were compared against a corrected 0.05 alpha criteria to account for multiple models

Note All interaction models were non-significant