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ORIGINAL PAPER

Retention in HIV Care Among HIV-Seropositive Pregnant and Postpartum Women in Uganda: Results of a Randomized Controlled Trial

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Abstract

We tested an intervention that aimed to increase retention in antiretroviral therapy (ART) among HIV-positive pregnant and postpartum women, a population shown to be vulnerable to poor ART outcomes. 133 pregnant women initiating ART at 2 hospitals in Uganda used real time-enabled wireless pill monitors (WPM) for 1 month, and were then randomized to receive text message reminders (triggered by late dose-taking) and data-informed counseling through 3 months postpartum or standard care. We assessed "full retention" (proportion attending all monthly clinic visits and delivering at a study facility; "visit retention" (proportion of clinic visits attended); and "postpartum retention" (proportion retained at 3 months postpartum). Intention-to-treat and per protocol analyses found that retention was relatively low and similar between groups, with no significant differences. Retention declined significantly post-delivery. The intervention was unsuccessful in this population, which experiences suboptimal ART retention and is in urgent need of effective interventions.

Keywords Pregnant women · Retention in HIV care · Clinical trials · Uganda

A subset of study findings was presented to government officials and non-government personnel in Uganda (Mityana, Entebbe, and Kampala, February–March 2018); at the 12th International Conference on HIV Treatment and Prevention (Miami, Floria, June 2017), and at the 13th International Conference on HIV Treatment and Prevention (Miami, Florida, June 2018). However, all findings presented previously were preliminary. The full results presented here are based on both intention-to-treat and per protocol analyses and have not been presented previously.

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Introduction

Antiretroviral therapy (ART) has dramatically reduced mortality among HIV-infected individuals who adhere to therapy [1–3]. However, despite the importance of retention in HIV care for optimal ART outcomes [4–6], continuing care over time remains a considerable challenge [7, 8]. Sub-Saharan Africa bears the greatest burden of HIV in the world [4, 5, 7]; in 2017, 25.7 million people were living with HIV [9]. The majority (81%) of those

who initiate ART in this region are retained in care at 12 months and, on average, roughly 65% remain in care at 36 months [10, 11], though recent analyses suggest that transfers may account for 15–20% of this reduction [12].

Pregnant and postpartum women (PPPW) are particularly vulnerable to poor retention in care [4, 13–18]. Although ART effectiveness in decreasing mortality among HIV-infected women is well-established [14, 15, 19], persistent societal, community, interpersonal, and individual level barriers weaken this impact [13]. A recent systematic review and meta-analysis of studies in Africa found that pooled estimates of retention in care at one year post-initiation ranged from 66.4% to 83.1% among PPPW [20]. Ensuring that women initiated on ART while pregnant stay on therapy beyond pregnancy remains a challenge, as current studies highlight the tendency for women to fall off the treatment cascade post-delivery [10, 13, 16, 21, 22].

Many patient-oriented interventions have been implemented to improve ART retention [2, 3, 23, 24], including among pregnant women [25–27]. Global expansion in mobile phone use offers new healthcare delivery opportunities to promote patient engagement in care [28, 29]. Among adherence interventions, eHealth approaches appear promising [24, 30–32]. Interventions using phone-based reminders also have potential to improve retention among PPPW 1–3 months postpartum [23, 30, 33], as shown by a trial in Kenya [34]. However, a cohort study found no association between text messages and phone calls and postpartum retention [23]. This mixed evidence highlights the need for further research to test specific eHealth approaches, especially in vulnerable populations such as PPPW [24, 31].

Wireless pill monitors (WPM), which enable real time adherence monitoring, are eHealth devices with potential to support both ART adherence and retention. WPM have been found acceptable and feasible in low-resource settings [35–39]. They have delivered real-time reminders resulting in improved adherence in China [40, 41] and Uganda [42], but not in South Africa, although such reminders resulted in fewer treatment gaps in South Africa [43]. To add to the evidence on eHealth interventions generally, and to knowledge regarding approaches to engage HIV-positive PPPW in care to improve retention in ART, we assessed the effect of a WPM-based intervention in this population. The intervention was guided by the IMB (Information, Motivation, and Behavioral Skills) model [44]. Our hypothesis was that engaging PPPW actively via real-time adherence reminders and data-informed counseling would improve information, motivation, and, ultimately, medication-taking behaviors, with a positive effect on ART retention. To our knowledge, this study was the first to target PPPW with a real-time reminder intervention to improve HIV treatment outcomes. Here we report on the results from this randomized controlled trial (RCT), which we conducted among PPPW at two hospitals in Uganda.

Methods

Study Design: Overview

This study implemented a RCT to assess the effect of the use of WPM to deliver personalized text reminders triggered by late dose-taking coupled with data-informed counseling on retention in ART among PPPW in central Uganda. Pregnant women were enrolled at two hospital sites; after an initial 1 month of WPM monitoring to confirm device use [45], participants were randomized to intervention vs. control group. The intervention was continued through delivery until 3 months postpartum.

Setting

In Uganda, approximately 1.4 million people were living with HIV in 2016, with women disproportionately infected: 7.6% of adult women compared to 4.7% of adult men [46]. With an estimated 120,000 HIV-positive pregnant women in 2013, Uganda was among the first sub-Saharan African countries to adopt Option B+, whereby all pregnant women who test positive for HIV initiate ART [47]. The program reached all antenatal care (ANC) facilities by March 2014 and is Uganda's standard of care [47, 48].

The trial was conducted at two government-operated ANC hospitals where women access integrated ANC/ART services: the Entebbe Grade B Hospital in Entebbe and Mityana District Hospital in Mityana. Entebbe is a major urban center, located 37 km (23 miles) southwest of Kampala, in Wakiso District, and home to 70,000 residents. The Entebbe study site serves a primarily urban, relatively well-educated, and mobile population. Mityana District, located 77 km (44 miles) west of the capital, Kampala, had a population of 329,000 in 2014 [49]. The district hospital, located in Mityana's main urban center, serves a population of primarily rural residents who may commute an hour or more for services. Each site provides ART to 1500–2000 individuals. At the start of the study in mid-2015, each site provided ART to 300–400 PPPW, with 15–25 women starting therapy monthly. Each site employed 6–8 physicians and nurses, supported by nurse midwives and lay counselors who assist with ART management. Uganda's provision of Option B+ follows international guidelines, which specify a first line regimen of efavirenz, lamivudine, and tenofovir in a single daily pill [50]. Per standard of care, all PPPW patients refill medications monthly at the integrated ANC/ART clinics until 1-year postpartum, after which time they are transitioned to the adult ART clinic on site.

Study Participants and Pre-intervention Period

Women were eligible to participate if they were pregnant; 18 years of age or older; between 12–26 weeks of gestation; ART-naive; initiating ART and receiving ANC at either study site; and had a mobile phone that could receive text messages and phone calls at home (there is no cost to receive text messages in Uganda). Eligible participants provided written informed consent before enrollment.

At enrollment by a study coordinator, each participant was given a WPM for her HIV medication and instructed on its use. The study utilized the Wisepill WPM (Wisepill Technologies, Cape Town, South Africa) [51], which records the date and time at each opening, transmitting these data immediately to a central server. Participants' WPM were then monitored daily for a 1-month pre-intervention period to confirm usage while they continued all aspects of usual HIV care. If a participant experienced a 2-day period without WPM openings, a study coordinator contacted her to learn the reason for non-openings. If the participant had poor reception or indicated an intention to not use the device, she was withdrawn from the study. Participants who did not attend the pre-scheduled standard 1-month clinic visit within a 4-week grace period were also withdrawn.

Randomization

At the 1-month visit, participants continuing in the study (as confirmed by their ability to use the WPM as intended and to attend the next scheduled monthly hospital visit) were given their randomization assignment by a study coordinator. For this purpose, block randomization was conducted by a study researcher, who used an electronic randomization tool to assign participants 1:1 to intervention vs. control group within blocks of 10, and then conveyed assignments to study coordinators in Uganda via a secure transfer system.

Overview of the Intervention

After randomization, intervention participants selected a text message from 10 options in consultation with a study coordinator. The message options had been developed during an earlier phase of the study with input from HIV-positive mothers and healthcare providers who conduct counseling with PPPW. No option referred to HIV or potentially stigmatizing topics, and all were in the local Luganda language, for example: "Time for prayers" or "Hello, it's time." Throughout the intervention period, failure to open the WPM within 120 min of scheduled dose time triggered a text message to the participant's mobile phone with the chosen reminder. In addition, support for patient engagement and improved adherence and retention was provided through data-informed counseling at monthly clinic visits. At each such visit, the participant and a nurse or counselor were given a WPM-generated report of the participant's adherence in the previous month, including a summary of doses taken 'on time' (defined as within 2 h of dose time). During counseling, the counselor reviewed retention and adherence issues with the participant, including whether adherence was $\geq 95\%$ in the previous month, challenges experienced with attending scheduled ART visits and regular pill-taking, as well as successful strategies to overcome them. Each counselor-participant pair also discussed strategies to improve retention in care and adherence in the next month. At 3 months postpartum, participants stopped receiving the reminders and data-informed counseling.

Control Group Procedures

The control group received all elements of standard of care for HIV-positive PPPW in Uganda, including monthly visits for pill collection and meetings with counselors at integrated ANC/HIV clinic sites. They continued to use the WPM regularly throughout the intervention period. The only difference between their care and the intervention group was that although they were monitored by WPM, they did not receive text message reminders, WPM-generated adherence reports, or report-informed counseling.

Given the nature of the intervention, blinding was not possible. To maximize consistency and uniform support, all counselors at clinic sites received training on retention and adherence counseling via a three-day workshop led by study clinicians. The training emphasized the importance of attending every scheduled clinic visit, taking all medications on time, supportive counseling strategies, and practice with counseling guides.

Outcomes

From randomization through postpartum month 3, study staff documented whether each scheduled ANC/HIV clinic visit was completed within one month of the scheduled date. If a participant missed a scheduled visit by > 1 month, it was documented as 'missed' and a hypothetical next 'scheduled' date was determined one month ahead for study purposes. Study staff tried to contact participants (regardless of randomization assignment) who missed a scheduled visit to remind them of their appointment. For the postpartum month 3 visit, we recorded both whether the visit was made and whether the participant returned before the final study visit at postpartum month 6. Those who missed the postpartum month 3 visit but attended a subsequent visit between postpartum month 3 and 6 were designated "completed the intervention period" but "missed postpartum month 3 visit."

Our primary outcome was a composite outcome "full retention," defined as meeting three criteria: (1) attended all

scheduled visits over the intervention period, pre- and post-delivery (within one month of scheduled appointment); (2) collected ART medications at each visit; and (3) delivered at the study hospital. We also measured the components of the composite measure separately and by major time periods: attendance at all scheduled visits in the pre-delivery period, attendance at all scheduled visits in the post-delivery periods, and delivery at the study hospital. (We did not measure pill collection separately as such collection accompanied all study visits.) Additional outcomes included "visit retention," which reflected the degree to which visits were completed, measured by the proportion of all scheduled visits which were attended (for the full intervention period and again for pre- and post-delivery periods separately), and "postpartum retention," which measured retention at 3 months postpartum, defined by participants missing ≤ 1 monthly clinic visits among the 3 possible post-delivery monthly visits.

Sample Size and Statistical Power

The trial was powered to detect a 25 percentage-point difference in proportion achieving full retention. Based on a conservative estimate that 50% of participants would achieve full retention in the absence of an intervention, 80% power, and alpha = 0.05, we estimated that a sample size of 120 pregnant women (60 per study group) would provide an adequate number to detect a significant difference in full retention of at least 25 percentage-points. To allow for up to 25% loss to follow-up, we aimed to recruit a total of n = 160 subjects.

Statistical Analysis

We first employed an intention-to-treat (ITT) analysis approach. We checked for randomization balance between intervention and control groups on a comprehensive list of variables: age (years); gestation age; marital status; education; if pregnant for the first time; if not, the number of previous pregnancies; whether HIV status had been disclosed to husband/partner at enrollment; and adherence in the pre-intervention period, defined by: (# of WPM openings within 2 h of scheduled dose time)/(# of prescribed doses), similar to a measure most significantly associated with viral suppression in a previous analysis [52]. The variables were distributed equally between study groups, except for previous pregnancies. We then compared outcomes across intervention and control groups, using Pearson's χ^2 tests for categorical variables (e.g. full retention) and Student's *t-tests* for continuous variables (e.g. visit retention, postpartum retention). We reported the results unadjusted for previous pregnancies since previous pregnancies were relevant to selected but not all participants: 52 participants in the intervention group and 44 in the control had previous pregnancies (adjusted results are unchanged and available upon request). Additionally, per protocol (PP) analyses were conducted among participants who followed primary study procedures, defined as a) completing the intervention period (according to the definition above) and b) having < 10% missing adherence data. Meeting the latter criterion required keeping the battery charged, since a depleted WPM was not able to monitor adherence and trigger text message reminders as needed.

Results

Study Profile and Sample Characteristics

A total of 165 HIV-positive women initiating ART were enrolled between June 2015 and January 2016, and participants were roughly equally represented from each site (Fig. 1). 133 were eligible to participate in the intervention at 1 month (66 in Entebbe and 67 in Mityana) and were randomized to intervention (n = 69) or control group (n = 64). Descriptive analysis of characteristics of those randomized to those who were excluded (n = 32) revealed no significant differences, with the exception that a higher proportion among randomized participants had disclosed their HIV status to someone else at enrollment (42% vs. 18%) (though the difference was smaller in proportions that had disclosed to husband or partner (28% vs. 11%)). A total of 108 completed the trial (Fig. 1); n = 53 participants met the criteria for PP analysis inclusion, 24 intervention and 29 control participants.

Sociodemographic characteristics were similar across intervention and control groups (Table 1). The average age was 25 years, with mean gestational age of approximately 21 weeks. Most were married; just over 50% had completed secondary schooling. About 30% were in their first pregnancy; mean pregnancies among those with > 1 pregnancy was 2.6 overall, but varied significantly between the two groups (2.2 in intervention and 3.0 in controls; $P = 0.02$). Approximately 25% had disclosed their HIV status to their husband/partner at enrollment. Mean adherence in the one-month pre-intervention period was just over 75% in both groups.

Effect of Real-Time Feedback on Retention in Care: Intention-to-Treat Analysis

Composite Outcome: Full Retention

The proportion of participants fully retained was low: 33/67 (49.3%) and 34/64 (53.1%) ($P = 0.66$) in intervention vs. control groups, respectively (Table 2), with no evidence of intervention effect. Mityana Hospital participants displayed

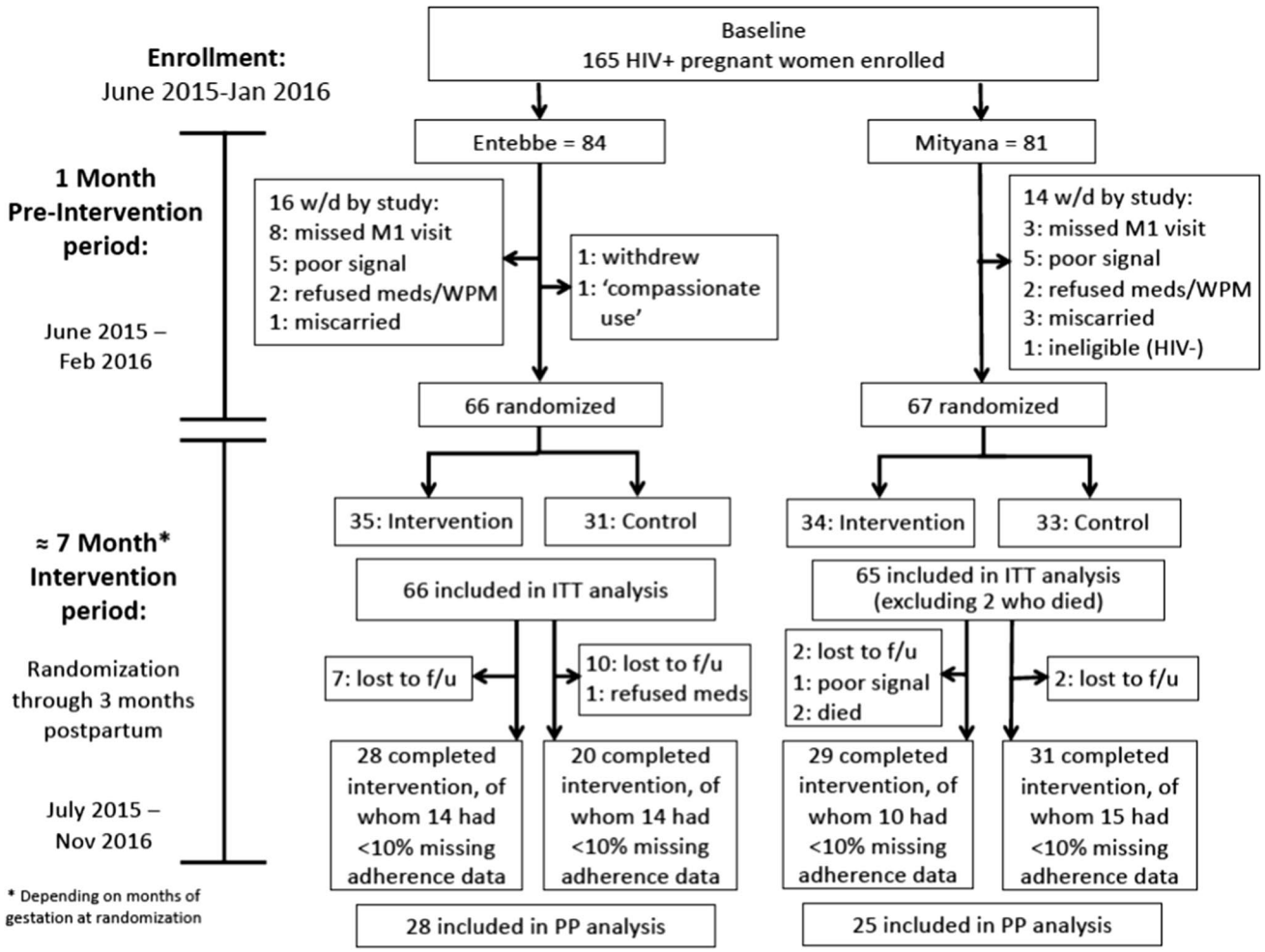

Fig. 1 Study flow diagram. *M1* month 1, *WPM* wireless pill monitor, *w/d* withdrawn, *f/u* follow-up, *ITT* intention to treat, *PP* per protocol

Table 1 Sociodemographic Characteristics

Characteristics	Intervention (n = 69)	Control (n = 64)	*P*
Age, years (mean, SD)	25.6 (6.8)	25.2 (4.6)	0.73
Gestation age, weeks (mean, SD)	20.4 (5.0)	21.9 (4.2)	0.06
Married (n, %)	49 (71.0)	49 (76.6)	0.47
Education level completed (n, %)			
Primary	31 (44.9)	25 (39.1)	0.50
Secondary	34 (49.3)	35 (54.7)	0.54
First pregnancy (n, %)	17 (24.6)	20 (31.3)	0.40
Mean pregnancies, among women with > 1 pregnancy (mean, SD)[a]	2.2 (1.4)	3.0 (2.1)	0.02
Others know of HIV status at enrollment (n, %)	30 (43.5)	26 (40.6)	0.74
Had disclosed HIV status to partner at enrollment (n, %)	22 (31.9)	15 (23.4)	0.28
Adherence,[b] pre-intervention (mean, SD)	78.6 (23.9)	75.9 (24.5)	0.52

[a]52 PPPW in the intervention group and 44 in the control group responded to this question

[b]Measured by: (# of WPM openings within 2 h of scheduled dose time)/(# of prescribed doses)

Table 2 Retention on ART: outcomes

Retention measures	Intention to treat			Per protocol		
	Intervention group (n = 67)	Control group (n = 64)	*P*	Intervention group (n = 24)	Control group (n = 29)	*P*
Composite outcome (full retention): % that attended all scheduled visits and delivered at study hospital, n (%)[a]	33 (49.3)	34 (53.1)	0.66	16 (66.7)	20 (69.0)	0.86
Retention over pre-delivery period[b]	54 (80.6)	55 (85.9)	0.31	23 (95.8)	28 (96.6)	0.89
Retention over post-delivery period[b]	40 (59.7)	43 (67.2)	0.38	18 (75.0)	24 (82.8)	0.50
Delivery at study hospital	60 (89.6)	52 (81.3)	0.18	21 (87.5)	24 (82.8)	0.64
Visit retention % of all scheduled visits completed, mean (St Dev)	82.7 (24.3)	86.7 (22.3)	0.33	94.7 (10.1)	95.5 (10.0)	0.78
Visit retention in pre-delivery period only	91.2 (20.3)	95.4 (12.6)	0.17	98.3 (8.2)	99.3 (3.7)	0.57
Visit retention in post-delivery period only	74.6 (37.2)	77.6 (37.1)	0.65	91.7 (14.7)	93.1 (16.4)	0.74
Postpartum retention % retained in care at Month 3 postpartum, n (%)[c]	54 (80.6)	52 (81.3)	0.93	24 (100.0)	28 (96.6)	0.36

[a]All attended visits were accompanied by ART pill collection; pill collection is not shown separately

[b]Defined by attendance at 100% of scheduled visits during the pre-delivery period and post-delivery periods, respectively, excluding delivery at study hospital

[c]Defined by missing ≤ 1 monthly clinic visits of the 3 total possible post-delivery monthly visits

slightly higher retention (53.1% vs. 60.6%, among intervention and control groups, respectively; $P = 0.55$) than those at Entebbe Hospital (45.7% vs. 45.2%; $P = 0.96$) (site-specific data shown in supplemental materials). The separate component of 100% attendance at clinic visits in the pre-delivery period was 80.6% vs. 85.9% for intervention vs. control groups ($P = 0.31$), higher than in the post-delivery period (59.7% vs. 67.2%; $P = 0.77$). The decline post-delivery was significant in intervention participants ($P = 0.03$, see Fig. 2a), but not in controls. Among intervention and control groups, 89.6% and 81.3% ($P = 0.18$), respectively, of women delivered at the study hospital. Although not significant, retention and delivery at the study hospital were generally 10% higher among participants in Mityana relative to Entebbe (site-specific data provided in supplemental materials).

Visit Retention

Visit retention (% visits attended) was also similar between intervention and control groups (82.7% vs. 86.7%; $P = 0.33$) (Table 2), with no evidence of an intervention effect. As shown in Table 2, visit retention in the pre-delivery period alone was 91.2% vs. 95.4% ($P = 0.17$) in intervention group vs. controls, respectively, and 74.6% vs. 77.6% ($P = 0.65$) in the post-delivery period. The decline in visit retention between the pre-delivery and postpartum periods was significant in each group (see Fig. 2b). Consistently, participants at Mityana Hospital had slightly higher visit retention (approximately 8%) than in Entebbe (see supplemental materials).

Postpartum Retention at Month 3

Among all participants, 80.6% of those in the intervention group compared to 81.3% in the control group were retained at postpartum month 3 ($P = 0.93$) (Table 2). Among both intervention and control groups, participants in Mityana again had somewhat higher retention (see supplemental materials).

Effect of Real-Time Feedback on Retention: Per Protocol Analysis

Fifty-three participants met inclusion criteria for the PP analysis, 24 and 29 participants in intervention and control groups, respectively (Table 2). Overall, full retention was approximately 15 percentage points higher in each group in this sub-sample compared to the ITT analysis (66.7% vs. 69.0% in intervention vs. controls, $P = 0.86$). Full attendance at study visits in the pre-delivery and post-delivery periods separately was 10–15 percentage points higher than in the ITT analysis: 95.8% vs. 96.6% in the pre-delivery period for intervention and control groups ($P = 0.89$) and 75.0% vs. 82.8% ($P = 0.50$) in the post-delivery period. The decline in the intervention group was significant (P = 0.04) (data not shown). A slightly higher proportion of participants in the intervention group delivered at the study hospital compared

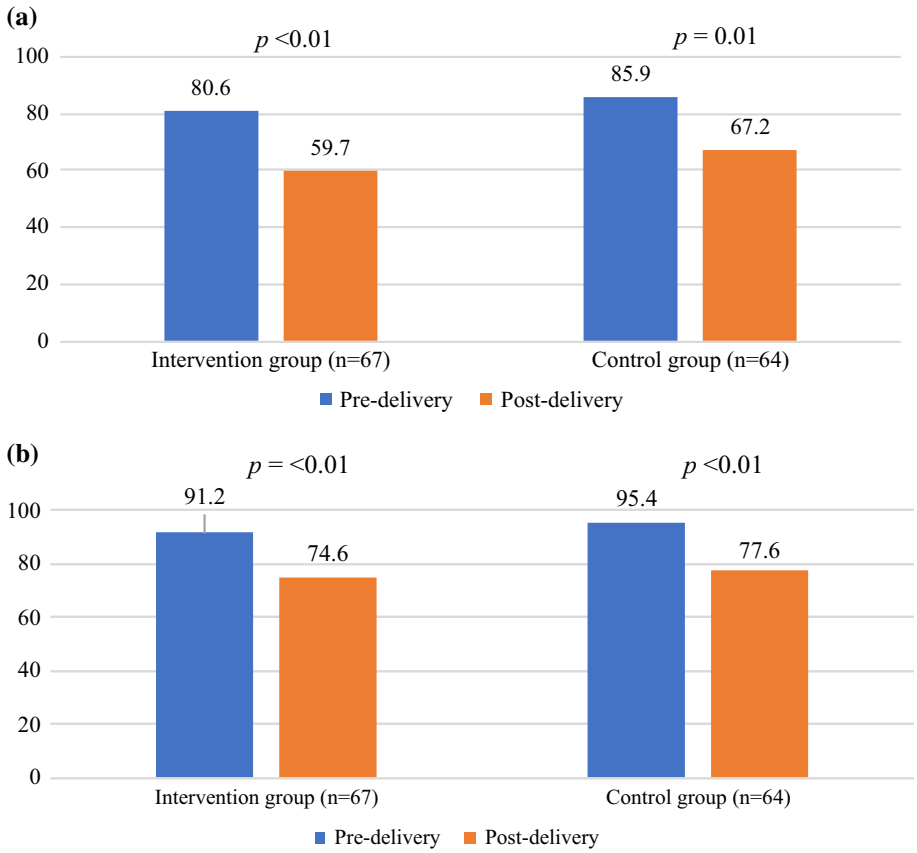

Fig. 2 Retention in care by pre- and post-delivery period and study group. **a** Full retention: proportion that attended all scheduled monthly clinic visits in the relevant study period (including collecting ART medications at each visit). **b** Visit retention: mean proportion of scheduled clinic visits in the relevant study period that were completed

to those in the control group (87.5% vs. 82.8%; $P=0.64$). Mityana participants again displayed slightly higher rates than those in Entebbe (see supplemental materials).

Visit retention was similarly higher compared to the full sample: 94.7% vs. 95.5% ($P=0.78$) in intervention and control groups, respectively, over the entire intervention period. This pattern continued over the separate pre- and post-delivery periods, with retention 10–15 percentage points higher than in the ITT analysis and not significantly different between groups. Retention again declined between the pre-delivery and post-delivery periods, though less substantially than in the full sample: from 98.3% to 91.7% in the intervention group and from 99.3% to 93.1% among controls. Retention was similar across the 2 study sites. Postpartum retention (at 3 months post-delivery) was 100% vs. 96.6% ($P=0.3$) in intervention vs. control groups.

Discussion

In this intervention trial, we assessed the use of real-time text message reminders and data-informed counseling on retention in care among PPPW in Uganda. Given our team's positive findings on ART adherence from a similar mHealth intervention in a HIV-positive population in China [41], we hypothesized that this approach might prove effective for other populations and that it might prove beneficial for retention in care, which is known to be a particular challenge for PPPW. The WiseMama study had several major strengths: the study population is known to be vulnerable, to experience poor ART outcomes, and to be understudied; we tested a novel intervention; and our use of multiple retention measures added rigor and depth. While the intervention's follow-up period was not lengthy, it was typical for behavioral interventions. Our findings show no significant effect on retention behaviors from real-time text reminders in our study population. However, two noteworthy patterns emerged. First, our measures of retention reinforce a common story: retention in HIV care is poor among PPPW in southern Africa and improving it is challenging [18, 20, 23]. Second, the decline in participants' retention between pre-delivery to post-delivery was sharp and consistent across measures [16]. These findings highlight the challenge of attaining the WHO's 90–90–90 goals and maximizing the benefits of Option B + [20, 53].

There are several potential reasons for our finding of no intervention effect. Examination of measured characteristics between intervention and control groups reveals few clues as they are well balanced: randomization was successful. Another potential issue is systematic underestimated

retention among PPPW in both groups. Recent research on loss to follow-up has found that retention indicators may be biased downward due to poor counting of patients who transfer to other locations for continued therapy [12]. Similarly, our retention estimates may have been affected because our study sites did not track patients lost to follow-up. We know from our efforts to contact participants who failed to attend clinic visits that some women attended nearby clinics for HIV care after returning to home villages to deliver or after delivery, though these reports are anecdotal. Study collaborators at the study sites also believe that the Entebbe-based study population may have been particularly mobile given that many were married to or the partners of military personnel, though we are unable to confirm this.

Several additional factors in our finding of a null effect warrant scrutiny. First, it is possible that use of the WPM alone changed subjects' behaviors, regardless of randomization group. This is likely, at least in the short run. Our participants were very enthusiastic about using the devices, and they may have been more motivated to take their pills and come back to the clinic as a result, though there is no reason to believe that such enthusiasm varied between the two groups. One advantage of the initial monitoring period is that it may have helped normalize such use. In previous successful intervention studies, we used slightly longer pre-intervention periods; longer lead-in periods may be useful in reducing the effect of intervention delivery modes alone. The actual intervention (text reminders and data-informed counseling) was not provided to controls, so they could not have benefited from provision of the intervention itself. Second, because the supported counseling provided to the intervention group was delivered by the same nurses who counseled all patients, it is possible that enhanced counseling techniques also benefited the control group. We conducted extensive training with all nurses and counseling staff at both clinics prior to beginning the intervention, and remained strongly supportive of counseling for all patients throughout the study. If such a cross-over effect took place, we would argue that this is not be a bad thing (though not ideal for observing an intervention effect). Third, as noted in the Methods section, study staff attempted to contact participants (regardless of randomization assignment) whenever they missed a scheduled visit. This may have diminished the intervention's effect by providing quasi-reminders to the control group. However, these actions are warranted by the need to support study procedures and ensure study validity.

Our study participants also experienced substantial challenges keeping their WPM batteries charged [45], which would prevent a device from triggering a reminder message. However, we did not find the intervention to be effective among PPPW who complied with intervention procedures. This finding contrasts with our analysis of adherence outcomes, in which it appears the intervention was effective among participants included in PP analyses (these results will be published separately) [54]. We hypothesize that adherence and retention behaviors are fundamentally different, with the possibility for different barriers to achieving positive outcomes. Adherence can be maintained at home, possibly with the aid of WPM-generated reminders, while traveling to a distant clinic presents a host of challenges, as discussed below. It is conceivable that, for women who could manage the WPM technology, the WPM-reminders and data-supported counseling provided sufficient motivation to maintain higher adherence, but could not overcome barriers to regular clinic attendance. Qualitative data collected during the course of the study (reported elsewhere) suggest substantial challenges to on-time clinic visits, particularly (a) structural barriers such as the cost and logistical challenge of traveling to the clinic and food shortages [55, 56] and (b) interpersonal barriers, including partner non-disclosure of HIV status [56, 57]. As noted at the beginning of the Results section, disclosure was low (42% of those randomized had disclosed to anyone at study enrollment, and only 28% had disclosed to their husband or partner). These barriers may have essentially outweighed the genuine enthusiasm expressed by the participants for using the adherence monitors. We would argue that these findings underscore a need for interventions that extend beyond individual-level behavior change to address critical interpersonal, structural, and societal level factors.

Despite widespread mobile phone use in sub-Saharan Africa, and excitement about the potential for mobile phone-based technologies to improve ART outcomes, the evidence on eHealth interventions as retention and adherence promotion tools remains mixed [3, 58–60]. In contrast to indications that ART outcomes in low-resource settings may be influenced positively by use of WPM-based interventions [41, 61, 62], our results among PPPW using real-time adherence monitoring found no improvement in ART retention. Given the potential of this technology to provide rapid feedback on critically important behaviors, further research to identify the best way to apply it to help achieve the WHO's 90–90–90 goals is an urgent priority. As such research progresses, we add to fellow researchers' recommendations that use of eHealth interventions, including those based on WPM technology, consider critical context-specific interpersonal and structural barriers [24, 63, 64]. Similar to a recent study in Malawi, our participants expressed the need for their husbands to be tested, which would facilitate disclosure of HIV status and safe access to treatment [65]. In light of evidence of positive impacts from male partner engagement on uptake of ANC services, PMTCT, HIV-free infant survival, as well as increased HIV testing and adherence among women [66–70], we believe that focusing efforts on male partner engagement testing and treatment in Uganda would support efforts to improve retention in care among

PPPW. Additionally, the possible over estimates of poor retention further highlights the need for improved patient tracking systems, as noted by other studies [12].

We acknowledge several study limitations. First, we were unable to blind participants and clinicians, who provided data-informed counseling to intervention participants. While counseling for control participants was possibly biased, we think this is unlikely due to the comprehensive counseling training provided to all clinicians as well as the null finding on intervention effect. Second, the intervention was implemented for only three months postpartum; a timeframe of one year or more after the critical delivery event might show a less sharp decline postpartum compared to pre-delivery as women regain a more regular schedule and return from their home villages in the months post-delivery. Third, our design and content of the triggered text messages did not include calls to action, a strategy now urged by the World Health Organization [71]. It is possible that more explicit calls to action in the messages might have encouraged participants to try harder to attend scheduled clinic visits. In message design during the study's formative phase, we solicited and used input from members of our study population to engage them in the intervention. In future communications-based research and programming of this type, we would urge incorporating the use of such 'calls' to maximize effectiveness. Fourth, our study sample was not large, and our statistical power was limited to observe relatively small but still meaningful differences. Fifth, it is not possible to tease out differences in impact between the text messages and counseling, as both activities were intervention features. Finally, the intervention was implemented in 2 sites only; expanding it in other regions of Uganda, or other low-resource settings where ART for pregnant and postpartum women may be better supported, might yield different results.

Conclusions

This study contributes useful findings regarding HIV treatment behaviors of pregnant and postpartum women in a low-resource setting in sub-Saharan Africa. We did not find improvement in ART retention resulting from an intervention that coupled real-time text message reminders when dose-taking was late with data-informed counseling. We also observed very low retention in HIV care in our study population, and a significant decline in retention after delivery, regardless of receipt of the intervention. These findings highlight the urgent need for effective interventions that can promote higher retention in critical ART care for this vulnerable population.

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Author Contributions LLS shared overall responsibility for overall study conception, design, and implementation and obtaining funding (with LJM), provided training and support during data collection, and helped manage and analyze data, interpret findings, and draft the manuscript. NH assisted with study design and implementation, led the data management and analysis, and helped interpret findings and draft the manuscript. DHH assisted with study conception, design, implementation, and obtaining funding, provided training to study site clinicians, and helped interpret findings and draft the manuscript. EMS assisted with data analysis, and helped interpret findings and draft the manuscript. SJ assisted with study design, helped interpret findings, and played a major role in drafting the manuscript. ALW assisted with study conception, design, implementation, and data analysis, and helped interpret findings and draft the manuscript. HC assisted with study design, played a key role in study implementation and data collection, and helped interpret findings and draft the manuscript. ALG assisted with study design and implementation, and helped interpret findings and draft the manuscript. RB assisted with study design and implementation, and helped interpret findings and draft the manuscript. PA assisted with study design, played a key role in study implementation and data collection, and helped interpret findings and draft the manuscript. MBD assisted with study conception, design, and implementation, provided training and support during data collection, and helped with data management, interpretation of findings and drafting of the manuscript. JG assisted with data collection, and helped interpret findings and draft the manuscript. BM assisted with study design, played a key role in study implementation and data collection, and helped interpret findings and draft the manuscript. LJM shared overall responsibility for overall study conception, design, and implementation and obtaining funding (with LLS), provided training and support during data collection, and helped interpret findings and draft the manuscript.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and review board at Boston University Medical Center, the research ethics committee of the School of Medicine (SOMREC) at Makerere University's College of Health Sciences in Kampala, Uganda, the Uganda National Council of Science and Technology (UNCST), and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all participants in this study.

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