Effectiveness of short message service (SMS) reminders on timely pick-up of antiretroviral therapy (ART) among consenting HIV-positive adults in Zambézia province, Mozambique

Final Report

***Date of release of report*:** Abstract submitted December 21, 2018; final report submitted February 2020

***Evaluators/authors and affiliation*:** Erin Graves[1], Caroline De Schacht[2], Wu Gong[3], Sara Van Rompaey[2], Maria Fernanda Sardella Alvim[2], Gaël Claquin[2*], Bryan E. Shepherd[3], Ann F. Green[1], Jose A. Tique[2], Eurico José[2], Hélio Machabane[2], Eusébio Maposse[2], Magdalena Bravo[2], Anibal Naftal Fernando[4], and C. William Wester[1,5]

[1]Vanderbilt University Medical Center, Institute for Global Health (VIGH), Nashville, TN, USA;
[2]Friends in Global Health (FGH), Maputo, Mozambique;
[3]Vanderbilt University Medical Center (VUMC), Department of Biostatistics, Nashville, TN, USA;
[4]Provincial Health Directorate of Zambézia (DPS-Z), Quelimane, Mozambique;
[5]Vanderbilt University Medical Center (VUMC), Department of Medicine, Division of Infectious Diseases, Nashville, TN, USA.

**at the time of evaluation*

Executive Summary

Informed by mHealth interventional studies showing improved combination antiretroviral treatment (ART) appointment attendance with cellphone messaging as well as newly developed systems in Mozambique, Friends in Global Health (FGH) piloted an intervention to provide short message service (SMS) reminders to consenting eligible adult patients enrolled in ART services with the goal of improving patients' adherence. Beginning in July 2016, an SMS reminders intervention was implemented in eight health facilities supported by FGH in Zambézia Province. We evaluated the effectiveness of this SMS reminder intervention by comparing ART pick-up rates among patients sent SMS reminders versus those patients not receiving SMS reminders at these locations.

All HIV-positive adults (≥15 years of age) enrolled in ART services reporting cellphone access were offered SMS reminders. Consenting patients were sent messages 15, 7, and 2 days prior to their scheduled ART pick-up appointment dates. Using routinely-collected program data (July 2016 - May 2018), mixed effect logistic regression was performed to determine the adjusted odds ratios (aOR) of ART pick-up within 2, 6, and 59 days of scheduled appointments (i.e. on-time, prior to defaulting, and prior to loss-to-follow-up, respectively), adjusting for sex, age, adherence support group status (i.e. receiving ART via Community Adherence Support Group [CASG] vs. not), partner HIV status, pregnancy, education, occupation, duration of ART, health facility (HF), weekday of appointment, and week of ART pick-up.

We compiled data regarding 18,941 scheduled ART pick-ups for 3,222 patients reporting cellphone access. Among these patients, 47% of males and 46% of females consented to receive SMS reminder services. Overall, females were more likely (~ 1.5 to 2-fold more likely) to pick up ART at all time points (i.e. within 2, 6, and 59 days of scheduled appointments) when compared to males (adjusted Odds Ratios [aOR] = [1.49; 95% CI: 1.34-1.66, p<0.001], [1.74; 1.50-2.00, p<0.001], and [1.93; 1.55-2.40, p<0.001], respectively), however, no additional supportive effect was seen with SMS reminders sent to female adults at any specific time (i.e. appointment reminder) interval. SMS reminders did provide a short term positive effect on timely ART pick-up among consenting males, although this effect attenuated over time, as males sent SMS reminders were 22% more likely to pick up ART within 2 days of scheduled appointments compared to males not receiving SMS reminders (aOR = 1.22 [95% CI: 1.09-1.37], p <0.001), but no significant effect was seen for males at later pick-up timepoint reminders, that is, for pick-ups within 6 (aOR=1.09, 95% CI: 0.95-1.25, p=0.2) and/or 59 (aOR=0.90; 95% CI: 0.74-1.10) days of scheduled appointments. Older adults, especially those greater than 50 years of age, were more likely to pick up their ART (with adjusted odds ratios ranging from 1.5 to 2.6 for the three SMS reminder evaluation timepoints) compared to the reference population of 15-24-year-old adults.

In Zambézia Province, SMS reminders provided a significant short-term positive effect on timely ART pick-up among consenting males, although this effect attenuated over time. Additional context-specific strategies need to be implemented to secure timely ART pick-up and improve retention in care.

Project Background

As the ownership and use of mobile phones becomes more ubiquitous, healthcare professionals will begin to incorporate mobile phone technologies, such as short message service (SMS) reminders, for the provision of various services.[1] SMS-based interventions for promoting engagement in health care services are largely acceptable among patient populations.[2-4] Among the various interventions aimed at improving adherence to prescribed combination antiretroviral treatment (ART), SMS reminder messages have been shown to be effective in increasing adherence in multiple studies.[4-8] Brief SMS messages sent on a scheduled basis as reminders for appointments have been shown to improve participation in health consultations compared to patients not being sent reminders.[6, 9-12] A 2017 study from Botswana investigating the effect of SMS reminders on timeliness for ART pick-up from urban pharmacies found a greater proportion (85%) of patients receiving SMS reminders had good pick-up timeliness compared to those not receiving reminders (70%), though results were not statistically significant.[13]

A randomized clinical trial (RCT) conducted in Maputo Province, Mozambique (2016) found that the provision of consistent SMS reminders reduced attrition among adult patients receiving HIV care in urban areas, with the greatest impact on clinic attendance rates being seen among adults who had initiated ART within the prior three months.[14]

Informed by mHealth interventional studies showing improved ART appointment attendance with cellphone messaging as well as newly developed systems in Mozambique,[15] FGH piloted an intervention to provide SMS reminders to consenting eligible adult patients enrolled in ART services with the goal of improving patients' ART medication pick-up adherence rates. Beginning in July 2016, an SMS reminders services intervention was rolled out to eight select health facilities (HF) supported by FGH in Zambézia Province by June 2018. These eight HF included three district capital HF sites of Namacurra, Mocubela and Maganja da Costa districts, and five peri-urban HF in the provincial capital of Quelimane City district: 17 de Setembro, 24 de Julho, 4 de Dezembro, Chabeco, and Coalane.

At these supported sites, the SMS reminders service was offered to all HIV-positive adults (≥ 15 years of age) enrolled in ART services at one of the HF piloting the SMS intervention if they reported access to a cellphone and provided informed consent to being contacted via mobile phone SMS messaging. Patients were excluded from the SMS services if they were HIV-negative, were less than 15 years of age, did not receive HIV care or treatment at one of the HFs included in this evaluation, reported not having access to a mobile phone to receive SMS messages, and/or if they did not consent to be contacted by telephone, or specifically not by SMS.

For standardized SMS service enrollment procedures, a written script was introduced to ensure that Health Counselors correctly covered issues and information related to the "Informed Consent" section on the *Psychosocial and Positive Prevention Assessment* form, detailing that contact could occur via home visits, phone calls and SMS reminders. The script highlighted that the SMS messages would be sent to remind patients about their scheduled ART refill or clinical

appointment, and to specify the timing and frequency of SMS reminders. Health Counselors (HC) were instructed to ensure that patients/caregivers had been fully informed regarding procedures related to staff and volunteers' provision of home visits, phone calls, and SMS reminders. Key messages from the informed consent process included a description of the purpose of the intervention, and an explanation of voluntary participation in the service. After obtaining informed consent from eligible adults, HC were instructed to immediately test the feasibility of the cell phone number provided by conducting a test call using the HF phone. If the call to that number was successful, the HC filled in the indicated phone number on the *Psychosocial and Positive Prevention Assessment* form. Finally, signature (or thumbprint and witness signature) and date was provided by the patient and the Health Counselor signed as the health care provider obtaining consent for the service.

Consenting patients were sent messages 15, 7, and 2 days prior to scheduled ART pick-up appointments. Messages sent to indicated cellphone numbers read "[*First, Last Name*] has an appointment at the [*indicated health facility*] on [*Day, Month, Year*]," with no further identifying information or reference to purpose of appointment, in order to protect patients' privacy and confidentiality. The content for the simple, uniform messages was reviewed and approved by technical team members with expertise in the local context.[16]

Evaluation Purpose and Questions

Our overall objective was to evaluate the effectiveness of SMS reminders on medication pick-up adherence rates among HIV-positive, ART-treated adults consenting to receive these reminders while engaged in clinical care at eight health facilities (HF) in Zambézia Province. We conducted an analysis to assess for any effects of the SMS reminders intervention on routine adherence-related outcomes by comparing ART pick-up rates among all patients who were eligible to receive SMS reminders (i.e., specifically comparing rates of those who were sent SMS reminders for their appointments and those who were not sent SMS reminders) at HF included in the scaled roll-out.

Evaluation Design, Methods, and Limitations

Type of evaluation

To evaluate the impact of the SMS intervention, we conducted a secondary data analysis on aggregated individual- and health facility-level data collected by district and provincial teams for routine programmatic monitoring and reporting purposes. We performed descriptive summaries of the data, univariate analysis, as well as adjusted mixed effect logistic regression analysis.

Summary of stakeholder engagement

FGH technical teams have ongoing collaborations with key stakeholders working in the health facilities and communities in which we are supporting and engaged. The implementation of SMS reminders for medication pick-up was piloted with awareness and support by our partners at the Zambézia Provincial Health Directorate (DPS-Z) as well as district-level partners in health and administrative agencies. The concept proposal and plan for secondary data analysis evaluation was approved by our sponsoring institution, namely CDC-MZ.

Sampling strategy

Data of adult (≥15 years of age) patients enrolled in ART services between July 2016 to May 2018 in the select eight HF where the SMS intervention took place were collected and included in the analysis. Since SMS services could only be delivered to persons with reported access to a cellphone, to account for the selection bias due to cellphone ownership, we restricted the analysis to data from patients reporting access to a cellphone. Variables of interest included but were not limited to all scheduled and completed visit dates to HF for ART pick-ups and consultations, as well as de-identified demographic data.

Methods for data collection and analytics, with rationale

All data included in the analysis for this evaluation were secondary data, collected by district- and provincial-level teams for routine programmatic monitoring and reporting purposes. Aggregated data were extracted from the OpenMRS electronic medical record database from those HF offering SMS services for the indicated evaluation period.

To compare the baseline characteristics of persons sent SMS reminders to those not sent SMS reminders, we selected as the population under analysis all patients from the eight involved health facilities having a scheduled ART pick-up during the period when SMS reminders were implemented.

The number of SMS messages sent were summarized per alert date, the date of the scheduled ART pick-up date being notified by the message. To be able to examine the odds for timeliness of ART pick-up (per the definitions used by the Mozambican Ministry of Health)[17], we analyzed all available scheduled and actual ART pick-up dates for patients included in the analysis to identify their likelihood of picking up their ART on-time, prior to defaulting status, and prior to loss-to-follow-up status (i.e., within 2, 6, and 59 days of their scheduled appointments, respectively).

To account for potentially different behavior between men and women and access to cellphones (i.e., potential differences in cellphone ownership), we included an interaction term between SMS service and sex into a likelihood ratio test, and did find a statistically significant interaction term between SMS service and sex on the outcome of ART pick-up within two days of scheduled appointment. Therefore, to be able to better interpret the results and detect if the effect from SMS

reminder service differed by sex, we re-parameterized the three variables (sex, SMS services, interaction term) into three new variables: sex, SMS effect on males, and SMS effect on females.

Data analysis plan

Adjusted odds ratios were derived from a mixed effect logistic regression of the ART pick-up data, restricted only to patients reporting access to a cellphone (not excluding patients who transferred out or were considered lost-to-follow-up [LTFU]). Adjustments were made for two types of random effects: i) one being the hierarchical structure of health facility nested by patients with multiple ART pick-ups; and secondly, ii) to account for the confounding effect from different times, the random effect of time was introduced into the model. The week in which the ART pick-up was scheduled was considered as a random effect to account for time variation including seasonal effects.

The unadjusted odds ratios were derived as the odds ratio by univariate analysis without adjustment for other variables and without consideration of hierarchical clustering of patients and repeated ART pick-ups by individual patients.

The statistical analysis was conducted using R statistical software [R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/]. The mixed effect logistic model was run using R package "lme4" (Douglas Bates, Martin Maechler, Ben Bolker, Steve Walker (2015). Fitting Linear Mixed-Effects. Models Using lme4. *Journal of Statistical Software*, 67(1), 1-48. doi:10.18637/jss.v067.i01.).

Limitations of design

We acknowledge several limitations for this analysis and evaluation. Since SMS reminder services could only be delivered to patients who reporting having access to a cellphone, to account for the selection bias due to the cellphone ownership, we conducted the analysis restricting the population to only those patients indicating access to a cellphone. Strictly speaking, this more conservative approach was adopted to achieve a more appropriate and representative comparison in the absence of being able to utilize matching comparisons. This limited our sample size for ART pick-ups, as well as our ability to understand the effect SMS service could potentially have on the general population, which in this region includes many individuals who report having no access to cellphone, especially females.

A further self-selection bias exists within the group who opted to receive SMS messages; despite matching for cellphone access, this difference between groups could not be adjusted for, as many factors can contribute to this difference, and it is not possible to collect further data/information to account for these differences (i.e., what contributes to patient having or not having access to a cellphone?).

Further, information regarding access, or not, to a cellphone was reported to HF personnel, and it was not possible to verify or confirm if a patient opted not to report cellphone access when in fact

they did have. Related to this, it was not always possible for HF staff to verify that the phone numbers provided at enrollment belonged to a cellphone owned by the patient, or if they were not the sole owner/user of the phone. Several other studies, including qualitative investigations, have highlighted the importance of addressing the contextual factor of phone sharing and confidential disclosures.[18]

The evaluation includes only a limited intervention implementation period in select sites, and we are limited to the inferences and interpretations based on the data available at the time of analysis. As such, we are limited in understanding individual patients' long-term behavior, or long-term outcomes such as LTFU, and if any LTFU outcome would possibly be related to death, or continued lag in pick-ups that eventually led to LTFU status.

Ethical considerations and assurances

All Health Counselors received specific training related to the intervention's standard operating procedures (SOP), including the standardized script and the process for obtaining informed consent, prior to commencing the implementation of SMS reminders in the respective HF.

In addition, all data managers received in-service trainings on established SOP to ensure comprehension of the intervention, objectives, procedures, and their responsibilities, including the importance of routinely checking the *Psychosocial and Positive Prevention Assessment* form for any new information and entering updating into OpenMRS in accordance with the patient's current preferences (e.g., if they were newly eligible to receive SMS reminders, or if they expressed a desire to stop receiving SMS reminders). All data included in this analysis were aggregated, de-identified programmatic data. The electronic databases outlined in the *Methods* section are stored on password protected and encrypted servers at FGH. De-identified data were extracted from these secure databases and sent via secure file transfer to relevant key personnel (e.g. the statistician).

Deviations from SOW/protocol (if any)

There were none related to this evaluation.

Data quality assurance

FGH technical teams were on-site and overseeing the fidelity of the implementation of this SMS reminder initiative. Programmatic data used in this evaluation was subject to routine data verification processes conducted by trained members of FGH's Monitoring and Evaluation (M&E) team and was stored securely on password-protected databases at district and provincial level offices. The performance of the program indicators was monitored by HF staff where the SMS reminder intervention was being implemented. All subsequent indicators were collected and internally reported monthly by the Health Information Systems (HIS) team, following the regular reporting period for program data. Data collection was completed by trained members of FGH and VUMC evaluation team.

Findings and Conclusions

Key findings for program improvement in relation to evaluation questions

Baseline characteristics

We compiled data regarding 18,941 scheduled ART pick-ups for 3,222 patients reporting cellphone access. These patients were almost equally female (1,664, or 52%) and male (1,558, or 48%). Among all patients included in analysis (all of whom were eligible for and informed of SMS services), 1,498 (46.5%) consented to receive SMS services and 1,724 (53.5%) declined. Among patients evaluated, 47% of eligible males and 46% of eligible females consented to SMS services. In this analysis, SMS reminder messages were sent (per intervention standard operating procedures) for 6,385 (34%) of the scheduled ART pick-ups, and not sent for 12,556 (66%) scheduled pick-ups (**Figure 1**).

Table 1 shows the baseline characteristics of the evaluation group. Median age at ART pick-up was nearly equal among those receiving SMS reminder services (median age = 30.2 years [IQR: 24.8, 37.0] versus those not receiving SMS reminder services (median age = 30.8 years [IQR: 25.3, 38.1]).

Patients opting to accept SMS reminder services were 51% female and 49% male; and in terms of age disaggregation, 23% were between 15-24 years of age, 70% were 25-49 years of age, and 8% were ≥50 years of age, with the latter group being classified as "older age" patients. Slightly more than 9% of evaluation participants reported having a partner who was also HIV-positive, compared to only 7% of patients who declined SMS services. Approximately 13% of patients enrolled in SMS reminder services reported a current pregnancy, compared to 15% of patients who declined receipt of SMS reminder services. The overwhelming majority (>99%) of patients consenting to receive SMS reminders had been enrolled in ART services for <6 months, compared to 97% of patients who declined.

Of patients who consented to receive SMS reminder services, 56% had completed some or all of secondary school, 30% had completed some or all of primary school, 9% reported having completed no schooling, and for 6% this information was missing; as compared to 52%, 34%, 7%, and 7%, respectively, for patients declining receipt of SMS reminder services. Of patients who enrolled to receive SMS reminder services, 44% reported being employed, compared to 42% of those who declined the service. Among SMS reminder service enrollees, 12% reported being a student at the time of enrollment, compared to only 10% of patients who declined SMS reminder services. Across health facilities implementing the SMS intervention during this evaluation period, acceptance rates to receive SMS reminder services among eligible patients ranged from 32% in Maganja da Costa *sede* (i.e., district capital) HF to 72% in the Mocubela *sede* HF, with an average acceptance rate of 48% across all sites.

With regards to ART pick-up characteristics (Table 2), the proportion of ART pick-ups that occurred within two days of the scheduled visit date (i.e., "on time") was greater for those for

which the patient was sent an SMS reminder for the scheduled visit (54%) compared to those for which the patient was not sent an SMS reminder for the scheduled visit (51%). For ART pick-ups for which an SMS reminder was sent, greater proportions of pick-ups took place on Wednesday through Saturday of the week (16%, 20%, 25%, and 6%, respectively) as compared to pick-ups for which an SMS reminder was not sent (15%, 19%, 21%, and 5%, respectively). For ART pick-ups by pregnant females, the proportion for which SMS reminders were not sent (16%) was greater compared to the proportion for which SMS reminders were sent (14%).

Effect on ART pick-up rates

Table 3 shows the adjusted odds ratios derived from mixed effect logistic regression on ART pick-ups. Overall, patients receiving SMS reminders were 13% more likely to pick up ART on or before their scheduled day of pick-up. Males who were sent SMS reminders were 22% more likely (aOR=1.22, 95%CI: 1.09-1.37, p<0.001) to pick up ART within two days of scheduled appointments compared to males not sent SMS reminders (**Figure 2**). For ART pick-up within 6 days of the scheduled pick-up date, this favorable association among males being sent SMS reminders was not significant (aOR=1.09; 95%CI: 0.95-1.25, p=0.2), and for ART pick-up within 59 days of the scheduled date, this positive association was not seen (aOR=0.90; 95%CI: 0.74-1.10).

Among all patients whose ART pick-up data was included in the analysis (i.e., those who received SMS reminders and those who did not), females were significantly more likely than males to pick up prescribed ART within two days (aOR=1.49, 95%CI: 1.34-1.66, p<0.001), six days (aOR=1.74, 95%CI: 1.50-2.00, p<0.001), and 59 days (aOR=1.93; 95%CI: 1.55-2.40, p<0.001) of scheduled appointments. Females, overall, were 16% more likely to pick up ART on or before their scheduled day for pick-up appointment, compared to males (**Figure 2**). Further, females who were pregnant at the time of the evaluation were significantly more likely to pick up their ART within 59 days of their scheduled appointment compared to non-pregnant females (aOR=1.50; 95%CI: 1.15-1.95, p<0.01). This positive association for timeliness of ART pick up was not seen, however, for pregnant females' pick-ups within 2 and 6 days of scheduled pick-up dates (aOR=0.89 and 0.95; 95%CI: 0.79-1.01 and 0.81-1.13; p=0.07 and 0.56; respectively).

Compared to younger adult patients (15-24 years of age), adults 25-49 years of age were more likely to pick up their ART within two days (aOR=1.15, 95%CI: 1.04-1.28, p<0.01), within six days (aOR=1.28, 95%CI: 1.11-1.47, p<0.001), and within 59 days (aOR=1.72, 95%CI: 1.40-2.12, p<0.001) of scheduled appointments. Older adults (≥50 years of age) were even more likely to pick up their ART within two days (aOR=1.43, 95%CI: 1.20-1.71, p<0.001), within six days (aOR=1.75, 95%CI: 1.38-2.22, p<0.001), and within 59 days of scheduled appointments (aOR=2.61; 95%CI: 1.82-3.75, p<0.001) compared to younger adults (15-24 years of age). Overall, older adults (≥50 years of age) were approximately 30% more likely than younger adults to pick up ART on or before their scheduled day of pick-up.

Independent of being sent SMS reminders, we found that patients receiving ART via Community Adherence Support Groups (CASG) were significantly more likely to pick up their ART within

two days (aOR=1.76, 95%CI: 1.46-2.12, p<0.001), within six days (aOR=2.24, 95%CI: 1.73-2.91, p<0.001), and within 59 days (aOR=9.09, 95%CI: 5.50-15.03, p<0.001) of their scheduled appointments compared to patients not receiving ART via CASG. In addition, patients who reported having an HIV-positive partner were significantly more likely to pick up their prescribed ART within 59 days of their scheduled pick-up date (aOR=1.51, 95%CI: 1.10-2.08, p=0.01) compared to patients who reported having an HIV-negative partner. Patients who had been on ART for 1-3 years were significantly less likely to pick up their ART within two days (aOR=0.85, 95%CI: 0.75-0.96, p=0.01), within six days (aOR=0.84, 95%CI: 0.73-0.97, p=0.02), and within 59 days (aOR=0.73, 95%CI: 0.59-0.92, p=0.01) of their scheduled appointments compared to patients who had been enrolled in ART services for less than six months.

Unanticipated findings

Unlike what was seen among males, there was no effect seen from SMS reminders on the timeliness of ART pick-up among females; moreover, females who received SMS reminders had similar ART pick-up rates when compared to females not sent SMS reminders (aOR=0.94, 0.90, 0.89; 95%CI: 0.85-1.05, 0.79-1.03, 0.72-1.10; respectively) (**Figure 2**).

Among females, pregnancy may be a protective factor for obtaining one's ART prior to defaulting in HIV care (i.e., within 59 days of the scheduled appointment, per definition recommended by Mozambique's MoH). However, with no significant association being found for SMS reminders sent within 2 and 6 days of scheduled appointment among pregnant women on ART pick-up, pregnancy status may not play a role for SMS reminders sent within the short time interval (i.e. 2 and 6 days) prior to scheduled pick-up.

The results demonstrated that only 43% of eligible patients consented for receiving SMS reminders. It should be explored whether access to a cell phone is a barrier issue or if certain patients prefer not to receive text messages for various reasons. The intervention showed a positive effect, but this was limited to those who have a phone and accepted being sent messages.

Conclusions

In Zambézia Province, SMS reminders provide a short-term positive effect on timely ART pick-up among consenting males (as seen by males being significantly more likely to pick up their ART within two days of their scheduled appointment when being sent SMS reminders), although this effect attenuated over time (with no significantly greater odds for ART pick-up within 6 or 59 days of scheduled appointment for males being sent SMS reminders). The proportion of on-time ART pick-ups was greater for those for which SMS reminders were sent compared to those for which SMS reminders were not sent.

Overall, HIV-positive females in Zambézia Province had a higher likelihood for ART pick-up at each time interval, however, no additive effect was seen with SMS reminders for females at any time interval. Older age also had a consistent positive effect on timely ART pick-up among all consenting adults. Additional context-specific strategies need to be implemented to ensure timely ART pick-up and improve retention in care.

These results could help inform continuation and/or adaptation of implementation strategies for SMS messaging programs within HIV services (for ART pick-up reminders and patient-centered messages for high-risk groups).

Graphical representation of results

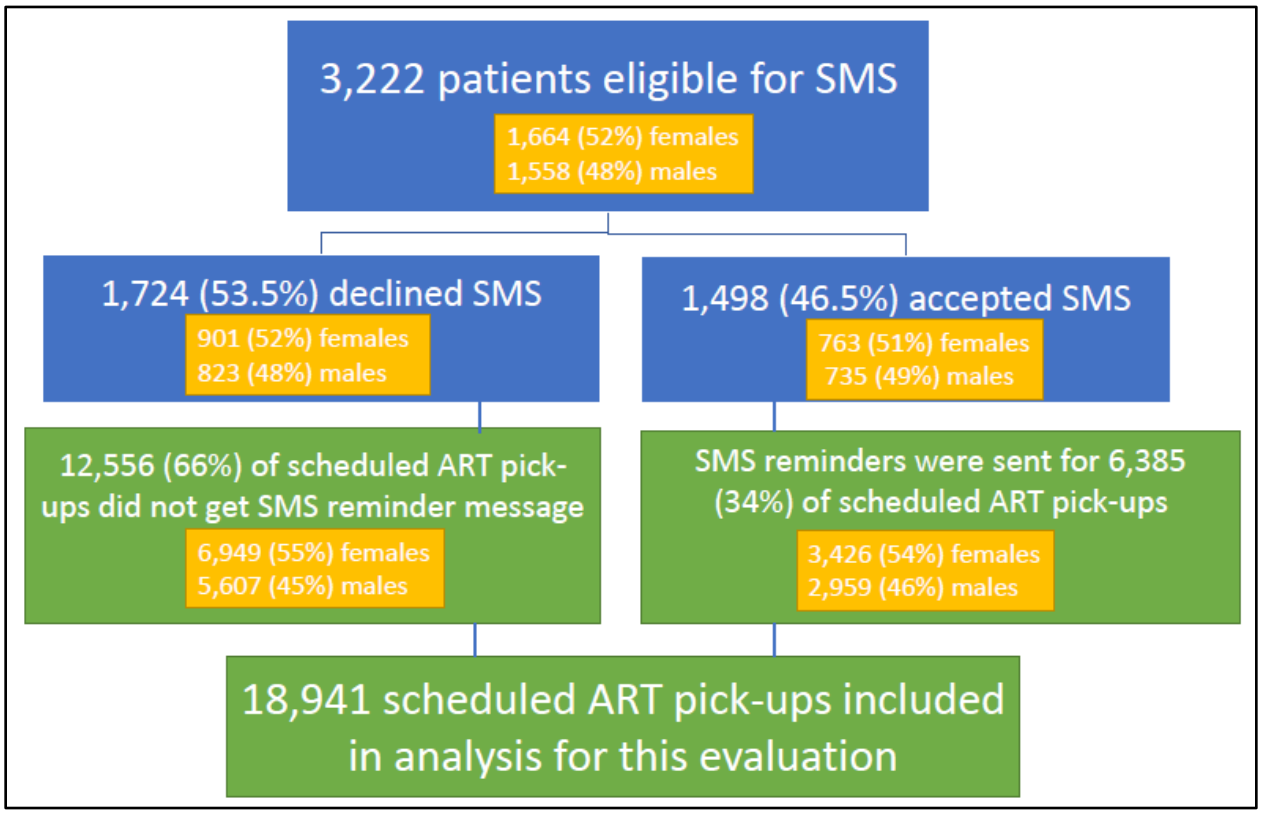

Figure 1. Data from July 2016 to May 2018 included in evaluation analysis

Table 1. Descriptive characteristics of SMS eligible patients

Variable	Level	Declined SMS	Accepted SMS	p-value
N		1,724	1,498	
Sex (%)	Male	823 (47.7%)	735 (49.1%)	0.474
	Female	901 (52.3%)	763 (50.9%)	
Age at ART pick-up (median [IQR])		30.2 [24.8, 37.0]	30.8 [25.3, 38.1]	0.008
Age at scheduled ART pick-up date (%)	15-24 years of age	441 (25.6%)	343 (22.9%)	0.163
	25-49 years of age	1,167 (67.7%)	1,041 (69.5%)	
	≥ 50 years of age	116 (6.7%)	114 (7.6%)	
Partner status (%)	Negative	1,599 (92.7%)	1,362 (90.9%)	0.067
	Positive	125 (7.3%)	136 (9.1%)	
Pregnancy Status (%)	No	1,461 (84.7%)	1,311 (87.5%)	0.027
	Yes	263 (15.3%)	187 (12.5%)	
ART Duration (%)	<6 months	1,678 (97.3%)	1,491 (99.5%)	<0.001
	<1 year	38 (2.2%)	6 (0.4%)	
	1-3 years	8 (0.5%)	1 (0.1%)	
Education level completed (%)	None	127 (7.4%)	128 (8.5%)	0.026
	Primary	592 (34.3%)	456 (30.4%)	
	Secondary	889 (51.6%)	831 (55.5%)	
	Missing	116 (6.7%)	83 (5.5%)	
Occupation (%)	Employed	731 (42.4%)	665 (44.4%)	0.137
	Homemaker	541 (31.4%)	451 (30.1%)	
	Farmer	190 (11.0%)	160 (10.7%)	
	Student	175 (10.2%)	173 (11.5%)	
	Unemployed	5 (0.3%)	5 (0.3%)	
	Retired	1 (0.1%)	1 (0.1%)	
	Missing	81 (4.7%)	43 (2.9%)	
Health facility (%)	Mocubela	33 (28%)	83 (72%)	
	Coalane*	182 (38%)	297 (62%)	
	4 de Dezembro*	295 (53%)	263 (47%)	
	Namacurra	250 (54%)	215 (46%)	
	17 de Setembro*	306 (55%)	249 (45%)	
	Chabeco*	184 (56%)	144 (44%)	
	24 de Julho*	269 (64%)	151 (36%)	
	Maganja da Costa	205 (68%)	96 (32%)	

Table 2. ART pick-up characteristics

Variable	Level	ART Pick-ups		
		SMS reminder was <u>not</u> sent	**SMS reminder was sent**	p-value
N		1,724	1,498	
Sex (%)	Male	5,607 (47.7%)	735 (49.1%)	0.474
	Female	6,949 (55.3%)	3,426 (53.7%)	
ART pick-up pattern (%) ** defined as number of days within next scheduled visit date*	≤ 2 days*	6,379 (50.8%)	3,453 (54.1%)	<0.001
	3-6 days*	3,347 (26.7%)	1,606 (25.2%)	
	7-59 days*	1,817 (14.5%)	827 (13.0%)	
	≥ 60 days*	1,013 (8.1%)	499 (7.8%)	
Age at ART pick-up (median [IQR])		30.7 [25.3, 37.7]	31.6 [26.3, 39.0]	<0.001
Age at scheduled ART pick-up date (%)	15-24 years of age	2,956 (23.5%)	1,293 (20.3%)	<0.001
	25-49 years of age	8,596 (68.5%)	4,501 (70.5%)	
	≤ 50 years of age	1,004 (8.0%)	591 (9.3%)	
Enrolled in CASG (%)	No	11,605 (92.4%)	5,978 (93.6%)	0.003
	Yes	951 (7.6%)	407 (6.4%)	
Partner status (%)	Negative	11,596 (92.4%)	5,862 (91.8%)	0.196
	Positive	960 (7.6%)	523 (8.2%)	
Pregnancy Status (%)	No	10,522 (83.8%)	5,499 (86.1%)	<0.001
	Yes	2,034 (16.2%)	886 (13.9%)	
ART Duration (%)	<6 months	7,779 (62.0%)	3,427 (53.7%)	<0.001
	<1 year	3,105 (24.7%)	2,235 (35.0%)	
	1-3 years	1,672 (13.3%)	723 (11.3%)	
ART Duration (median [IQR])		0.3 [0.2, 0.7]	0.5 [0.2, 0.7]	<0.001
Health facility (%) ** Quelimane City District*	Maganja da Costa	1,759 (14.0%)	500 (7.8%)	<0.001
	Mocubela	559 (4.5%)	446 (7.0%)	
	Namacurra	2,115 (16.8%)	809 (12.7%)	
	17 de Setembro*	1,753 (14.0%)	1,065 (16.7%)	
	24 de Julho*	1,542 (12.3%)	639 (10.0%)	
	4 de Dezembro*	2,254 (18.0%)	1,119 (17.5%)	
	Chabeco*	1,132 (9.0%)	539 (8.4%)	
	Coalane*	1,442 (11.5%)	1,268 (19.9%)	
Weekday of scheduled ART pick-up (%)	Monday	2,772 (22.1%)	1,051 (16.5%)	
	Tuesday	1,462 (11.6%)	622 (9.7%)	
	Wednesday	1,839 (14.6%)	1,038 (16.3%)	
	Thursday	2,413 (19.2%)	1,291 (20.2%)	
	Friday	2,657 (21.2%)	1,571 (24.6%)	
	Saturday	634 (5.0%)	410 (6.4%)	
	Sunday	779 (6.2%)	402 (6.3%)	<0.001

Table 3. Results from logistic regression model

Factor		ART pick-up within 0-2 days of scheduled		ART pick-up within 6 days of scheduled		ART pick-up within 59 days of scheduled	
		Adjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
Sex	Male	REF		REF		REF	
	Female	1.49 [1.34-1.66]	<0.001	1.74 [1.50-2.00]	<0.001	1.93 [1.55-2.40]	<0.001
Age	15-24 years	REF		REF		REF	
	25-49 years	1.15 [1.04-0.18]	0.01	1.28 [1.11-1.47]	<0.001	1.72 [1.40-2.12]	<0.001
	50+ years	1.43 [1.20-1.71]	<0.001	1.75 [1.38-2.22]	<0.001	2.61 [1.82-3.75]	<0.001
SMS effect (Overall)		1.06 [0.98-1.15]	0.14	0.99 [0.90-1.09]	0.85	0.92 [0.80-1.06]	0.26
SMS effect on Males		1.22 [1.09-1.37]	<0.001	1.09 [0.95-1.25]	0.20	0.90 [0.74-1.10]	0.29
SMS effect on Females		0.94 [0.85-1.05]	0.28	0.90 [0.79-1.03]	0.12	0.89 [0.72-1.10]	0.28
Enrolled in CASG	No	REF		REF		REF	
	Yes	1.76 [1.46, 2.12]	<0.001	2.24 [1.73, 2.91]	<0.001	9.09 [5.50, 15.03]	<0.001
Partner HIV status	Negative	REF		REF		REF	
	Positive	0.97 [0.84, 1.13]	0.72	1.20 [0.98, 1.47]	0.07	1.51 [1.10, 2.08]	0.01
Pregnancy status	No	REF		REF		REF	
	Yes	0.89 [0.79, 1.01]	0.07	0.95 [0.81, 1.13	0.56	1.50 [1.15, 1.95]	<0.01
Education level completed	None	REF		REF		REF	
	Primary	1.08 [0.92, 1.26]	0.37	1.03 [0.83, 1.27]	0.8	1.07 [0.77, 1.47]	0.69
	Secondary	1.15 [0.98, 1.35]	0.08	1.17 [0.94, 1.45]	0.15	1.26 [0.91, 1.73]	0.16
ART duration	<6 months	REF		REF		REF	
	<1 year	0.93 [0.86, 1.01]	0.09	0.88 [0.80, 0.97]	0.01	0.85 [0.73, 0.99]	0.04
	1-3 years	0.85 [0.75, 0.96]	0.01	0.84 [0.73, 0.97]	0.02	0.73 [0.59, 0.92]	0.01

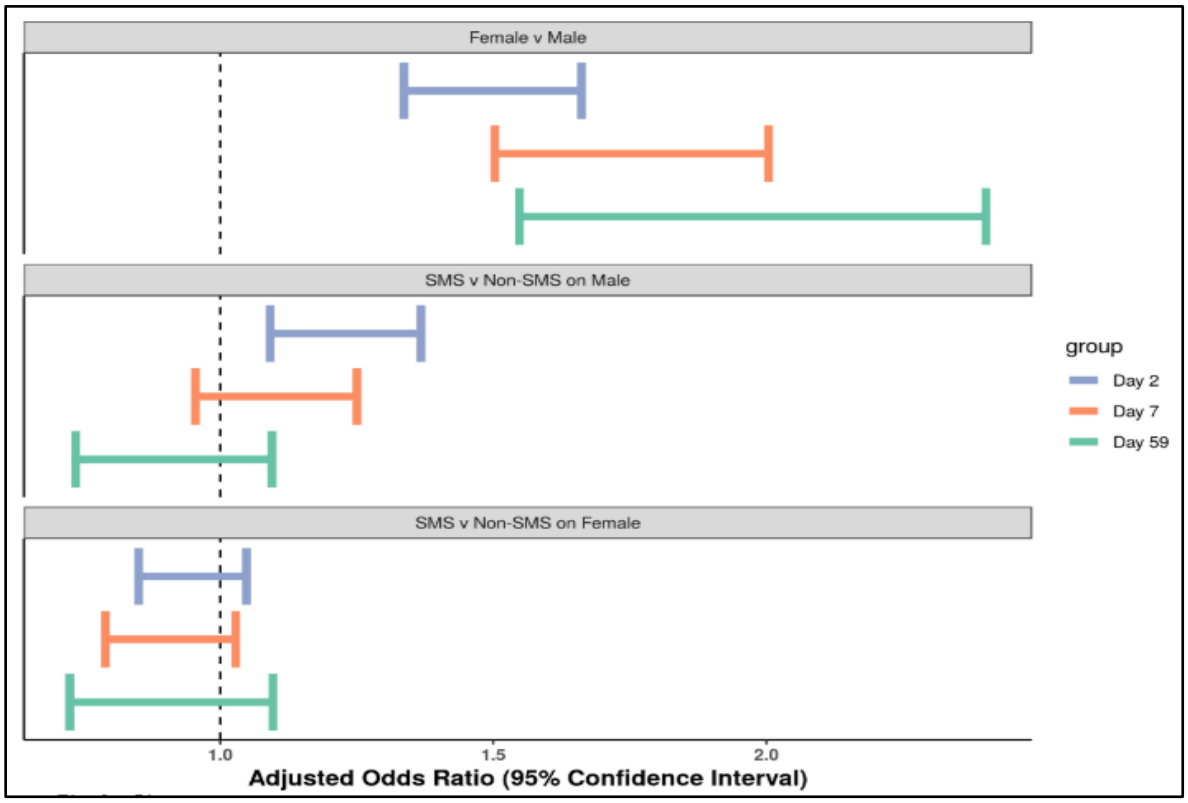

Figure 2. Forest plot for CI of Adjusted Odds Ratio, by sex and SMS effect

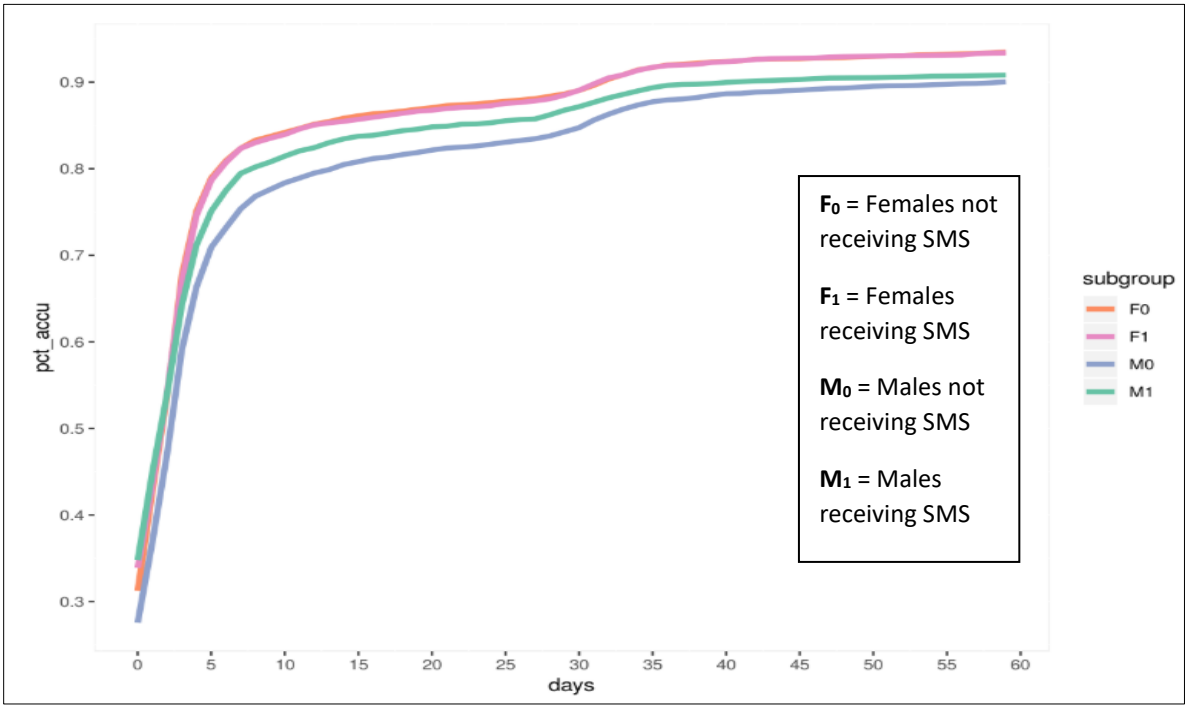

Figure 3. Cumulative ART pick-up by Sex

Recommendations

Our results show that in select sites in Zambézia Province, slightly less than half of all adult patients eligible for SMS reminders accept these services, with eligible males being slightly more likely to accept SMS reminders than eligible females. Our findings demonstrate that a considerable proportion of eligible patients are inclined to uptake the SMS reminders service. Further investigation is necessary to identify facilitating factors for SMS service uptake, especially among males and young adults.

Among those sent SMS messages, the reminders appeared to have a short-term positive effect on improving the timeliness of ART pick-up rates among males. A 2017 program evaluation analyzing HIV continuum of care outcomes among adolescents and young adults in Zambézia found that in this region, males are less likely to adhere to ART pick-ups, and younger males in particular need additional support to improve ART adherence, overall retention in care rates and reduce their mortality risk.[19] We consider the SMS intervention to be a formidable strategy, as it appears to be efficacious among those consenting to receive SMS reminder services, particularly among males.

Given this, we plan to continue efforts to inform public health officials and policymakers in the region of these contextual findings of this evaluation for consideration of adopting a similar and/or expanded SMS reminder strategy in attempts to improve patient adherence in these communities.

Additionally, we advocate that in this region certain high-risk groups, specifically pregnant and lactating women, children exposed to HIV, and patients who are defaulting from ART care, may need additional support to attend their clinical appointments.[15] As a potential additional adherence support service, there is a considerable need to explore the effects of sending tailored support SMS messages and/or reminders to patients defaulting or at risk for defaulting from their HIV care. Similarly, an SMS service aimed at pregnant and lactating females and their male partners, with tailored messages for promoting prevention of mother-to-child transmission (PMTCT) care and service uptake should be piloted in the region to assess efficacy at improving maternal and infant outcomes and potential for increasing male partner engagement and support in this critical time frame.[18, 20, 21]. A systematic review showed consistent evidence that an SMS reminder and a promotional health information is more effective in reducing missed appointments at the health facility than a simple reminder.[22] In addition, a meta-analysis of controlled trials showed that interventions that used personalized messages for patients had greater effects on adherence results versus uniform or generalized message content.[23]

Dissemination plan

FGH has shared results with provincial-level MoH authorities to advocate for rollout of automated SMS appointment reminders in remaining facilities; we also aim to share at MoH national-level.

In an effort to share best practices and lessons learned from this novel strategy, a CDC-MZ-approved abstract with these findings was presented in a poster format at the IAS 2019 Conference

in Mexico City, Mexico (July 2019) and the INTEREST 2019 Conference in Accra, Ghana (May 2019), as well as an oral presentation at the Provincial Scientific Conference in Zambézia, Mozambique (July 2019). Additionally, a peer-reviewed publication detailing these important finding is being finalized, with plans for submission to a high impact public health journal for broader dissemination of results and recommendations.

Appendices

Approved evaluation SOW/protocol

The approved concept note is submitted along with this final report for reference. This evaluation is covered by and was approved by CDC-Mozambique Associate Director for Science (ADS) under the VUMC/FGH blanket protocol for secondary data analyses to evaluate and improve program outcomes using routine HIV Care and Treatment data (CGH HSR #: 2016-163a).

Data collection instruments/tools

Not applicable.

Informed consent

There was no consent form necessary for use of data for this evaluation, as only routinely collected, de-identified, aggregated programmatic data was included in the analysis for this evaluation. As such, a waiver of consent was approved, as the evaluation involved no more than minimal risk, would not have been possible without the waiver, and the waiver did not adversely affect the rights nor welfare of the patients whose data was included in the evaluation.

Biosketches

Not applicable.

Conflict of interest statement

The collaborators in this evaluation have no conflicts of interest to declare.

Evaluation costs

Not applicable.

Results or Logical Framework

Not applicable.

References

1. Aranda-Jan, CB, Mohutsiwa-Dibe N, and Loukanova S, *Systematic review on what works, what does not work and why of implementation of mobile health (mHealth) projects in Africa.* BMC Public Health, 2014. **14**: p. 188.
2. Muwonge TR, Ngure K, Katabira E, et al., *Short Message Service (SMS) Surveys Assessing Pre-exposure Prophylaxis (PrEP) Adherence and Sexual Behavior are Highly Acceptable Among HIV-Uninfected Members of Serodiscordant Couples in East Africa: A Mixed Methods Study.* AIDS Behav, 2019. **23**(5): p. 1267-1276.
3. Venables E, Ndlovu Z, Munyaradzi D, et al., *Patient and health-care worker experiences of an HIV viral load intervention using SMS: A qualitative study.* PLoS ONE, 2019. **14**(4): p. e0215236-e0215236.
4. Ware NC, Pisarski EE, Tam M, et al., *The Meanings in the messages: how SMS reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda.* AIDS, 2016. **30**(8): p. 1287-94.
5. Barnighausen T, Chaiyachati K, Chimbindi N, et al., *Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies.* Lancet Infect Dis, 2011. **11**(12): p. 942-51.
6. Mills EJ, Lester R, Thorlund K, et al., *Interventions to promote adherence to antiretroviral therapy in Africa: a network meta-analysis.* Lancet HIV, 2014. **1**(3): p. e104-11.
7. Mayer JE and Fontelo P, *Meta-analysis on the effect of text message reminders for HIV-related compliance.* AIDS Care, 2017. **29**(4): p. 409-417.
8. Haberer JE, Musiimenta A, Atukunda EC, et al., *Short message service (SMS) reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda.* AIDS, 2016. **30**(8): p. 1295-300.
9. Bigna JJ, Noubiap JJ, Plottel CS, et al., *Effect of mobile phone reminders on follow-up medical care of children exposed to or infected with HIV in Cameroon (MORE CARE): a multicentre, single-blind, factorial, randomised controlled trial.* The Lancet Infectious Diseases, 2014. **14**(7): p. 600-608.
10. Pop-Eleches C, Thirumurthy H, Habyarimana JP, et al., *Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders.* AIDS, 2011. **25**(6): p. 825-34.
11. Horvath T, Azman H, Kennedy GE, Rutherford GW, *Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection.* Cochrane Database Syst Rev, 2012(3): p. Cd009756.
12. Amankwaa I, Boateng D, Quansah DY, et al., *Effectiveness of short message services and voice call interventions for antiretroviral therapy adherence and other*

outcomes: A systematic review and meta-analysis. PLoS ONE, 2018. **13**(9): p. e0204091-e0204091.

13. Reid MJA, Steenhof AP, Thompson J, et al., *Evaluation of the effect of cellular SMS reminders on consistency of antiretroviral therapy pharmacy pickups in HIV-infected adults in Botswana: a randomized controlled trial.* Health Psychol Behav Med, 2017. **5**(1): p. 101-109.
14. Joseph Davey D, Nhavoto JA, Augusto O, et al., *SMSaude: Evaluating Mobile Phone Text Reminders to Improve Retention in HIV Care for Patients on Antiretroviral Therapy in Mozambique.* J Acquir Immune Defic Syndr, 2016. **73**(2): p. e23-30.
15. Nhavoto JA, Gronlund A, and Chaquilla WP, *SMSaude: Design, Development, and Implementation of a Remote/Mobile Patient Management System to Improve Retention in Care for HIV/AIDS and Tuberculosis Patients.* JMIR Mhealth Uhealth, 2015. **3**(1): p. e26.
16. Kerrigan A, Kaonga NN, Tang AM, et al., *Content guidance for mobile phones short message service (SMS)-based antiretroviral therapy adherence and appointment reminders: a review of the literature.* AIDS Care, 2019. **31**(5): p. 636-646.
17. Republic of Mozambique, MoH, National Directorate for Medical Assistance, *Guia de Tratamento Antiretroviral e Infecções Oportunistas no Adulto, Criança, Adolescente e Grávida*. 2014: Maputo, Mozambique.
18. Jennings L, Ong'ech J, Simiyu R, et al., *Exploring the use of mobile phone technology for the enhancement of the prevention of mother-to-child transmission of HIV program in Nyanza, Kenya: a qualitative study.* BMC Public Health, 2013. **13**: p. 1131.
19. Ahonkhai A, Aliyu MH, Audet CM, Bravo M, Simmons M, Claquin G, et al. , *Poor retention and care-related sex disparities among youth living with HIV in rural Mozambique (oral presentation).* in *9th International AIDS Society (IAS) Conference*. 2017: Paris, France.
20. Odeny TA, Hughes JP, Bukusi EA, et al., *Text messaging for maternal and infant retention in prevention of mother-to-child HIV transmission services: A pragmatic stepped-wedge cluster-randomized trial in Kenya.* PLoS Med, 2019. **16**(10): p. e1002924.
21. Odeny TA, Newman M, Bukusi EA, et al., *Developing content for a mHealth intervention to promote postpartum retention in prevention of mother-to-child HIV transmission programs and early infant diagnosis of HIV: a qualitative study.* PLoS ONE, 2014. **9**(9): p. e106383.
22. McLean SM, Booth A, Gee M, et al., *Appointment reminder systems are effective but not optimal: results of a systematic review and evidence synthesis employing realist principles.* Patient Prefer Adherence, 2016. **10**: p. 479-99.

23. Finitsis, DJ, Pellowski JA, and Johnson BT, *Text message intervention designs to promote adherence to antiretroviral therapy (ART): a meta-analysis of randomized controlled trials.* PLoS ONE, 2014. **9**(2): p. e88166.