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Effect of Text Messaging Plus Peer Navigation on Viral Suppression Among Youth With HIV in the iCARE Nigeria Pilot Study

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Abstract

Background—Consistent with the global trend, youth with HIV (YWH) in Nigeria have high rates of viral non-suppression. Novel interventions are needed.

Setting—Infectious Diseases Institute, College of Medicine, University of Ibadan, Nigeria.

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Methods—In a single-arm trial, participants aged 15–24 years old received 48 weeks of a combination intervention, comprising daily two-way text message medication reminders plus peer navigation. The primary outcome measure was viral suppression below 200 copies/mL. Secondary outcomes measures included self-reported adherence on a visual analogue scale and medication possession ratio (MPR), each dichotomized as ≥90% (good) or < 90% (poor) adherence. Outcomes were analyzed using McNemar's test. Retention in care, intervention feasibility and acceptability, and participants' satisfaction were also assessed.

Results—Forty YWH (50% male) were enrolled: mean age 19.9 years (SD=2.5), 55% perinatally-infected, and 35% virologically suppressed at baseline. Compared to baseline, the odds of virologic suppression was higher at 24 weeks (OR = 14.00, p < 0.001) and 48 weeks (OR = 6.00, p = 0.013). Self-reported adherence (≥90%) increased from baseline at 24 weeks (63%, p = 0.008) and 48 weeks (68%, p = 0.031). MPR ≥90% increased at weeks 24 and 48 (85% and 80%, respectively), achieving statistical significance at 24 weeks only (p = 0.022). Retention in care at 48 weeks was 87.5%. All (37/37) participants at week 48 were fully or mostly satisfied with the intervention.

Conclusion—Daily, two-way text message reminders plus peer navigation is a promising combination intervention to improve viral suppression among YWH in Nigeria.

Keywords

viral suppression; youth; phones; peers; adherence

INTRODUCTION

Since 2016, guidelines in Nigeria, Africa's most populous country, have recommended antiretroviral treatment (ART) regardless of CD4 cell count for all people with HIV.[1] Suppression of HIV-1 viremia curbs AIDS-related morbidity and mortality, limits viral transmission, and is essential to end the epidemic.[2–4] Consistent with the global trend, youth (15–24 years of age) in Nigeria have not benefited from ART as much as adults.[5–8] In 2017, fewer than half of youth with HIV (YWH) receiving care at the Infectious Disease Institute, College of Medicine, University of Ibadan, Ibadan, Nigeria (IDI/CoMUI) were virologically suppressed (unpublished data). Evidence-based interventions are needed to optimize ART outcomes in YWH.[9]

Mobile phones are powerful tools for ART-related interventions,[10–11] and there were over 190 million active mobile phone subscriptions in Nigeria in April 2020.[12] The widespread preference for text messaging among youth make it uniquely promising for youth-directed interventions. In 2016, the United States (U.S.) Centers for Diseases Control (CDC) endorsed an innovative two-way text message reminder intervention (TXTXT) for promoting ART adherence in YWH.[13] This endorsement was based on a study by Garofalo et al., in which 16–29-year-olds who received the TXTXT intervention were more than twice as likely to report >90% adherence to ART over the 6-month intervention period, and the improvements were sustained at 6-months post intervention.[14] TXTXT has not been evaluated outside the U.S.

Engagement of peers is another potential way to improve ART outcomes in youth, particularly adolescents (10–19 years of age), because peer influences on health and well-being are greatest during this stage of life.[15–18] Indeed, peer navigation and support is recommended by the World Health Organization (WHO) as an evidence-based approach to improve ART outcomes in youth across the HIV care continuum.[19] Peer support ranks high among potential facilitators of ART adherence among YWH in sub-Saharan Africa,[20,21] which harbored 78% of the global population of YWH in 2017.[22]

Studies of interventions to improve ART outcomes among 15–24-year-olds in sub-Saharan Africa have failed to demonstrate improvement in ART adherence and loss to follow up, even when the same interventions were effective in older individuals.[23–26] While these results can reflect challenges in addressing the unique struggles of youth, they may also indicate the limitations of single interventions in addressing complex multi-dimensional determinants of ART success. Combination interventions may be more effective than single interventions,[27] but this is not a consistent finding.[28]

The Intensive Combination Approach to Rollback the Epidemic in Nigerian Adolescents Study (iCARE Nigeria) is a two-phase trial with HIV testing and treatment intervention arms, each incorporating mobile health technology (mHealth) and peer navigation. iCARE Nigeria was adapted for Nigerian youth through broad input from local YWH and other stakeholders.[29] Here, we report the findings of the first (pilot) phase of the treatment intervention arm of the iCARE study, where we hypothesized that the investigational combination intervention will improve the odds of viral suppression among YWH aged 15–24 at IDI/CoMUI. We also tested, as secondary outcomes, effects of the combination intervention on adherence and retention in care, as well as intervention feasibility and acceptability, and participants' satisfaction.

METHODS

Setting

This study was conducted at IDI/CoMUI, which receives support from the CDC-funded AIDS Prevention Initiative in Nigeria (APIN) Public Health Initiatives, and provides ART to over 6000 persons with HIV, aged 14 or older. Antiretroviral drugs are dispensed through an on-site pharmacy, and routine viral load and CD4 cell monitoring is also provided, at no cost to YWH. Youth with viral load > 1000 copies/mL after at least 6 months of ART receive enhanced adherence counseling. Those with persistent viremia despite 3 months of enhanced adherence counselling are evaluated for an empiric switch to second- or third-line ART regimens. A YWH youth club meets on-site every other month for peer interaction, support, and education.

Study Design

A collaborative working group of community and governmental stakeholders and two YWH focus groups were conducted in December 2018, in Ibadan, Nigeria to adapt the combination peer navigation and text message reminder intervention to the local context. Findings from this formative research suggested that the combination intervention

should include low navigator-peer ratio (1:5) and volunteer-based navigators to promote sustainability and altruism, and flexible matching of navigator to peer and low requirements for mobile phone data use to promote engagement. With the findings from this formative research,[29] we designed a locally-adapted combination intervention consisting of daily, two-way, personalized text message medication reminders (TXTXT) plus peer navigation, then conducted a single-arm study of its effect on viral suppression and other HIV care continuum outcomes over 48 weeks.

Study Participants—In order to be considered eligible, the potential participant had to be 15–24 years old, HIV seropositive, a registered patient at IDI/CoMUI, on ART for at least 3 months, understand and read basic English and/or Yoruba, able to provide consent, and intend to remain a patient at IDI/CoMUI during the 48-week follow-up period. In compliance with the 2014 Nigeria Federal Ministry of Health Guidelines, minors aged 16 or 17 years, or 15 years old and emancipated, provided consent for themselves without parental involvement.[30]

Recruitment procedures—To recruit participants, we created a sampling frame of potentially eligible youth from medical records at IDI/CoMUI, stratified into virologically suppressed (HIV-1 RNA <200 copies/mL) or viremic (≥200 copies/mL) groups. A random sample was then selected as every "n^{th}" YWH based on the ratio of target sample size to number of YWH in the sampling frame. Enrollment was monitored to ensure that no more than 35% of selected individuals were virologically suppressed, in order to reflect the clinic's proportion of virologically suppressed youth. Youth selected from the sampling frame were approached by study staff to determine their interest and eligibility for the study. As needed based on refusals or no-shows, the sampling frame was re-constituted as a ratio of remaining sample needed to remaining YWH in the sampling frame. These procedures were followed until the accrual target of 40 was reached.

Text message reminders—YWH worked with study staff to develop the text message library, and ensure it contained expressions understood and commonly used by youth. The text messages, which were designed to promote ART adherence, were delivered via the Dimagi Commcare platform (https://www.dimagi.com/commcare/). Participants used their own phones for text messaging; however, a phone was provided to those without one. The daily text messages included a personalized initial medication reminder that coincided with the individual's chosen time for antiretroviral drug ingestion. This was followed by a second message 15 minutes later, asking whether they took their medication, with a request for reply ("yes" or "no"). An encouraging automated message (based on the message library) was then triggered by their reply. Both the initial and follow-up messages were chosen by each youth and personalized to reflect content meaningful to them. To protect confidentiality, messages were worded in a way that would not reveal the participant's HIV status if read by a third party See Supplemental Digital Content Table 1).

Peer navigation—Peer navigators were selected from the IDI/CoMUI clinic. Requirements for this role included being virologically suppressed in the prior 12-month period (if available), aged 18–30 years, and clinically stable, according to their physician's

subjective assessment. The peer navigators received didactic lectures and practicums over the course of two weeks, delivered by the study investigators and staff supervisors, covering general professionalism, privacy and confidentiality, basic HIV education, human rights and protections, mental health, self-care, and roles and responsibilities of peer navigators (see Supplemental Digital Content, Table 2). In line with the findings from formative YWH focus groups, we matched each peer navigator to 4 or 5 study participants based on salient shared characteristics, including gender, age, residence location and religion.[29] We allowed older ages for peer navigators than participants.[29] After assessment of the participant's needs and development of an action plan by clinic staff, peer navigators made at least one contact (in-person or phone) every two weeks with participants to support goals of the action plan. Peer navigators also collaborated with clinic staff to facilitate referrals to mental health and other services, accompanied participants to appointments as needed, and provided general peer support (see Supplemental Digital Content, Table 3). Also based on formative research, peer navigators were considered volunteers in order to promote altruistic motivations and enhance sustainability. Accordingly, they received nominal stipends, primarily to cover transportation and communication expenses.

Ethics—Institutional Review Board approval was obtained from Northwestern University, Lurie Children's Hospital, and the joint University of Ibadan/University College Hospital Ethics Committee.

Data Collection and Outcomes Measures

Data were collected for this study via interviewer-administered electronic questionnaires, medical records abstraction, and blood specimen collection at baseline, and at 24 and 48 weeks post baseline. Collected demographic characteristics included age, sex, ethnic group, highest level of education, religion, and phone ownership or access. Medical history abstracted from records included mode of infection, current ART regimen, and drug pick-up information from 24 weeks prior to baseline through 48 weeks on study. Each participant was asked to provide approximately 100 strands of hair at baseline, week 24 and week 48 to measure antiretroviral drug levels.

The primary study outcome was viral suppression, defined as viral load <200 copies/mL. Viral load quantification occurred at an HIV Reference Laboratory, using real-time HIV-1 COBAS® assay (Roche Molecular Systems, Inc.) with a lower detection limit of 20 copies/mL.

The secondary outcomes included medication adherence and retention in HIV care. The adherence measures were i) self-reported 30-day adherence on a visual analogue scale (VAS) of 0 to 100,[31] ii) drug pick-up adherence based on medication possession ratio (MPR) calculated from pharmacy records,[32–34] and iii) antiretroviral drug levels in hair.[35] MPR was calculated, using drug-pick records over the 24-week period preceding the evaluation date, as total number of days' supply obtained including the last fill, divided by number of days between first fill and last day of the observation window (also known as continuous multiple-interval measures of medication availability).[36] Values greater than 100% were truncated to 100%. We evaluated adherence to the regimen rather than individual drugs since

the antiretroviral drugs in each participant's regimen were always dispensed together. Both VAS and MPR values were created into dichotomous indicators of ≥90% adherence (good) or < 90% adherence (poor).[37]

Retention in care was defined as two HIV care related visits to IDI/CoMUI in each 24-week observation period. We also assessed intervention feasibility, acceptability and satisfaction, using a modified version of the client satisfaction questionnaire (CSQ-8).[38] Feasibility was measured by the ratio of assigned peer navigator to participants compared to the planned ratio of 1:5, and number of navigator-participant encounters compared to plan of one every two weeks. Acceptability and satisfaction were measured at 48 weeks by assessing whether the intervention activities were: delivered to the participant as they expected, intrusive or bothersome, and met expectations for privacy. Overall satisfaction with the intervention was assessed as well.

Data Analyses

Changes between pre and post-intervention periods were compared using McNemar's test. We used an intent-to-treat approach (ITT) for the primary analysis; therefore, participants who were deceased or lost to follow-up were coded as not suppressed. We pre-specified that the combination intervention would be considered clinically-significant and merit further investigation if we observed a greater than 30% increase from baseline in the proportion of youth with viral load <200 copies/mL after 48 weeks of the intervention, estimated to correspond to an odds ratio (OR) of ≥1.5. For descriptive statistics, percentages were calculated for dichotomous outcomes and mean values for continuous outcomes.

RESULTS

Participant Characteristics

A total of 46 YWH were selected from the sampling frame, out of whom 5 refused to participate and 1 was ineligible. The 40 participants (20 males) enrolled (Table 1) had a mean age of 19.9 years (SD=2.5, range=15–24). At baseline, thirty-six participants (65%) owned or had access to a cell phone to receive the intervention; the study provided phones to the remaining 14 participants; 3 additional phones were distributed to replace lost or malfunctioning personal (n=2) or study-provided (n=1) phones. All participants completed the week 24 visit, while 37 completed 48 weeks (1 died, 2 lost to follow up).

Virologic outcomes

The proportion of YWH with viral suppression was 35% at baseline, and 68% at 24 weeks, an increase of 94%. At 48 weeks, 60% were suppressed, an increase of 71% from baseline. Viral suppression rates overall and in subgroups are detailed in Table 2. Compared to baseline, the odds of being virologically suppressed were substantially higher at 24 weeks (OR = 14.00, $p < 0.001$), and at 48 weeks (OR = 6.00, $p = 0.013$) of the combination intervention.

Increases in viral suppression rates were seen across subgroups: men versus women; perinatally versus non-perinatally infected participants; first-line versus second-line

regimens; and owned/had access to cell phone or not at baseline. Transition from suppressed to viremic status was rare; of the 16 participants who were not virologically suppressed or were deceased or lost to follow up at week 48, only 2 were suppressed at baseline.

Adherence and retention in care

Self-reported ART adherence ≥90%, based on VAS, was 43% at baseline. This increased from baseline levels to 63% (p = 0.008) at 24 weeks and 68% (p = 0.031) at 48 weeks. Self-reported adherence was not significantly correlated with viral suppression at 24 (r = 0.014, p = 0.933) or 48 weeks (r = 0.305, p = 0.056).

MPR indicated that 63% of participants had ≥90% drug pick-up adherence at baseline. Compared to baseline, the proportion with MPR ≥90% increased numerically at both weeks 24 and 48 (85% and 80%, respectively); statistical significance was achieved at 24 weeks (p = 0.022), but not 48 weeks (p = 0.092). MPR was not significantly correlated with viral suppression at 24 weeks (r = 0.306, p = 0.054), but was significantly correlated at 48 weeks (r = 0.357, p = 0.024).

Hair samples were provided by 23% of participants. Due to this low uptake, antiretroviral drug concentrations were not measured. Retention in care was 98% at 24 weeks and 88% at 48 weeks.

Feasibility, acceptability, satisfaction

We identified 9 peer navigators (8 original and one replacement) with a mean age of 22.6 years (3.7). The assignment ratio of peer navigators to peers was 1:5. Each peer navigator contacted their assigned peers an average of 1.8 times in each two-week period, which was above the expected average of at least one contact. The proportion of participants who were provided a phone at some point during the study was 40%. After an adjustment period due to technical challenges, text message reminders were successfully deployed to 100% of participants on a consistent basis by study week 7.

In terms of acceptability, at week 48, 5% of participants reported the text messages as sometimes or always “intrusive or bothersome” and 10% found peer navigation sometimes or always “intrusive or bothersome.” No participant experienced inadvertent disclosure of HIV status or any other unexpected adverse events as a result of either aspect of the intervention.

At 48 weeks, 100% (n=37 of 37 retained) of participants indicated that they were very satisfied or mostly satisfied with the combination intervention and 100% (n=37 of 37) would refer a friend to receive it.

DISCUSSION

In a heterogeneous cohort of YWH in Nigeria, the iCARE combination intervention, comprising daily, two-way text message reminders and peer navigation, led to a six-fold increase in the odds of viral suppression from baseline to 48 weeks. The combination intervention was feasible and acceptable with high satisfaction and retention in HIV care

documented. These remarkable results were obtained even though the last 14 weeks of the study occurred during the Coronavirus Disease 2019 (COVID-19) pandemic. Two of the participants with viral non-suppression at week 48 had achieved viral suppression at week 24, which they subsequently lost as a result of interstate travel lockdown that affected antiretroviral drug pick-up from the clinic pharmacy. Given the increasing popularity of text messaging across sub-Saharan Africa,[39] the iCARE combination intervention may have broad relevance and impact if our pilot results are confirmed in larger studies.

Previous studies in 15–24-year-olds across sub-Saharan Africa highlight the challenges of influencing HIV care outcomes in this population. In a retrospective cohort study in South Africa, loss-to-follow-up did not significantly improve among youth, aged 16–24 years, who received a community health worker-led, nurse-assisted intervention.[25] Another study, conducted in Uganda, showed no significant effect of one-way or two-way text messaging on ART adherence among YWH aged 15–22 years.[26] Our study differs from these earlier studies in that we deployed two distinct interventions (two-way text message reminders and peer navigation) concurrently, and used viral suppression as the primary outcome measure. We chose a combination approach on the premise that automated text message reminders would address some drivers of poor ART adherence, such as forgetfulness, while barriers related to stigma, mental health, or social instability would be better addressed by needs-based peer support. This combination approach may explain our positive results in a heterogeneous youth population of perinatally and non-perinatally infected youth, young women and young men, those on first- and second-line regimens, and those with or without personal phones. In addition, it is likely that the selected text-messaging approach independently promoted success since it was based on a validated, CDC-recommended intervention (TXTXT),[14] which we further adapted to the study population.[29] Nevertheless, the fact that forty percent of YWH in our study were either viremic, dead, or lost to follow up, despite 48 weeks of the combination intervention, suggests additional interventions are needed for some YWH. Baseline antiretroviral drug resistance may explain the poor outcomes in some of these youth,[40] along with intractable barriers to ART access and adherence that we documented, such as food insecurity, housing instability, and non-disclosure.

By integrating formative research, we designed an intervention that prioritized the needs and preferences of YWH, while factoring in local social and health infrastructure realities. Thus, we assigned 5 YWH to each peer navigator. This standardization is important, given heterogeneity around the operationalization of peer support in the literature.[41] The peer navigators were volunteers and received nominal stipends, which makes the intervention scalable and sustainable. Also, as recommended by YWH in the formative focus groups, we selected navigators who were older, on average, than participants (mean age of 22.6 versus 19.9 years). This aligns with local culture, which assigns greater responsibility to older individuals, and is similar to the Zvandiri model in Zimbabwe, where 18–24-year-olds served as treatment supporters to 10–15-year-old adolescents.[42] Each youth in our study was asked to choose the text message they received, thereby supporting youths' desire for autonomy.[17] Finally, the study intervention did not require clinic visits. As a result, it was convenient for youth who lived far from the study site to take part.

The age range of participants in our study spans the latter half of adolescence into young adulthood. As such, an important question is whether the results can be extrapolated to adolescents under 15 years old. We caution against such extrapolation in the absence of evidence. Compared to 15–24 year-olds, adolescents under 15 are at a different cognitive developmental stage, and have different challenges and needs with treatment adherence when confronted with a chronic condition like HIV.[43–45] Moreover, it is doubtful that the younger adolescents can be expected to have, or maintain, personal phones for the combination intervention. There are already interventions targeting adolescents younger than 15 years, such as facility-based peer support[46] and community-based peer support,[47] without text-messaging.

Our study is not without limitations. First, we enrolled only 40 YWH in this single-arm study; however, this sample size and design were adequate to determine whether the combination intervention is sufficiently promising to justify advancing it to the second phase of the iCARE study, a larger, randomized trial of the intervention's effectiveness. Second, though there were improvements in self-reported adherence by VAS, the correlations with viral suppression were weak and not statistically significant; however the level of correlation are consistent with prior research among PWH.[31] Drug pick-up adherence (MPR) correlated with virologic suppression at week 48, though the numerical improvement in adherence at this timepoint did not achieve statistical significance. Reasons for these results may include the small sample size, and inherent limitations of adherence measures, such as VAS and MPR, that do not capture actual drug ingestion.[48–50] We had planned to directly measure antiretroviral drug levels in hair,[51] but less than a quarter of participants provided hair sample, likely linked to Nigerian men's preference for short hair, plus fears among Nigerians that hair may be used for rituals.[52] Antiretroviral drug levels in dried blood spots will be used to objectively measure adherence in the next phase of our study. Lastly, it remains to be seen whether already stretched health systems will be able to provide resources such as mobile phones that the study purchased for forty percent of participants. Overall, the combination intervention consumed little resources, and, importantly, remarkable results were obtained at IDI/CoMUI, which has a well-established youth club. Youth-friendly services are advocated for ART programs that cater to YWH as such services may improve outcomes.[53, 54] Our results suggest that the combination intervention employed in this study may be synergistic with other youth-targeted programs, and thereby save more lives and costs in the long run. Cost-effectiveness studies are needed to clarify this.

In conclusion, this 48-week pilot study demonstrates that the iCARE combination intervention is promising for improving ART outcomes among YWH aged 15–24 years in Nigeria. Based on these positive results, a large, fully-powered, randomized, step-wedge study, with implementation science and cost-effectiveness components, is underway at six sites in four Nigerian cities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic characteristics of iCARE Nigeria study participants (N=40)

	Total n (%)
Age	
M (SD)	19.9 (2.5)
Median (Range)	19 (15–24)
Sex	
Male	20 (50.0)
Female	20 (50.0)
Ethnic group	
Hausa	1 (2.5)
Igbo	4 (10.0)
Yoruba	35 (87.5)
Religion	
Christian	27 (67.5)
Islam	13 (32.5)
Highest Level of Education	
No formal education	1 (2.5)
Primary school	1 (2.5)
Junior secondary school	0 (0)
Senior secondary school	24 (60.0)
Tertiary institution	14 (35.0)
Mode of Infection	
Behavioral	11 (27.5)
Perinatal	22 (55.0)
Blood transfusion/other medical	2 (5.0)
Unknown	5 (12.5)
Viral Load <200 copies/ml	
Yes (suppressed)	14 (35.0)
No (viremic)	26 (65.0)
Visual Analogue Scale	
≥ 90% adherent	17 (42.5)
Medication Possession Ratio	
≥ 90% adherent	25 (62.5)
Antiretroviral Regimen	
First-line	26 (65.0)
Second-line	14 (35.0)
Cell Phone (baseline)	
Own/possess cell phone	26 (65.0)
Did not own/possess cell phone	14 (35.0)

Note. First-line regimens = two nucleoside reverse transcriptase inhibitors (NRTIs) plus efavirenz (17), dolutegravir (8), or nevirapine (1). Second-line regimens= two NRTIs plus atazanavir/ritonavir (11) or lopinavir/ritonavir (3)

Table 2.

Participants with viral suppression overall and in subgroups (N=40)

Virological Suppression (copies/mL)	Baseline n (%)	24 Weeks n (%)	48 Weeks n (%)
Overall			
< 200	14 (35)	27 (68) **	24 (60) *
< 1000	19 (48)	31 (78) **	28 (70) *
Perinatally Infected (< 200)	5 (23)	15 (68)	15 (68)
Non-perinatally Infected † (< 200)	5 (45)	7 (64)	6 (55)
First-line Regimen (< 200)	11 (42)	21 (81)	18 (69)
Second-line Regimen (< 200)	3 (21)	6 (43)	6 (43)
Owned cell phone (< 200)	10 (38)	16 (62)	16 (62)
Did not own cell phone (< 200)	4 (29)	11 (79)	8 (57)

Note: P-values represent Exact McNemar tests for viral suppression indicating differences from baseline. Participants who did not complete a visit at 48 weeks were considered non-virologically suppressed. Statistical tests were not performed for subgroups given small cell counts.

* $p < 0.05$,

** $p < 0.01$

† Excluding 7 participants who reported blood transfusion (2) or unknown (5) mode of transmission