

Development and Pilot Testing of Daily Interactive Voice Response (IVR) Calls to Support Antiretroviral Adherence in India: A Mixed-Methods Pilot Study

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Abstract This two-phase pilot study aimed to design, pilot, and refine an automated interactive voice response (IVR) intervention to support antiretroviral adherence for people living with HIV (PLH), in Kolkata, India. Mixed-methods formative research included a community advisory board for IVR message development, 1-month pre-pilot, post-pilot focus groups, and further message development. Two IVR calls are made daily, timed to patients' dosing schedules, with brief messages (<1-min) on strategies for self-management of three domains: medical (adherence, symptoms, co-infections), mental health (social support, stress, positive cognitions), and nutrition and hygiene (per PLH preferences). Three ART appointment reminders are also sent each month. One-month pilot results ($n = 46$, 80 % women, 60 % sex workers) found significant increases in self-reported ART adherence, both within past three days ($p = 0.05$) and time since missed last dose ($p = 0.015$). Depression was common. Messaging content and assessment domains were expanded for testing in a randomized trial currently underway.

Keywords Antiretroviral adherence · Intervention · Interactive voice response · Mobile phone · India

Introduction

India has one of the largest populations of people living with HIV (PLH) in the world, estimated at 2.09 million [47], second only to South Africa. High adherence to antiretroviral therapy (ART) remains a challenge for PLH globally, with approximately 62 % of PLH reporting ≥ 90 % adherence across studies and regions [28], and estimated at 70 % in India [24]. India has made significant investments in offering universal access to ART, but has limited resources to provide behavioral counseling for adherence, prevention, and self-management support that is typical in high resource settings. Although newer ART regimens may not require 90 to 95 % adherence rates for efficacy [2], such high rates remain the typical target in research and intervention programs [28]. In a typical twice-a-day regimen, 90 to 95 % adherence translates to missing only three to six doses in a month, which could jeopardize treatment efficacy, particularly if missed doses occur over two or more consecutive days [10, 29]. Support for ART adherence must become integrated into the daily routines of PLH.

Mobile phones are integrated into our daily routines and have proliferated rapidly over the last 5 years in low-resource settings, approaching 100 % penetration rates, even among low-income individuals [25]. Mobile phone "teledensity" (i.e., proportion of mobile phones to population) has reached 140 % in urban India and 40 % in rural areas [45]. These always on, always carried, communication tools are creating many new opportunities to provide low-cost, massively scalable, disruptive innovations to support HIV treatment and prevention [33]. Traditional behavioral counseling modalities are costly, difficult to access and deliver, and typically do not result in sustained changes over time [41, 42]. Automated, mobile phone

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interventions have the potential to reach PLH at any time and location and be sustained for extended periods, or as needed on-demand, at relatively low costs. This paper reports on the mixed-methods formative development, pilot testing, user-experience feedback, and iterative development of an automated interactive voice response (IVR) intervention for adherence and self-management support for PLH in Kolkata, India.

The emerging evidence-base on automated electronic reminders (e.g., pagers, text-messaging) for medication adherence finds promising results for short-term effectiveness in about half of studies identified [48], including for antiretroviral adherence [7, 38, 49]. Non-automated telephone reminder interventions have also demonstrated efficacy in randomized controlled trials (RCTs) in the United States [11], but the two efficacious studies identified also included counseling follow up by a nurse [31] or social worker [16]. Three RCTs to date have assessed short message service (SMS) reminders for ART adherence in low resource settings. Two studies in Kenya demonstrated efficacy in improving ART adherence with newly initiated ART patients via a simple weekly SMS query or reminder (e.g., “Are you well?” or “This is a reminder”) over 12-months [18, 30]. One study also included healthcare worker follow-up by telephone if responses to the SMS query were not received [18]. A third trial in Cameroon with a smaller sample and 6-month follow-up period reported no efficacy for improved adherence with weekly SMS reminders with more diverse messaging content, but also not with newly initiated ART patients [20]. These SMS interventions notably required some degree of functional and technological literacy to use SMS, which impacted study eligibility and intervention efficacy, as identified in a patient-level meta-analyses of these three studies [21]. Other potential limitations of mobile phone delivered intervention include possibility of phones being shared, turned off, or out of range for reception, but the potential ubiquity and scale of the delivery platform still holds great potential.

In India, two other mobile phone ART adherence interventions have been tested or are under way, both using IVR primarily instead of SMS. One, non-experimental cohort study found that optimal (i.e., 90 %) adherence rates increased from 81 % of participants at baseline to 91 % at 6-months [32]. The intervention used a weekly IVR query on whether ART was missed in the previous day and a weekly picture SMS as a second reminder. The study found preference for IVR over picture SMS, and text SMS infeasible due to functional and technological literacy limitations. Another project, called TAMA, has developed a more complex daily IVR ART reminder, reporting, and information system that provides detailed menus for information seeking and sharing (e.g., symptoms and side effects), accessing test results, and requesting healthcare

provider follow-ups using a personal identification number (PIN) to access the system and protect confidentiality [15]. Although meta-analyses of nine SMS interventions in other settings identify greater effects for weekly versus daily messaging to support ART adherence [21], user feedback in the TAMA project in India found that PLH preferred daily messaging over weekly messaging [15].

The current study further examines the potential of daily messaging for ART adherence. In addition, most of the IVR and SMS interventions for PLH implemented to date have had a relatively simple and narrow focus on reminders for ART adherence. Although forgetfulness is a commonly cited reason for non-adherence, many other factors are also associated with adherence such as depression, social support, stigma, substance use, treatment beliefs, provider relationships, and to a lesser extent, structural barriers such as costs and accessibility [17, 23, 24, 27]. In high-resource settings like the United States, these multiple factors are typically addressed by effective ART adherence interventions [19, 37, 41, 42] and evidence-based “prevention for positives” interventions [6, 14, 34]. A narrow focus on medication reminders may miss opportunities to support other aspects of self-management of HIV/AIDS in addition to treatment adherence [5, 44]. Therefore, the current study also fills a gap in the literature by developing a simple and broadly accessible IVR messaging intervention for PLH with content focusing on multiple domains of self-management in addition to adherence reminders.

Methods

Collaboration and Funding

This study is a collaboration between researchers and intervention specialists at UCLA, the Sonagachi Research and Training Institute (SRTI) in Kolkata, India, and Dimagi Inc., a mobile health company specializing in development and applications of mobile health technologies globally. SRTI is a unit of Durbar (www.durbar.org), a community-based organization led by a collective of sex workers. SRTI, or the Sonagachi Project, has been an innovator and leader in HIV prevention and community development programs in India since 1992. Dimagi provided technical engineering support, programming, server hosting, and coordinating with an IVR service provider. The intervention was also based on a prior pilot conducted with Dimagi in the United States that used SMS and engaging but non-HIV-related messaging content [12].

The study proposal was funded by an Indo-US bilateral R21 funding mechanism, a collaboration between the National Institutes of Health (NIH) and the Indian Council of Medical Research (ICMR). Parallel proposals were

submitted to NIH and ICMR, which were peer-reviewed independently and then jointly. The study was reviewed and approved by the Durbar Ethical Review Board and the UCLA Institutional Review Board.

Pilot Study Aims

The pilot study phase had four primary aims: (1) assess feasibility, acceptability, and technological functioning of the IVR intervention; (2) preliminarily assess intervention impact on self-reported ART adherence and related factors; (3) assess engagement and user fatigue in terms of answering, listening to, and responding to IVR calls; and (4) gather user-experience feedback to iteratively develop the intervention for the RCT. In addition, the number of initial messages was limited to assess whether repetition of messages during the 1-month pilot would result in decreased engagement in answering and listening to messages.

Theoretical Underpinnings

Two broad theoretical perspectives guided intervention development, self-determination theory [36] and common factors of core elements in evidence-based interventions [35]. Self-determination theory (SDT) focuses attention on social-contextual factors that influence motivation, self-regulation, mental health and well-being, such as competence, autonomy, and social relatedness. SDT guided decisions to enable participants to schedule and opt in and out of different message types and to incorporate the Community Advisory Board's (CAB's) and pilot users' feedback to add nutrition and hygiene messages in lieu of sexual and alcohol risk reduction messages. Common Factors is a syncretic meta-theoretical approach to intervention design, similar to the information, motivation, and behavioral skills (IMB) meta-theory [8], which highlights motivating framing, applied information, feel-think-do skills (i.e., cognitive-behavioral and affective), but also adds emphasis on addressing barriers, social support, and sustainability. Common Factors was used in this study because it is grounded in the HIV prevention evidence-base and was developed to apply across contexts and targeted outcomes [35]. Technology design was guided by participatory design principles [40] which influenced plans for CAB and pilot study feedback, and by similar user experience design principles [9] that emphasize user feedback based on actual use of technology rather than anticipated preferences of hypothetical scenarios.

Intervention Mechanism Hypotheses

The intervention has three potential mechanisms of action. Most simply, the twice a day calls function as alarms or

dosing reminders, regardless of whether or not a call is answered. Second, the aim of the messaging content is to be engaging for participants to sustain their participation and prevent burnout and fatigue. Third, messaging content aims to inform, motivate, and influence behaviors to support improved adherence and potentially related factors such as social support and depression.

Community Advisory Board

A CAB of PLH was formed to guide formative development of the intervention and messaging content. The CAB members were invited from the Mamata network of positive women (MNPW), a peer support network comprised of sex workers, their male partners (clients and/or husbands/boyfriends), and other non-sex worker residents of communities served by Durbar. MNPW member networks are seeded from clients of Durbar's Mamata Care and Treatment Center (MCTC), a HIV voluntary counseling, testing, and treatment linkage center staffed by peer sex worker community health workers. Fourteen PLH volunteered to participate in the CAB, including several men and women not engaged in sex work. Three meetings were convened to participate in formative development of the intervention during year 1.

Pilot Intervention Messaging and IVR System Design

An initial set of 40 messages was developed with the CAB for pilot testing the IVR system. Message topics included medication adherence, healthcare provider communication, nutrition, hygiene, active coping, positive cognitions, social support, relaxation, and a few messages on alcohol, condoms, and STI. Cognitive-behavioral messages were also adapted from two SMS-based RCTs for depression prevention [50] and comorbid depression and alcohol use disorder [1]. Messages were recorded in Bengali (local language) and Hindi (common national language), and in male and female voices to match participant gender to minimize adverse responses from spouses or partners. Message durations averaged 40 seconds (range 33–44 seconds). A query played at the end of each call ("Did you like this message? Press 1 for yes, 2 for no"), to test the IVR functionality and assess in-the-moment message preferences. Messages were randomly sorted into a queue that was the same for all participants. If a call was not answered, the IVR system made two more attempts at 5-min intervals. Once a call was answered, the next message in the queue played at the next call. Three appointment reminder messages were also sent at 7, 2, and 1 day prior to the scheduled 1-month follow-up assessment as a proxy for monthly ART Center appointment reminders.

Calls were timed based on each participant's morning and evening ART dose times as reported in the baseline interviews collected on smartphones, which automatically links data to the IVR system in real-time. The baseline assessment also included queries to adjust the call times if the default ART dosing time was not acceptable, and the preferred time for the separate appointment reminder calls.

Pilot Study Recruitment and Eligibility

Participants for the pilot study were recruited from the Durbar Mamata network. Eligibility criteria included aged 18 years or older, confirmed HIV+ serostatus, currently taking ART, able to provide voluntary informed consent, and a client or member of the MCTC or MNPW.

Baseline and Follow-Up Surveys

Participants were surveyed on ART attitudes and adherence, social support, HIV-status disclosures, sexual behaviors, alcohol use, mental health, and messaging preferences. The follow-up survey was administered 4 weeks after the baseline survey with nearly identical content, but with timeframe for recall questions covering the past month instead of past 2 months as in baseline in order to capture only the follow-up period. Unless stated otherwise, all questions were developed by the India team with an international consultant for a preliminary ART adherence survey conducted prior to the funding of the current study. A major concern of the India team was survey burden based on experiences in the preliminary adherence study, therefore, brief measures were prioritized for this pilot study. Specific measures include the following:

AIDS Clinical Trial Group (ACTG) Adherence Measures [4]

In addition to querying doses missed over past 3 days and the prior weekend, the measures include assessment of related domains such as treatment barriers and beliefs.

Alcohol Use AUDIT-C [3]

Alcohol use was assessed with an adaptation of the AUDIT-C problem drinking screening, which includes general frequency of consuming alcohol and problem drinking.

Hospital Anxiety and Depression Scale (HADS; [43])

The HADS is a brief mental health measure consisting of 14 items with seven items each assessing anxiety and

depressive symptoms using a 4-point likert response scale from “not at all” (0) to “most of the time” (3). The HADS has good reliability and validity with more detailed mental health measures and has been used cross-culturally in many settings including India [13, 26, 46]. The HADS was translated into Bengali and tested in a prior pilot study with sex workers at Durbar.

Sexual Behaviors

Questions were adapted from the India team's annual point prevalence and risk behavior surveys with sex workers. Questions included whether participants had none, one, or multiple partners; marital and HIV status of primary partner (if applicable); and “How often you used condoms” with primary and other partners (two questions) with response options ranging from “Never (0)” to “Regular—100 % (3).”

Route of HIV Transmission

Four questions assessed potential source of HIV acquisition by asking, “Have you ever...” “paid for sex services?,” “injected drugs?,” “had sex with another man (for men)?,” and “had a blood transfusion?”

Social Support

Social support for taking ART was measured with one item from the ACTG measure asking, “To what extent do your friends or family members help you remember to take your medication? Not at all (0) to A lot (3).” Six other social support for ART questions were also asked. One question asked, “What is the attitude of your family members about taking ART?” with response options for “Family members do not know HIV-status,” “Discourage to take medicine,” “Angry and irritating,” “Cold,” or “Positive/encouraging.” Five questions asked “What sort of support you receive from each of these other types of relations for taking ART?” for neighbors, colleagues/coworkers, friends, extended family, and HIV-positive peers with response options “No support, discriminating, emotional support, and financial support.” Responses for “Discriminating” and “Financial Support” were rare (i.e., one and three, respectively), so variables were dichotomized as support for taking ART or not.

HIV Status Disclosures

Ten questions assessed disclosure, including, if spouse/partner knows HIV status, number of children and household members that know, recent active and passive

disclosure (i.e., “have you disclosed” and “did anyone find out other ways,” respectively), and if there were problems or benefits resulting from disclosures.

HIV-Related Stigma

Several questions indirectly assessed stigma-related factors, such as, how many household members the participants has to hide ART from, experiencing problems from disclosures, perceived non-acceptance of HIV-status by spouse/partner and children, and a “discriminating” response option in the social support questions.

IVR Call Log and Response Data

The IVR system automatically logs and time-stamps call attempts, calls answered, message number, duration of call and responses to an IVR query at the end of each message, “Did you like this message, press 1 for yes or 2 for no.” Web-based, downloadable reports are available in real-time for monitoring system functioning, individual participant IVR message exposure, and IVR responses.

Focus Group Discussions

After the follow up interviews, all participants were invited to participate in focus group discussions (FGD). Four FGDs were conducted with a total of 22 participants with up to 8 study participants in each FGD. Discussion began with an open-ended and non-directive question, “First, share with us your feedback and experiences with the IVR messages.” More directive probes were used as discussions waned, which included: what liked most about the messages, what liked least, what problems were experienced, concerns or worries, suggestions for message topics and content, and suggestions for the system more broadly. The focus group discussions were audio recorded, and transcribed.

Statistical Data Analysis

Statistical analyses were conducted in SAS version 9.3 [39]. Simple frequency distribution methods (means, mode, ranges, and standard deviations) were used to analyze the baseline survey. The follow-up survey was analyzed with pre-post comparisons using McNemar’s tests for dichotomous variables, Wilcoxon ranked-sum tests for count variables, and T-tests for means comparisons. Visual plots and frequency distributions were examined for IVR call data.

Qualitative Data Analysis

The four transcribed FGD were coded in Atlas.ti (version 7.5, Berlin, Germany) using a grounded approach working

from the data to identify key themes or descriptive codes and subthemes within the data [22]. Key themes were informed both by the themes outlined in the description of the FGD above but new themes and subthemes emerged based on issues raised by the participants. These themes and subthemes were developed by a trained research assistant in consultation with the anthropologist leading the data coding and analysis. The code book developed was reviewed and revised in consultation with the PI. Revisions were based on consensus agreement among the team. Key themes included study participation experience, HIV concerns, clinic service issues, and messaging recommendations. We then ran analyses to identify major trends and associations in the coded data.

Results

CAB Feedback on Intervention Design

The original aims of the study proposed to focus on sexual risk behaviors, substance use, and mental health and coping strategies, in addition to ART adherence, however, the CAB advised that drug and alcohol abuse were not significant problems in their communities. Furthermore, messages on HIV or ART, alcohol, condom use, and sexually transmitted infections (STIs) were not likely to be acceptable due concerns around to stigma, disclosure, and children answering calls. The CAB also advised that information on nutrition and hygiene was desired, and that depression was a significant problem for their peers. Finally, the potential feasibility of personal identification numbers (PINs) was discussed, that is, an IVR call is received and first a PIN needs to be entered before the message content plays. This would further protect privacy but also allow messaging content that specifically mentioned HIV and other potentially stigmatizing domains. The CAB was confident that most of their peers could not remember or use PINs. Furthermore, it would be a barrier to being exposed to the IVR messages more broadly because action would be required to enter a PIN and it would be easier to ignore the call.

Baseline Demographic and Background Factors

Over a 2-month period, from July to August 2013, we enrolled 46 participants, approximately half of the PLH on ART in the Mamata network. Table 1 shows demographic characteristic details. Participants were primarily female (80 %; n = 37 of 46). The mean CD4 count at last test (within prior 6 months) was 473 cells/ml (SD 225, Range 123–1,001 cell/ml). Route of HIV acquisition was primarily from heterosexual partners, with 16 participants reporting having a blood transfusion in lifetime, only one

Table 1 Demographic and background characteristics of participants at baseline (n = 46)

	n	%
Age in years (mean, range)	36	[22, 65]
Female	37	80.40
Highest level of education		
Illiterate	18	39.10
Literate (can sign name, not necessarily reading)	12	26.10
Class 5	9	19.60
Class 10	7	15.20
Present profession		
Unemployed	2	4.55
House wife	2	4.55
Professional	2	4.55
Sex worker	30	68.18
Daily labourer	3	6.82
Other	9	20.45
Household Situation		
Live with others?	29	63.04
Live with your children?	15	32.61
Have a spouse / partner?	24	52.20
Live with spouse / partner?	18	75.00
Spouse / partner is HIV+?	12	50.00
Others sometime answer phone (If yes, who else?):	12	26.70
Parents	2	18.20
Spouse	7	63.60
Children	6	54.50
Others	2	18.20
Perceived attitude of family members-towards ART		
Family members do not know HIV status	22	47.8
Cold	1	2.2
Positive / encouraging	23	50.0
Years since HIV diagnosis (mean, SD; range 2 months to 16 years)	4.59	4.37
Years since initiate ART (mean, SD; range 0–11 years)	2.07	2.58
Last CD4 Count (mean, SD; range 123–1,001 cells/ml)	473	225
How long to travel from home to ART center?		
Less than 50 min	27	58.70
30–60 min	9	19.57
1–2 h	4	8.70
Greater than 2 h	6	13.04
How often go to ART center?		
Monthly	28	60.87
Every 2 months	17	36.96
Barriers (“Difficulties”) collecting medicine		
None	23	43.40
Long waiting hours in the hospital	14	26.42
Cost of travel	0	0.00
Attitude of medical doctor	3	5.66

reporting a history of intravenous drug use, and none of the men reporting having sex with other men. Six of nine men reporting paying for sex services in lifetime but only one recently, and none were sex workers. PLH had been on ART an average of 2 years and diagnosed about 4.5 years ago (range up to 16 years).

Education, Occupation, Income

Participants had low levels of education with 39 % illiterate, another 26 % with no formal education, only 16 % completing class 10 or above (i.e., 10th grade, considered equivalent to high school graduation in India). Most were female sex workers (65 %) but also housewives, daily laborers, and professionals. Participants were from the lower end of the socioeconomic spectrum and the breadwinners in the household. All participants but one had their own personal mobile phones, but 27 % reported that other people sometimes answer the phones, primarily spouses or children.

Household Composition, Social Support, and HIV Status Disclosure

Most participants (63 %) lived with others, including one-third with their children and one-third with a partner or spouse (shown in Table 1). HIV-status disclosure was modest but not universal. About 65 % reported having PLH peers who knew their HIV-status and 25 % reported that co-workers, neighbors, friends, or family knew their HIV status. Of those with spouses/partners (52 %), almost all (92 %) were aware of the participant's HIV-status and half of spouses/partners were also HIV-positive. None reported not being accepted by partners/spouses for their HIV status. Of the 12 PLH with children who knew their parent's HIV status (26 % overall, 2/3 of those with children), none reported not being accepted by their children because of their HIV status. Only five PLH reported recent active HIV disclosures within the past 2 months at baseline with three at follow up. There were seven recent passive disclosures at baseline and five at follow up.

Structural Barriers to ART Adherence

Also shown in Table 1, about 57 % of PLH reported structural barriers to adherence. The primary barriers to receiving ART medications were long waiting lines at the ART centers followed by issues related to perceived provider attitudes or disclosure concerns. The majority of participants lived within 30 or 60 min travel to their ART center and had monthly or bi-monthly appointments, but 13 % lived more than 2 hours away. None reported missing doses because the ART center had short supply.

Pre-Post Follow-Up Results

Table 2 shows results of primary outcomes of ART adherence and messaging preference variables. Table 3 shows alcohol use, condom use, and mental health results with potential changes from baseline to follow.

ART Adherence, Attitudes, and Social Support

Self-reported missed doses decreased by two ACTG adherence measures, as shown on Table 2 and in Fig. 1a and b. Missing any dose in the past 3 days decreased from 39 to 18 % of participants by follow-up. Also, the time since last missed a dose increased (Fig. 1b), for example, with the majority of participants (52 %) reporting last missed dose 1–3 months ago at follow-up compared to 44 % reporting last 1–2 weeks at baseline. Reasons for missed doses also decreased from about 44 % to about 17 % for “being busy” and “concerned others might see” (see Table 2). Reports of social support for taking ART also decreased except for increasing with HIV-positive peers. There were no significant changes in other related variables, such as reasons for missing or stopping ART, side effects, nor ART attitudes (e.g., resistance, optimism).

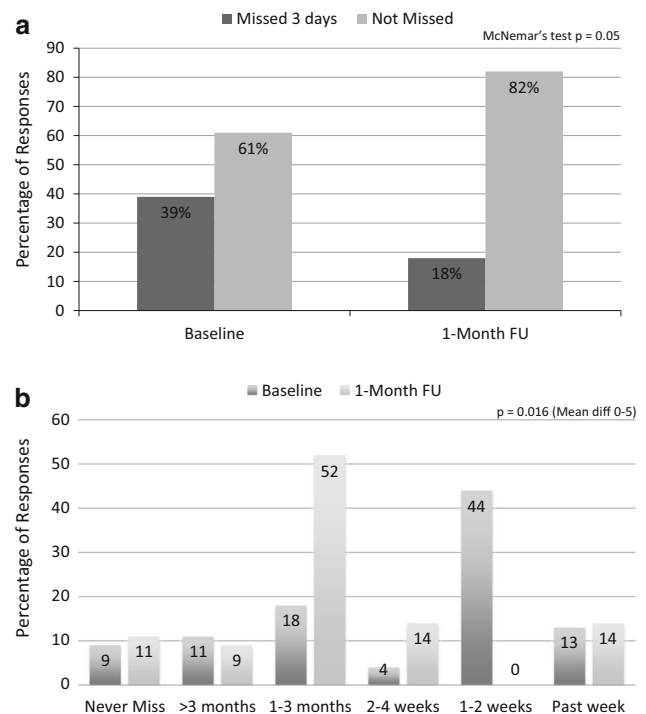


Fig. 1 **a** Missed any ART dose today or past 3 days. **b** How long ago last missed dose (%)

Messaging Preferences

Only four participants preferred to receive HIV-specific messages at baseline and follow up. Almost all participants preferred general health messages at baseline (98 %) and follow-up (100 %). Table 2 shows other messaging preference results. Briefly, potential disclosure concerns increased slightly but not significantly, by about 10 % from baseline to follow-up. Notably, the proportion of people who anticipated the potential for problems from receiving general health messages being overheard or answered by others increased from 20 % at baseline to 48 % at follow-up ($p = 0.05$). The proportion of participants wanting to receive messages timed to their doses also increased from baseline to follow up. The proportion of participants wanting to receive messages about medication usage and importance of high adherence decreased somewhat from baseline (98 %) to follow-up (91 %), but not statistically significant and still strongly supported.

Alcohol Use

Table 3 shows alcohol use reports increasing at follow-up. There was a non-significant trend in increased reports of recent alcohol use from 44 % at baseline to 55 % at follow up, and a statistically significant increase in frequency of recent drinking comparing means treating the seven categorical responses as an approximately continuous scale. The trend is a result of fewer “never” drinking reports at follow but toward occasional drinking rather than increased daily drinking reports.

Sexual Behaviors and Condom Use

About half (52 %) the participants reported a steady sexual partner and over half of those ($n = 13$) were HIV+. About half (52 %) also reported multiple sexual partners in the past 2 months. There were trends for lower reports of condom use based on mean comparisons of likert-response options, primarily reflecting reports of “regular (100 %)” condom use decline with primary partners (68–39 %) and other partners (88–75 %) from baseline to follow up.

Mental Health

Table 3 also shows depression, but not anxiety, increasing significantly from baseline to follow-up via increases in mild and moderate levels of depression from none.

IVR Message Query Approval Responses

IVR call preference responses (i.e., in response to “Did you like this message? Press 1 for Yes or 2 for No”) were

primarily positive. All but one message had 84–100 % “yes” responses. The message with the lowest approval rate (76 % yes vs. no responses) was the longest message and mentioned sharing both positive and negative events with social supports. There were no observable trends in differences in message content for messages with 100 % approval ratings compared to messages with 85–90 % approval ratings.

Focus Group Discussions

Four FGDs included 22 of the 46 pilot study participants. Thirteen female FGD participants identified as sex workers, two as retired sex workers, and three as housewives. Four were male clients of sex workers (not primary partners). Their ages ranged between 28 and 60 years with over half in the 30s. Two focus groups were all female and two had two men each. The dominant themes in the discussions were instrumental technical challenges, concerns about privacy and disclosure, preferences for non-HIV specific messages on health and wellness, and the medication reminder functions.

Instrumental Technical Challenges

Focus group discussions identified that participants with low call answer rates ($n = 3$ participants total) were due to poor reception issues due to the location of their home or the quality of their phone, for example,

Actually I live in such a damp room and I do not get mobile tower that is why I was not able to hear any messages. [FGD 2, Male, 30, Client]

I had a Nokia mobile. But my son broke the phone and I had to buy a Micromax phone. Since then I am facing this mobile connectivity problem. [FGD 3, Male, 30, Client and Primary Partner]

In addition, prompted discussions explored feasibility of responding to IVR queries. Participants who did not respond to queries (i.e., by pressing 1 for yes or 2 for no) had low literacy and could not reliably demonstrate their recognition of the roman numerals on their phones, which also led to discussions about the infeasibility of using and remembering PINs for many PLH.

Privacy and Disclosure Concerns

The greatest challenge participants reported centered on other family members or friends accessing their phone. For those living with others to whom they had not disclosed their HIV status, others potentially answering their phone or overhearing

Table 2 Antiretroviral adherence and related variables, over 1-month

	Baseline (n = 46)		Followup (n = 44)		Difference	
	n	%	n	%	+/-	<i>p</i> value ^a
Missed any ART doses in past 3 days?	18	39.1	8	18.2	–	0.050
Last time missed taking any medications?						
Median on 0–5 scale from days to months	4		2		–	0.015
Missed dose recently because:						
Other might notice medication	20	43.15	7	15.9	–	0.005
Felt drug was harmful	5	10.9	4	9.1		
Busy with other things	20	43.5	8	18.2	–	0.005
Change in daily routine	11	23.9	13	29.5		
Had no medicine	1	2.2	1	2.3		
Out of home	11	23.9	13	29.5		
Stopped taking medication recently because...						
Felt better?	1	2.2	1	2.3		
Felt worse?	3	6.5	8	18.2	+	0.096
Difficult to remember whether have taken medicine?	22	47.8	21	47.7		
Receive support for taking ART from:						
HIV+ peers	35	76.1	44	100.0	+	
Neighbors?	18	39.1	10	22.7	–	0.046
Colleagues/coworkers?	19	42.2	12	27.3	–	0.020
Friends?	20	43.5	17	38.6		0.405
Extended family?	14	30.4	4	9.3	–	0.020
Friends or family help remind you to take medication?						
Not at all (0)	17	37.0	18	40.9		
A little (1)	5	10.9	5	11.4		
Somewhat (2)	4	8.7	8	18.2		
A lot (3)	20	43.5	13	29.5		
Mean, SD	1.59	1.37	1.36	1.29		0.383
Think HIV in your body will become resistant if not adherent?						
No	3	6.5	7	15.9		
Do not know or not sure	1	2.2	0	0.0		
Yes	42	91.3	37	84.1		
How sure ART has positive effect on health?						
Not at all (0)	5	10.9	1	2.3		
A little (1)	8	17.4	3	6.8		
Somewhat (2)	8	17.4	14	31.8		
A lot (3)	25	54.3	26	59.1		
Mean, SD	2.15	1.07	2.48	0.73		0.079
Suffered side effects from medications recently?	20	43.5	14	31.8		0.197
Messaging preferences						
Think other people around could hear messages?	10	21.7	13	29.5		0.406
If overheard HIV-specific message, possible problems?	37	80.4	40	90.9		0.480
If overheard general health message, could result in problems?	9	19.6	21	47.7	+	0.050
Want medication messages (e.g., importance of high adherence)?	45	97.8	40	90.9		0.180
Want to receive messages at time take medication?	16	34.8	29	65.9	+	0.001
Want ART center appointment reminders?						
No	2	4.3	1	2.3		
Yes, if no mention of ART or HIV	21	45.7	34	77.3	+	
Yes	23	50.0	9	20.5	–	0.007

^a Unless otherwise noted, *p* values are calculated using McNemar's test for binary variables, Wilcoxon signed-rank test for ordinal variables, and paired t-tests for continuous variables

Table 3 Potential secondary outcome variables and changes over 1 month

	Baseline (n = 46)		Followup (n = 44)		Difference	
	n	%	n	%	+/-	p value ^a
Alcohol						
Drink alcohol, ever?	35	76.1	29	65.9		0.157
Drank alcohol, recently?	20	43.5	24	54.5		
How often drink alcohol?						
Never (0)	15	42.9	5	17.2		
During festivals (1)	11	31.4	8	27.6		
Once a month (2)	1	2.9	3	10.3		
2 or 3 times a month (3)	5	14.3	7	24.1		
Once or twice a week (4)	3	8.6	4	13.8		
3 or 4 times a week (5)	0	0.0	1	3.4		
Nearly every day (6)	0	0.0	0	0.0		
Daily (7)	0	0.0	1	3.4		
Mean, SD	1.14	1.35	2.17	1.73	+	0.013
On days drank recently, how many drinks? (mean, SD)	2.6	1.8	3	1.8		0.567
How often 5+ drinks within 4 h, recently?						
Never (0)	17	85.0	14	58.3		
Once a month (1)	0		4	16.7		
2 or 3 times a month (2)	3	15.0	2	8.3		
Once or twice a week (3)	0		2	8.3		
3 or 4 times a week (4)	0		1	4.2		
Daily (5)	0		1	4.2		
Mean, SD	0.30	0.73	1.00	1.59	+	0.0952
Condom use						
With primary partner recently?						
Never (0)	2	10.5	4	30.8		
Sometime (less than 50 %) (1)	2	10.5	1	7.7		
Often (greater than 50 %) (2)	1	5.3	2	15.4		
Regular (100 %) (3)	13	68.4	5	38.5	-	0.010
Mean, SD	2.39	1.09	1.67	1.37		0.168
With other partner recently?						
Never (0)	0		1	4.2		
Sometime (less than 50 %) (1)	1	4.2	4	16.7		
Often (greater than 50 %) (2)	2	8.3	1	4.2		
Regular (100 %) (3)	21	87.5	18	75.0		
Mean, SD	2.83	0.48	2.50	0.93		0.110
Mental health (HADS)						
Total score (mean, SD)	16.5	6.3	18.4	5.8	+	0.047
Anxiety (total) (mean, SD)	7.1	3.9	7.2	3.7		
Depression (total) (mean, SD)	9.4	3.6	11.2	3.0	+	0.002
Depression (level)						
None (<8)	17	37.0	4	9.1		
Mild (8–10)	12	26.1	15	34.1		
Moderate (11–14)	13	28.3	21	47.7		
Severe (≥15)	4	8.7	4	9.1		
Median (depression score)	9		11.5		+	0.004

^a p values are calculated Using McNemar's test for binary variables, Wilcoxon signed-rank test, for ordinal variables, and paired t-tests for continuous variables

calls resulted in preferences to not receive messages that specifically mention HIV or sexual behaviors, for example,

No one in my family knows anything about my HIV status. So it would raise certain issues of embarrassment for me. [FGD 1, Female 32, Sex Worker]

Some participants reported that they had disclosed their HIV status to their spouses or partners but had not yet disclosed to children.

Interviewer: What about your views on these (condoms and STIs) type of messages?

Sometimes my son picks up my phone and listen the message. I do not like messages on condoms and STIs. [FGD 2, Female, 28, Housewife].

My son might know about the disease but I also do not like messages on condoms and STIs. [FGD 2, Female 35, Ex Sex Worker]

Thus, even if they had disclosed to their children, some were still concerned about message content specifically mention HIV or sex. However, those who lived alone and/or had disclosed their HIV status to adults close to them were comfortable receiving messaging specifically mentioning STIs, HIV/AIDS, ART, etc. For example,

I don't have any problem receiving messages on condoms and STIs as I stay alone...If by mistake any one of my friends received the call then I tell them that the phone message has come from mobile company. [FGD 3, Female, 26, Sex Worker]

Preferences for General Health and Wellness Messages

Nearly all participants reported preferences for general health messages. Participants appreciated messaging related to hygiene, nutrition, physical and psychological wellbeing/health, as well as adherence reminders. For example,

I received messages such as, "Did you take water? Drink plenty of water", that one I liked most...I would like to receive...general messages which do not contain HIV or anything related to that. If by any chance any neighbour listened, it might create problems for me. [FGD 3, Female, 28, House Wife]

Responses to the prompted question about messages that were liked or preferred included,

I liked all of them, such as "take your medicine timely", "It is time to take your medicine", "eat more vegetables", "drink plenty of water", "stay

cheerful", "spend time with friends, so you would feel better". [FGD 3, Male, 65, Client]

I liked the message which reminds me to take my medicine, eat green leafy vegetables. [FGD 1, Female, 30, Sex Worker]

Medication Adherence Messages

Participants also noted that calls functioned sufficiently as reminders, without needing to hear a message. Participants noted that the reminders helped them be more consistent in taking their medications on time on a regular basis. For example,

Previously we hardly take our medicine at the right time but after receiving these messages we could take it on time. [FGD 1, Female, 38, Sex Worker]

Previously I was unable to take my medicines at the right time as I was busy with some household chores. The phone calls remind me to take my medicines. So I liked it. [FGD 3, Female 28, House Wife]

Although most participants appreciated medication reminder messaging, a few participants had mixed responses to medication messages that mentioned HIV. Similar feedback was given for the monthly ART center appointment reminder. For example,

Interviewer: So in that sense, should we send this type of message or its better not to send?

It's better to say doctor's chamber in place of ART [Female, 37, Sex Worker, FGD 4]

Agreed [Female, 40, former Sex Worker. FGD 4]

Finally, although burnout on repetition of messages did not emerge as a salient theme or subtheme in the focus group analyses, directed querying in the focus groups indicated that participants were aware of the repeated messages in the last 10 days of the pilot period. Responses suggested that message content be expanded to minimize repetition of messages over 2 months at least.

Final IVR Message Design

The IVR message set was expanded to 120 for use in the RCT. Messages were broadly categorized in three domains with about 40 messages each; medical, health promotion, and mental health. Medical messages focus on self-management of treatment (medication adherence, doctor communication), symptoms (nausea, diarrhea, dehydration), and co-infections (tuberculosis). Health promotion messages focus on nutrition and hygiene. Mental health

messages focused on positive cognitions, social support and stress reduction. Messages were randomized within specific category, then domain, and then formed into a queue alternating medical, mental health, and health promotion messages.

Message delivery design remains the same as the pilot, with two IVR messages per day (morning and evening, ideally timed to dosing schedule) and three ART appointment reminder calls. In addition, based on modest IVR responses and technical proof of concept, a weekly assessment IVR call was added that asks four yes/no questions on missing medication in prior week, experiencing symptoms, and two on depression (feeling hopeless, good spirits). Participants can opt-out or -into morning calls, evening calls, appointment reminders, or weekly assessment calls by calling the interviewer and making a request, which is being tracked as an outcome related to sustainability and burnout in the RCT.

Adaptation to IVR Regulatory Changes

Just prior to original date to launch the RCT in November 2013, the Telecom Regulatory Authority of India (TRAI) implemented a “do not disturb” phone number registration system to block commercial SMS and telemarketer calls (including IVR). In addition, no commercial calls can be made between 9 pm and 9 am, regardless of registry status. Protocols were adapted accordingly, including IVR design to fit within the 9 am to 9 pm timeframe if dose time or preferred call time is outside that range.

Discussion

This study demonstrates feasibility, acceptability, and potential efficacy of an automated IVR messaging intervention for improving ART adherence, and potentially related outcomes, via more comprehensive messaging content than has been examined previously. Overall there was high acceptability of the intervention, except for messages specifically mentioning HIV/AIDS and sexual risk behaviors. Less than 10 % (4 of 46) participants desired messages that specifically mention HIV/AIDS, sexual risk, or alcohol, but they also desired general health messages. IVR technology and Dimagi’s communication platform are designed to enable customized message banks tailored to participants’ preferences. However, since so few participants desired specific messages, we opted not to implement personalized messaging strategies at this time. Messaging preferences are being assessed in the RCT to gauge the potential scale of interest in specific messages and broader message domains in a larger sample for a future iteration of the intervention.

This study is further testing the potential of daily messaging, which one prior study using SMS found was less efficacious in improving adherence than weekly messaging [30] while another in India found preferences for daily versus weekly ART reminders by IVR [15]. Daily messaging that includes diverse and engaging messaging content may be more acceptable in some contexts, and may also be more efficacious in providing continuous support to prevent multi-day treatment interruptions that can impact viral suppression and which could occur between weekly reminders. The RCT currently underway is utilizing the weekly IVR query on adherence and symptoms in the control group, which will further elucidate the potential efficacy of weekly versus daily messages for adherence and related outcomes. In addition, it may not be sustainable or acceptable to continue to receive daily messages over an extended period of time for some PLH. The potential for burnout reflected in opt-out (and opt-in) requests, call answer rates, and IVR response rates are being tracked in the RCT over 6 months as a secondary outcome.

The primary limitations of this study are reliance on self-report only, short timeline, brief assessments, small sample size, and lack of control group, limiting statistical power and inferences on intervention effects. Self-report measures of adherence, in particular, have been found to be unreliable, but more objective measures were not feasible with funding in this pilot or the RCT. The RCT is collecting pills counts and provider’s adherence percentage ratings from medical charts, as well as baseline and 6-month follow up CD4 counts by enrolling participants at the date of one of their biannual routine CD4 count visits. Furthermore, feedback from the CAB and India research team emphasized that survey instruments needed to be brief, less than 60 min to administer, in order to limit burden of participation and ensure assessments were completed without fatigue and related potential biases in response. Therefore, brief measures were used and not all domains potentially targeted by the intervention were assessed in the pilot. Since the assessment burden in this pilot experience was not found to be problematic, the RCT assessment has been expanded to directly assess stigma, coping skills, and social support more robustly. A related limitation is the use of 2-month recall period at baseline and 1-month recall in the follow up to not have overlap with the baseline period, which makes comparisons less reliable in this analysis.

There were also somewhat counterintuitive results for increased reports of depressive symptoms and alcohol use at follow up, and decreasing social support for ART reports and trends for condom use. These results are likely due to a combination of social desirability at baseline relative to follow-up, and assessment reactivity (i.e., becoming more aware of behaviors after the baseline interview). Participants were

relatively naïve to research involving detailed questionnaires and the research team members were newly hired and not acquainted with the community. Trust and rapport likely increased at follow-up. Social desirability for depressive symptom reports was suggested by the research team as participants wanting to show a positive or aspirational image at first impression, followed by assessment reactivity and perhaps exacerbated by biases at follow up toward eliciting support in a context of a CBO service setting and intervention ending. Notably, themes related to depression did not emerge in the focus group discussions. Social support decreases were most likely due to assessment reactivity, reflecting on actual support received after querying in baseline assessment. Such trends are being closely monitored in the RCT.

Future directions of this line of research include tailored messaging content for those willing to receive messages specifically addressing HIV, alcohol use, sexual risk behaviors, and other sensitive topic domains. Other possibilities include incorporating the intervention more directly into ART treatment settings as is being done in the TAMA study in India [15], and linking data for healthcare provider or peer counselor follow up when participants do not answer calls or respond to weekly queries, as done some prior studies [16, 18, 31], although this was not suggested by participants in the study. The current intervention, however, is ultimately designed to be simple and broadly scalable, without burdening healthcare providers, and accessible to the large numbers of PLH on ART in India with low technical and functional literacy. Although this general messaging intervention approach is limited in that it does not directly address structural barriers to treatment and adherence (e.g., costs and supply limitations, distance to clinic, transportation, and healthcare provider attitudes), these were not common barriers in this formative study. The potential impact of this intervention on improved ART adherence is promising but whether or not other outcomes can also be impacted remains to be demonstrated.

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