

Effectiveness of a mHealth intervention with short text messages to promote treatment adherence among Mexican adults patients with HIV: A randomized clinical trial

Luis Eduardo Del Moral Trinidad, Jaime Federico Andrade-Villanueva, Pedro Martínez Ayala, Rodolfo Ismael Cabrera Silva, Melva Guadalupe Herrera Godina, Luz Gonzalez-Hernandez

Submitted to: JMIR mHealth and uHealth
on: February 19, 2024

Disclaimer: © The authors. All rights reserved. This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on its website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressly prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript..... 5
Supplementary Files..... 18
 Figures 19
 Figure 1..... 20

Effectiveness of a mHealth intervention with short text messages to promote treatment adherence among Mexican adults patients with HIV: A randomized clinical trial

Luis Eduardo Del Moral Trinidad^{1*} MPH; Jaime Federico Andrade-Villanueva^{2*} IDP, MCR; Pedro Martínez Ayala^{2*} IDP; Rodolfo Ismael Cabrera Silva^{3*} MSci; Melva Guadalupe Herrera Godina^{4*} phDPH; Luz Gonzalez-Hernandez^{2*} IMD, PhDIM

¹Universidad de Guadalajara Public Health Sciences Guadalajara MX

²HIV Unit Hospital Civil de Guadalajara "Fray Antonio Alcalde" Guadalajara MX

³Department of Medical Sciences University of Guadalajara Guadalajara MX

⁴Biomedical Sciences Research Institute Universidad de Guadalajara Guadalajara MX

* these authors contributed equally

Corresponding Author:

Luz Gonzalez-Hernandez IMD, PhDIM

HIV Unit

Hospital Civil de Guadalajara "Fray Antonio Alcalde"

Sierra Mojada

Guadalajara

MX

Abstract

Background: In 2022, 39 million people lived with HIV, and efforts target the 95-95-95 goal by 2030. In Mexico, key affected populations include men who have sex with men, drug users, sex workers, and transgender individuals. Adherence to treatment is vital, influenced by patient-provider relationships and access to care. eHealth interventions, notably SMS reminders, show promise in enhancing adherence.

Objective: To evaluate the effectiveness of a mHealth intervention on ART adherence amongst adult PLWHIV

Methods: A randomized clinical trial on adult patients who attended the tertiary care from the university hospital "Hospital Civil de Guadalajara – Fray Antonio Alcalde" to initiate ART. mHealth intervention included the use of short message service (SMS) to interact with the patient and as a reminder system for upcoming medical examinations or ART resupply during a 6-month period. A control group (n=40) received medical attention by the standard protocol used in the hospital. Intervention effectiveness was assessed by quantifying CD4+ T cells, viral load, and a self-report of adherence by the patient.

Results: The intervention group had greater adherence to ART than control (96% vs 92%, $p = < .0001$). In addition, the intervention group had better clinical characteristics, including lower viral load (141 cop/mL vs 2413 cop/mL, $p = < .0001$) and a tendency for a major number of CD4+ T cells (399 vs 290 cells/uL).

Conclusions: These results show that mHealth intervention significantly improves ART adherence. Implementing mHealth programs can improve the commitment of PLWHIV to their treatment. Clinical Trial: NCT05187741

(JMIR Preprints 19/02/2024:57540)

DOI: <https://doi.org/10.2196/preprints.57540>

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

☒ Please make my preprint PDF available to anyone at any time (recommended).

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.

Only make the preprint title and abstract visible.

No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain visible

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <http://www.jmir.org/preprint/57540>



Original Manuscript

Effectiveness of a mHealth intervention with short text messages to promote treatment adherence among Mexican adults patients living with HIV: A randomized clinical trial

Keywords: HIV, Treatment adherence, mHealth, randomized clinical trial, Mexico

Abstract

Purpose: To evaluate the effectiveness of a mHealth intervention based on short messages service (SMS) to increase ART adherence on adult PLWHIV.

Methods: A randomized clinical trial on adult patients who attended to the hospital “Hospital Civil de Guadalajara – Fray Antonio Alcalde” to initiate ART. mHealth intervention included the use of short message service (SMS) to increase adherence as a reminder system for upcoming medical examinations or ART resupply, this was given for a 6-month period. A control group (n=40) received medical attention by the standard protocol used in the hospital. Intervention effectiveness was assessed by quantifying CD4+ T cells, viral load, and a self-report of adherence by the patient.

Results: The intervention group had greater adherence to ART than control (96% vs 92%, $p = < .0001$). In addition, the intervention group had better clinical characteristics, including lower viral load (141 cop/mL vs 2413 cop/mL, $p = < .0001$) and a tendency for a major number of CD4+ T cells (399 vs 290 cells/uL, $p = .1526$).

Conclusions: These results show that mHealth intervention significantly improves ART adherence. Implementing mHealth programs can improve the commitment of PLWHIV to their treatment.

1. Introduction

On 2022, there were 39 millions of people living with HIV (PLWHIV), of which 37.5 million were over the age of 15 years. Most of the PLWHIV are female (53%) and 630,000 died from AIDS-related illness in that year (1). International efforts have been implemented to achieve the 95-95-95 goal by 2030. This goal aims for 95% of all PLWHIV to be aware of their HIV status, 95% of all diagnosed PLWHIV to be treated with antiretroviral therapy (ART), and 95% of treated PLWHIV to have an undetectable viral load (2).

The HIV landscape in Mexico reflects global trends, with key populations being men who have sex

with men, injection drug users, sex workers and transgender individuals. As of the close of 2020, there were 3,389 new HIV cases reported. Males accounted for 80.2% of cases and females 19.8%, with a gender ratio of 4:1 (2,3,5).

Adherence is not only an important pillar for achieving viral suppression but also prevents the spread of the disease in a community level. Moreover, it is a major player in improving the life quality of PLWHIV (3). The world health organization (WHO) defines treatment adherence as “the extent to which a person’s behavior taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (4,5).

Treatment adherence is complex and is influenced by the personal behavior that a PLWHIV has toward the disease, and the relationship the PLWHIV has with the health care provider and the health institutions (6,7). Several factors that impact treatment adherence have been described, including the patient's lack of understanding of the disease, the presence of treatment adverse effects, the lack of treatment efficiency as perceived by the patient, the trust of the patient to the indications prescribed by the health provider, financial and social availability to obtain ART, mental health, lack of support from the family or community, being young, among others (8,9).

Improving treatment adherence is beneficial to the overall health of PLWHIVH, by reducing disease progression, and the development of complications. In addition, treatment adherence is favorable for health systems as it reduces the number of infected patients, diminishes the need for specialized medical attention, reduces the need for alternative treatments due to treatment failure, and prevents patients' disability (10).

The literature has reported a wide range of interventions to improve adherence, including digital interventions also known as electronic health (eHealth). eHealth is defined as the cost-effective and secure use of information and communications technologies supporting health and health-related fields. An integral part of the eHealth is using wireless technologies like phones, tablets, and smartphones for public health, known as mobile Health (mHealth) (11).

eHealth and mHealth strategies have been proposed for many aspects of health services, including adherence, diagnosis, training, recruitment, follow-up, prevention, and guidance about the disease or treatment (12). In a systematic review analyzing 27 studies regarding the usage of mHealth for PLWHIV in low and middle-income countries, it was shown that 56% of the studies had a significant positive impact on treatment adherence. The most common intervention was the usage of reminders through short message service (SMS) (13).

One of the main reasons why SMS has been used is due to its extensive coverage in areas where wireless internet is not available. Additionally, SMS can be received by users even if they do not

have a data plan. This intervention allows patients to stay connected despite coverage limitations they may face. Thus, the aim of this study was to evaluate the efficacy of mHealth intervention based on short messages service to increase ART adherence on adult PLWHIV in contrast to standard medical attention.

2. Methods

We performed a randomized clinical trial in which we assessed the efficacy of using SMS to improve treatment adherence. PLWHIV were recruited from the HIV clinic of the tertiary care hospital 'Hospital Civil de Guadalajara – Fray Antonio Alcalde' from February to November 2022.

Inclusion criteria: The study included individuals who were diagnosed with HIV and had less than six months on ART therapy, both men and women aged 18 years or older. Additionally, participants should have a mobile device capable of receiving SMS-type messages and must willingly sign the informed consent to participate.

Exclusion criteria: Excluded from the study are individuals currently enrolled in another clinical trial, pregnant women, minors, individuals with a mobile phone capable of receiving SMS messages but lacking coverage or service in their residential area.

Using Openepi software, sample was calculated for 40 individuals to each group (control and intervention). Patients were recruited and assigned randomly among the control and treatment groups. Randomizations was done as it follows: a simple random allocation method was employed, utilizing a table of random numbers for patient assignment. Participants were assigned to either the intervention or control group based on whether their assigned number was even or odd, respectively. This straightforward approach ensured that each patient had an equal chance of being allocated to either group, enhancing the randomization process and minimizing selection biases.

Protocol was approved by the ethics committee in research of the Hospital Civil de Guadalajara' Fray Antonio Alcalde' with registry number 095/18 and registered on clinical trials (NCT05187741). All patients signed an informed consent prior to enrollment, this consent form provided complete information about the protocol and any concerns from potential participants were addressed before signing the informed consent.

2.1 Variables of the study

Sociodemographic variables were obtained at the time of recruitment with a form that was fill with the aid of the research team. Viral load and number of CD4+ T cells were measured at the time of enrollment and after the 6-month follow-up.

Self- adherence measure: This was measure at the six months follow up. For measuring adherence, the four-day adherence index was employed, which is calculated using the following formula:

$$\text{Four-day adherence index} = 1 - (\text{Forgotten pills} / \text{Prescribed pills}) \times 100$$

For the measurement of variables, employment was considered when patients reported engaging in paid work, whether formal or informal. Tobacco, alcohol, and illicit drug consumption were considered positive if patients reported consumption more than twice a week in the last month. The duration of living with HIV and the duration of antiretroviral therapy (ART) were calculated as of the study's completion date.

2.2 mHealth strategy

The intervention consisted of the following procedures: participants received two messages per week on Mondays and Thursdays in the morning. These messages were pre-validated by a research group, and their content can be found in the corresponding publication (14). Additionally, participants received reminder messages for appointments or prescription refills 24 hours before the scheduled date. Moreover, participants had the option to communicate with the researchers to address any queries, which were resolved through consensus among the research team with support from relevant departments. To ensure ongoing communication, the telephone line accepted collect messages and collect calls, enabling participants to stay connected throughout the study. The control group received the standard medical treatment offered in the hospital.

2.3 Statistical analysis

Proportions were analyzed by chi-squared and T-student for continuous variables. Relative risk based on treatment adherence (>95% or >90%) was measured and Fisher's exact test was implemented for statistical evaluation. A multivariate analysis was done to calculate relative risks of variables associated with adherence. All statistical analysis was performed on SPSS version 25 and a p-value of <.05 was considered significant.

3. Results

From 217 potential candidates, 80 patients fulfilled the inclusion criteria and agreed to participate in the study. The 80 participants were randomly assigned to the intervention or control group (40 in each). In each group, 2 participants were lost to follow-up, and 2 were removed from the study because they transferred to another clinical care unit. (Figure 1). Intervention and control groups had a median age of 31 and 37.5 years. Both groups were mostly men (95.5% and 92.5%, respectively). At the time of enrollment, the intervention group had more CD4+ T cells (227 vs 169 cells/uL) and

viral load (65,050 vs 57,800 copies/mL) than the control. In addition, the intervention had more days living with HIV and more days on ART when compared to control group (Table 1). Tobacco consumption was greater in the control group (37.5% vs 57.5%). Most of the participants were single, employed, and reported alcohol consumption (Table 1).

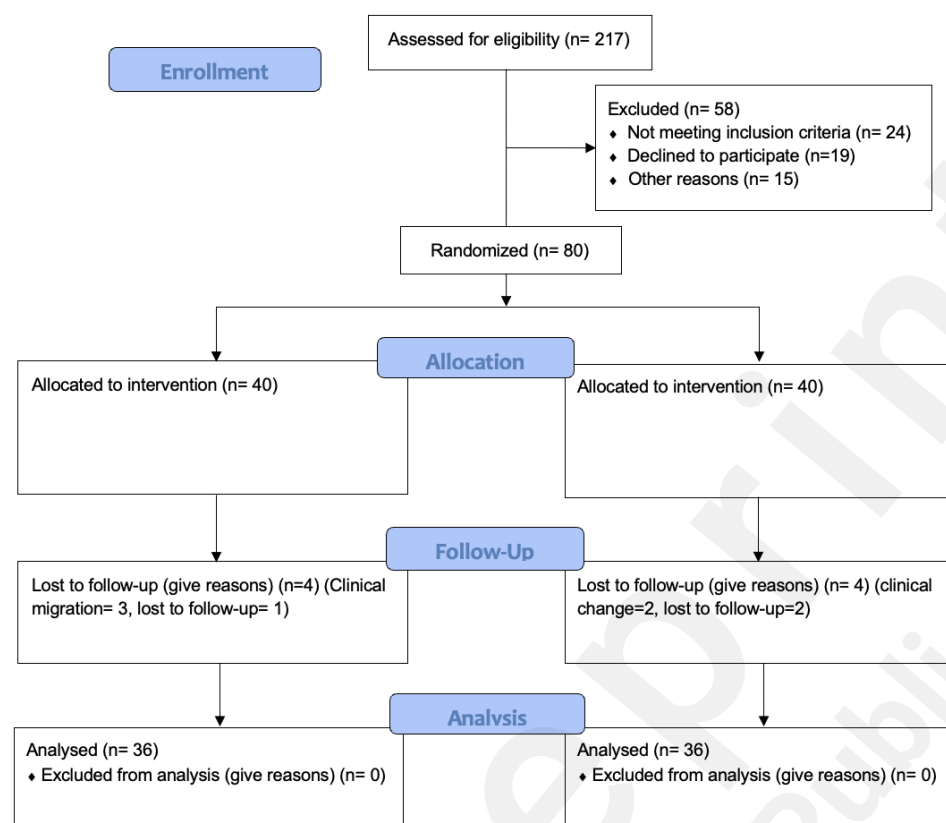


Figure 1. Flow diagram CONSORT flow diagram of the intervention.

Table 1. Participants' Clinical and Socio-Demographic Characteristics.

	Intervention Group (n=40)	Control Group (n=40)	p-value
Clinical Variables			
Age (years)	31.0	37.5	.0011
Median (IQR)	(27.8-36.0)	(30.0-49.5)	
Male n(%)	38 (95.5%)	37 (92.5%)	
Days after HIV Diagnosis	283.5	303	.5042
Median (IQR)	(58.3-519.3)	(101.3-1128)	
Day on ART	122	51	.7286
Median (IQR)	(15.75-192.3)	(19.75-171.0)	
CD4+ T cell count (cells/uL)	227	169	.0879
Median (IQR)	(88-435)	(25-291)	
Viral Load (copies/mL)	65,050	57,800	.4601

greater chance of reaching the desired adherence, almost 3 times more likely to reach a 95% adherence than the control (Table 3).

Table 3. Comparison on Treatment Adherence Among Groups

Group	>95% Adherence		RR	95% CI	p-value
	Yes	No			
Intervention	26	10	2.6	1.48-4.57	<.001
Control	10	26			

To identify if other variables impacted the probability of reaching 95% adherence, we performed a binary logistic regression of all analyzed variables. Aside from the SMS intervention, no other variables had statistically significant in reaching the 95% adherence (Table 4).

Table 4. Logistic Regression Variables To Reach 95% Treatment Adherence

Variable	Relative Risk	95%CI	p-value
Age >45 years	0.728	0.15-3.60	.693
Employed	0.392	0.10-1.41	.153
Tabaco Consumption	1.56	0.436-5.60	.492
Alcohol Consumption	2.31	0.59-8.98	.225
Use of Illegal Drugs	0.81	0.25-2.62	.730
Detectable Viral Load	04.26-	0.67-26.83	.122
CD4+ T Cell Count >200	4.09	0.38-43.05	.244
Study Intervention	11.655	2.88-47.05	.001

4. Discussion

This study aimed to evaluate the effectiveness of mHealth with ART adherence on adults starting or restarting treatment. As mentioned before, adherence plays a key role in PLWHIV allowing them to

reach viral suppression and increasing life quality overall. This highlights the importance of exploring interventions to support patients recently diagnose to reach optimal adherence.

This study enrolled patients with an age ranging from 30 to 40, which correspond with the national and worldwide age with the most HIV prevalence. Also, our participants were mostly men, like Mexico national trend, as men who have sex with men and transgender people are the main groups affected for HIV in Mexico (15).

Both groups shared previously reported factors that can impact adherence like alcohol consumption and being single (4,6,10,16). Although it was out of the scope of this study to further analyze the factors associated with adherence, the descriptive results found in this study provide a preliminary view for further investigations targeted to study the importance of these factors on patient's adherence to treatment.

Even though the participants were randomly assigned to each group, our intervention group had a lesser age than our control group. We believed that this is related to the recruitment process, older patients were most likely to reject the invitation of the study due to the concern of digital means over in-person attention. Giebel et.al mentions that interventions must be adapted to the different age groups due to the diversity of the users (17). These findings need to be explored and contemplated in further studies.

Regarding clinical findings, the control group had a lower CD4 T cell count (168 cells/uL), suggesting a delay in HIV detection. The fact that one of our groups had less than 200 cell/uL highlights the relevance of findings methods to improve early detection in high-risk populations, and, as is our study, strategies to prevent bad adherence to ART or abandonment (18).

In this study, we show that mHealth strategies improve adherence to treatment by 4% ($p < .0001$) and increases 3 times the probability of reaching a 95% of treatment adherence. However, we wanted to evaluate the impact of age and other variables in the probability of reaching 95% of treatment adherence. For this, we performed a multivariate analysis, in which the mHealth intervention statistically correlates with adherence regardless of other independent variables like age, marital status, and employment. These results suggest that mHealth strategies can be beneficial in multiple scenarios.

As previously demonstrated, simply sending SMS messages had minimal to no impact on enhancing treatment adherence (19,20), we implemented a mHealth strategy based on the usage of interactives SMS, in which the patients had the opportunity to interact by text or phone call with a health professional. Interactive SMS have been showed to be effective and participants are most likely to develop a compromise with their treatment (21-23).

Another fundamental aspect of the intervention was the frequency of the texts. We implemented two weekly messages and appointment reminders for the first three months and only appointment reminders for the last three months. The goal was to help develop a habit in the patients, while still providing access to help if required. Also, it has been reported that a high frequency of messages over a long period of time becomes repetitive and stops having a beneficial impact (24-26).

Although other studies have used similar strategies, this is the first study in Mexican population to use strategies of mHealth with decreasing message frequency to increase adherence. In addition, we implemented messages that were validated by a Mexican group of health professionals, researchers, and PLWHIV on ART (14). Few studies looking into the efficacy of mHealth SMS use validated messages for their population (27-29).

Like other studies, we identified an improvement in treatment adherence by using SMS (13,20,30-32). However, it is important to consider that adherence evaluation is mainly assessed by a self-report provided by the patient, which has an intrinsic bias. As a method to address this bias, we measured the HIV viral load and the four-day adherence index, which has been reported to have adequate sensitivity and specificity in Mexican populations (33).

Although we identify increased adherence using mHealth strategies, further studies on a bigger population are required to confirm our results. It is also important to recognize the variability among different populations and regions (34). This study was performed in the State of Jalisco, and we found 93% of treatment adherence in our control group. These results are similar to a study performed in the state of Mexico (93% adherence) (35) but double the one found in the state of Tamaulipas (46% adherence) (36), these differences by state highlight how treatment adherence is contextual, and is determined, in a big portion, by the conditions surrounding the patients (37).

5. Conclusions

In summary, this study demonstrates that integrating mHealth strategies as a supplementary approach to existing interventions can enhance treatment adherence among people living with HIV. Additionally, our findings highlight significant results that may inform the implementation of larger and more intricate interventions aimed at bridging the communication gap between healthcare clients and medical service providers.

Declarations

Competing interests: The authors declare no competing interests.

Acknowledgements: We would like to thank our institution for allowing us to carry out the protocol and giving us the support for its implementation. Also, most importantly, to the patients whose

participation was vital for this research.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Funding: No funding was secured for the implementation of this protocol, and all associated costs were covered independently.

Ethics approval: Protocol was approved by the ethics committee in research of the Hospital Civil de Guadalajara' Fray Antonio Alcalde' with registry number 095/18 and registered on clinical trials (NCT05187741). All patients signed an informed consent prior to enrollment, this consent form provided complete information about the protocol and any concerns from potential participants were addressed before signing the informed consent. Clinical Trials Number: NCT05187741

References

1. Unaid. Fact sheet 2022: HIV update. 2022.
2. UNAIDS. GLOBAL COMMITMENTS, LOCAL ACTION. After 40 years of AIDS, charting a course to end the pandemic. 2021;52.
3. Espinosa Aguilar A, Sánchez MÁ, Lamadrid MDPG. An updated understanding of adherence to antiretroviral treatment. *Rev Cubana Enferm.* 2018;34(1):220–32.
4. B. Nachega J, C. Marconi V, U. van Zyl G, M. Gardner E, Preiser W, Y. Hong S, et al. HIV Treatment Adherence, Drug Resistance, Virologic Failure: Evolving Concepts. *Infect Disord Drug Targets.* el 1 de abril de 2011;11(2):167–74.
5. Lo TO. Adherence to Longterm Therapies. *World Health.* 2003;
6. Maria Isabel Peñarrieta, Tamil Kendall NM. Adherencia al tratamiento antirretroviral en personas con vih en tamaulipas, méxico. *Rev Peru Med Exp Salud Publica.* 2009;26(3):333–7.
7. Gr C, Faria S de, Pj O cortez. Factors associated to the Control of viral Load in HIV positive patients. *Archivos de Medicina.* 2021;21(1):13–23.
8. Miller TA. Health literacy and adherence to medical treatment in chronic and acute illness: A meta-analysis. *Patient Educ Couns.* 2016;99(7):1079–86.
9. Sánchez-Rivero I, Madoz-Gúrpide A, Parro-Torres C, Hernández-Huerta D, Mangado EO. Influence of substance use and cognitive impairment on adherence to antiretroviral therapy in HIV+ patients. *Adicciones.* 2020;32(1):7–18.
10. Schaecher KL. The importance of treatment adherence in HIV. *American Journal of Managed Care.* 2013;19(12 SUPPL.):231–7.
11. Kampmeijer R, Pavlova M, Tambor M, Golinowska S, Groot W. The use of e-health and m-

health tools in health promotion and primary prevention among older adults: A systematic literature review. *BMC Health Serv Res*. 2016;16(Suppl 5).

12. Bervell B, Al-Samarraie H. A comparative review of mobile health and electronic health utilization in sub-Saharan African countries. *Soc Sci Med [Internet]*. 2019;232(October 2018):1–16. Disponible en: <https://doi.org/10.1016/j.socscimed.2019.04.024>

13. Demena BA, Artavia-Mora L, Ouedraogo D, Thiombiano BA, Wagner N. A Systematic Review of Mobile Phone Interventions (SMS/IVR/Calls) to Improve Adherence and Retention to Antiretroviral Treatment in Low-and Middle-Income Countries. *AIDS Patient Care STDS*. 2020;34(2):59–71.

14. Pérez-Sánchez IN, Iglesias MC, Rodriguez-Estrada E, Reyes-Terán G, Caballero-Suárez NP. Design, validation and testing of short text messages for an HIV mobile-health intervention to improve antiretroviral treatment adherence in Mexico. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*. 2018;30:37–43.

15. Consejo Nacional para la Prevención y Control del Sida. Guía Nacional para la Prevención del VIH y el SIDA. 2014;6–11.

16. Soares R de CA, de Brito AM, Lima K, Lapa TM. Adherence to antiretroviral therapy among people living with HIV/AIDS in Northeastern Brazil: A cross-sectional study. *Sao Paulo Medical Journal*. 2019;137(6):479–85.

17. Giebel GD, Speckemeier C, Abels C, Börchers K, Wasem J, Blase N, et al. Problems and Barriers Related to the Use of Digital Health Applications: Protocol for a Scoping Review. *JMIR Res Protoc*. 2022;11(4):1–7.

18. Johnson DE, Sorvillo FJ, Wohl AR, Bunch G, Harawa NT, Carruth A, et al. Frequent failed early HIV detection in a high prevalence area: Implications for prevention. *AIDS Patient Care STDS*. 2003;17(6):277–82.

19. Linnemayr S, Huang H, Luoto J, Kambugu A, Thirumurthy H, Haberer JE, et al. Text messaging for improving antiretroviral therapy adherence: No effects after 1 year in a randomized controlled trial among adolescents and young adults. *Am J Public Health*. 2017;107(12):1944–50.

20. Georgette N, Siedner MJ, Petty CR, Zanoni BC, Carpenter S, Haberer JE. Impact of a clinical program using weekly Short Message Service (SMS) on antiretroviral therapy adherence support in South Africa: a retrospective cohort study. *BMC Med Inform Decis Mak*. 2017;17(1):1–9.

21. King E, Kinvig K, Steif J, Qiu AQ, Maan EJ, Albert AYK, et al. Mobile text messaging to improve medication adherence and viral load in a vulnerable canadian population living with human immunodeficiency virus: A repeated measures study. *J Med Internet Res*. 2017;19(6):1–15.

22. Jopling R, Nyamayaro P, Andersen LS, Kagee A, Haberer JE, Abas MA. A Cascade of Interventions to Promote Adherence to Antiretroviral Therapy in African Countries. *Curr HIV/AIDS Rep.* 2020;17(5):529–46.
23. Hendricks L, Eshun-Wilson I, Rohwer A. A mega-aggregation framework synthesis of the barriers and facilitators to linkage, adherence to ART and retention in care among people living with HIV. *Syst Rev.* 2021;10(1):1–28.
24. Bartlett YK, Farmer A, Newhouse N, Miles L, Kenning C, French DP. Effects of Using a Text Message Intervention on Psychological Constructs and the Association Between Changes to Psychological Constructs and Medication Adherence in People With Type 2 Diabetes: Results From a Randomized Controlled Feasibility Study. *JMIR Form Res.* 2022;6(4):1–12.
25. Lin B, Liu J, He W, Pan H, Ma Y, Zhong X. Effect of a Reminder System on Pre-exposure Prophylaxis Adherence in Men Who Have Sex With Men: Prospective Cohort Study Based on WeChat Intervention. *J Med Internet Res.* 2022;24(8):1–14.
26. Griffie K, Martin R, Chory A, Vreeman R. A Systematic Review of Digital Interventions to Improve ART Adherence among Youth Living with HIV in sub-Saharan Africa. *AIDS Res Treat.* 2022;2022:1–7.
27. Kibu OD, Siysi VV, Albert Legrand SE, Asangbeng Tanue E, Nsagha DS. Treatment Adherence among HIV and TB Patients Using Single and Double Way Mobile Phone Text Messages: A Randomized Controlled Trial. *J Trop Med.* 2022;2022.
28. Kawichai S, Songtaweasin WN, Wongharn P, Phanuphak N, Cressey TR, Moonwong J, et al. A Mobile Phone App to Support Adherence to Daily HIV Pre-exposure Prophylaxis Engagement Among Young Men Who Have Sex With Men and Transgender Women Aged 15 to 19 Years in Thailand: Pilot Randomized Controlled Trial. *JMIR Mhealth Uhealth.* 2022;10(4):1–13.
29. Garofalo R, Kuhns LM, Hotton A, Johnson A, Muldoon A, Rice D. A Randomized Controlled Trial of Personalized Text Message Reminders to Promote Medication Adherence Among HIV-Positive Adolescents and Young Adults. *AIDS Behav.* 2016;20(5):1049–59.
30. Haberer JE, Musiimenta A, Atukunda EC, Musinguzi N, Wyatt MA, Ware NC, et al. Short message service (SMS) reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda. *Aids.* 2016;30(8):1295–9.
31. Controlado A. Envio de mensajes de texto para mejorar la adherencia de pacientes en TARGA: Ensayo aleatorizado controlado. *Rev Peru Med Exp Salud Publica.* 2019;36(3):400–8.
32. Karen S. Ingersoll¹, Rebecca A. Dillingham, Jennifer E. Hettema¹, Mark Conaway, Jason

Freeman, George Reynolds and SH. Pilot RCT of Bidirectional Text Messaging for ART Adherence Among Nonurban Substance Users with HIV Karen. *Physiol Behav*. 2017;176(3):139–48.

33. Balandrán DA, Gutiérrez JP, Romero M. Evaluación de la adherencia antirretroviral en México: Adherencia de cuatro días vs. índice de adherencia. *Revista de Investigacion Clinica*. 2013;65(5):384–91.

34. Camacho G, Kalichman S, Katner H. Anticipated HIV-Related Stigma and HIV Treatment Adherence: The Indirect Effect of Medication Concerns. *AIDS Behav* [Internet]. 2020;24(1):185–91. Disponible en: <https://doi.org/10.1007/s10461-019-02644-z>

35. Santillán C, Torija T, Cruz GV, Noguez Noguez S, Cecilia A, Hernández J, et al. Indicadores de adherencia al tratamiento antiretroviral de una población mexicana VIH+. *Alternativas en psicología*. 2017;88–106.

36. Bastán JEP. Adherencia al tratamiento antirretroviral de personas con VIH/sida en la Atención Primaria de Salud. *Revista Habanera De Ciencias Medicas*. 2007;6(5):1–15.

37. Giuliani M, Donà MG, La Malfa A, Pasquantonio MS, Pimpinelli F, Cristaudo A, et al. Ensuring retention in care for people living with HIV during the COVID-19 pandemic in Rome, Italy. *Sex Transm Infect*. 2020;0(0):1–2.

38. Pou C, Maculuvé S, Ceden S, Luis L, Rodri J, Clotet B, et al. Determinants of virological failure and antiretroviral drug resistance in Mozambique. *Journal of Antimicrobial Chemotherapy*. 2015;(June):2639–47.

Supplementary Files

Figures

Flow diagram CONSORT flow diagram of the intervention.

