Review Article

THE INDONESIAN
JOURNAL OF INFECTIOUS DISEASES

p-ISSN: 2354-6077), e-ISSN: 2599-1698

Digital Medication Reminders to Improve Antiretroviral Therapy Adherence in Children Living with HIV: Literature Review

Atika Rahmawani[1,2*], Ina Islamia[1], Risna Ningsih[1]

[1]Master of Nursing Science, Faculty of Nursing, Universitas Indonesia, Depok, Indonesia
[2]Sulianti Saroso Infectious Disease Hospital, Jakarta, Indonesia

ARTICLE INFO

Received: 5 August 2024
Reviewed: 10 January 2025
Accepted: 18 January 2025

Keywords:
HIV-Children, Adherence, Medication, Reminder, Technology

*Corresponding author:
Atika Rahmawani
Email: atikarahmawani84@yahoo.com

ABSTRACT

Background: *Antiretroviral treatment is the treatment for people infected with human immunodeficiency virus (HIV) using anti-HIV combinations that are used for life. The main factors determining the success of ARV treatment are sustained and optimal adherence to therapy. Adherence to ARV treatment can be challenging for children and especially adolescents with HIV because ARVs must be taken for life. There are several ways to improve adherence to ARV medication directly, namely through comprehensive educational pressure, other ways can be done by utilizing technology that uses medication reminder applications such as the use of smartphones, android-based application development, electronic monitoring, Short Message Service (SMS), social media-based support, and mass media campaigns. This paper reviews the scientific evidence on technology-based ARV treatment adherence.*
Methods: *This article is based on scientific journal searches conducted through online databases, namely Scopus, Proquest, PubMed, and Scholar, published in 2019-2023.*
Results: *showed that using technology as a reminder to take medication can improve adherence of children with HIV in taking ARV drugs.*
Conclusion: *The use of technology can improve adherence in children with HIV, can also reduce viral load rates, and increase CD4 levels.*

INTRODUCTION

Children and adolescents represent a significant portion of the global population living with human immunodeficiency virus (HIV). According to the World Health Organization (WHO), as of 2020, there were 1.8 million children (under 15 years old) and 1.8 million adolescents (aged 10–19 years) living with HIV worldwide [1]. In Indonesia, 31 adolescents aged 10–19 years were receiving antiretroviral (ARV) therapy as of March 2018. However, only 51.61% of them adhered

to ARV therapy, while the rest were categorized as "defaulting." Overall, adolescents show lower adherence rates compared to younger children [2].

Antiretroviral (ARV) therapy involves a lifelong combination of medications aimed at improving the quality of life of people living with HIV, reducing viral load, and increasing CD4 cell counts. The primary factors determining the success of ARV therapy are sustained and optimal adherence. Poor adherence increases the risk of virological failure, viral resistance, and adverse effects such as substance abuse, depression, and transmission of the infection. Missing more than three doses per month is considered suboptimal adherence, defined as less than 95% adherence [3]. Effective ARV therapy introduced in the 1990s significantly reduced AIDS-related mortality and morbidity. Adherence to ARV treatment remains one of the most important predictors of long-term survival. Moreover, optimal adherence is necessary for ARV therapy to serve as a key strategy in preventing further disease transmission at the population level. Medication adherence presents particular challenges for children and adolescents. Children depend on caregivers for their health care, while adolescents undergo rapid physical and psychosocial transitions, leading to unique developmental struggles. In resource-limited settings, optimal adherence rates among this population range from 49% to 100%, influenced by varying sociocultural contexts and the lack of standardized methods to measure ARV adherence [4]. Adherence to ARV therapy has been critical in transforming AIDS into a manageable chronic illness. In response, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the Fast-Track strategy in 2014, aiming to end the global AIDS epidemic by diagnosing 95% of all people living with HIV, providing ARV treatment to 95% of those diagnosed, and achieving viral suppression in 95% of those on treatment [5].

In Indonesia, as of 2018, 52% of children with HIV had received lifelong ARV therapy. Administration of ARV medications must comply with specific parameters, including correct dosing and timely intake. Patient adherence to ARV treatment is critical to the success of HIV management, as stated in the Ministry of Health Regulation [6]. Consistent and long-term adherence is particularly challenging for adolescents due to various barriers, including forgetfulness, HIV-related stigma, mood fluctuations, and substance use. Furthermore, recent research suggests that the clinical social environment plays an important supportive role for adolescents living with HIV, influencing health outcomes [7].

Several approaches can be employed to improve patients' adherence to ARV medication. One approach involves comprehensive educational interventions that emphasize the importance of health issues and encourage patients to take personal responsibility for following ARV treatment. Such educational strategies aim to raise awareness and commitment among patients to consistently and diligently take ARV medications as prescribed by health professionals, which is key to effective HIV/AIDS management. Another method involves the use of technology to

support ARV medication adherence. This includes technology-based medication reminder models such as smartphone apps, Android-based applications, electronic monitoring systems, short message service (SMS), social media-based support, and even mass media campaigns. Among these, SMS reminders have proven to be one of the most effective tools for enhancing adherence to ARV therapy among adolescents living with HIV.

In Nigeria, the development and use of ARV medication reminders among adolescents have been implemented through an application specifically designed as a daily ARV treatment reminder. The Android-based smartphone application, *PEERNaija*, functions as a bidirectional daily medication reminder. This smartphone app was designed to leverage peer-based social environments to improve treatment adherence. It offers a multifaceted adherence intervention including peer-based social features, financial incentives, virtual peer support, and clinic-based early outreach for non-adherent adolescents [8].

Through technological advancements, adherence to ARV medication can be promoted and developed in various ways, particularly through the development of reminder technologies that enhance medication adherence among children living with HIV. One of the strategies to improve treatment adherence among People Living with HIV/AIDS (PLWHA) is through education. This is because PLWHA require detailed and comprehensive information regarding their ongoing treatment. In the Society 5.0 era, people are inseparable from internet connectivity and social networks. Therefore, utilizing health information through smartphones can serve as a means to improve knowledge, attitudes, motivation, self-efficacy, and adherence to treatment among PLWHA [9]. Accordingly, this literature review was conducted to provide an overview of ARV treatment adherence among adolescents, focusing on various models based on medication reminder technologies.

METHODS

In this study, the method used is a literature review, which is a study approach aimed at analyzing selected literature from various sources in order to draw conclusions or generate new ideas. The journals used in this review focus on a specific topic. Journal searches were conducted using five categories of keywords: Children-HIV, Adherence, Treatment, Reminder, and Technology. Scientific journal searches were carried out through online databases, including Scopus, ProQuest, PubMed, and Google Scholar, covering the period from 2019 to 2024.

RESULTS

A total of 2021 records were identified through systematic searches of four electronic databases. Records were exported in CSV, nbib, and RIS formats. After removing 122 duplicates, 1899 unique records remained. Nine full-text articles were assessed for eligibility and were reviewed for

inclusion. A Preferred Reporting Items for Systematic Reviews and Meta-analyses flow chart (Figure 1).

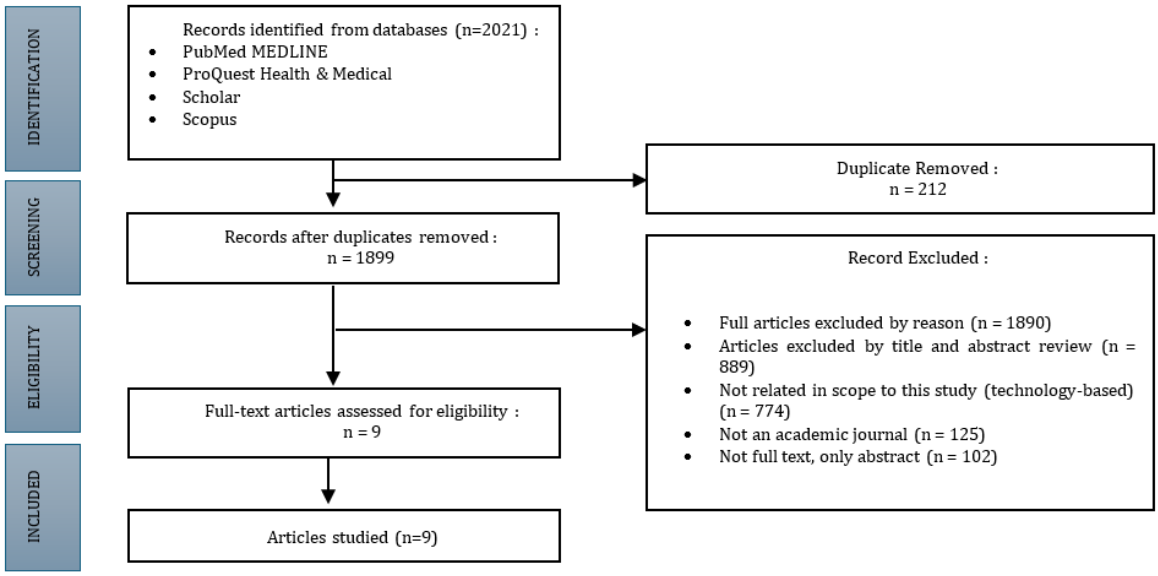

Figure 1. PRISMA flowchart

We synthesize nine studies evaluating digital adherence tools (DATs) for HIV treatment, primarily using RCTs in Sub-Saharan Africa. Key technologies include SMS reminders (5 studies), electronic monitors (Wisepill™/RTMM, 3 studies), and apps/social media (3 studies), targeting mostly adolescents. Findings indicate DATs especially SMS and monitors effectively improve ART adherence and viral suppression in this population, with high feasibility/acceptability (e.g., >95% in pilots). However, social media interventions showed limited impact, and small sample sizes constrain generalizability. Overall, DATs demonstrate significant potential in resource-limited settings, though successful implementation requires reliable infrastructure and context-appropriate design, often enhanced by human support (e.g., peer navigation). Detailed summaries are presented in Table 1.

Table 1. The following are selected articles analyzed

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
1	Sumari-de Boer, et all (2023), Tanzania [10]	*Effect of a customized digital adherence tool on retention in care and adherence to antiretroviral treatment in*	RCT Mixed Method	Children aged 0–14 and their caregivers; Adolescents aged 15–19; Breastfeeding women	Objective: To investigate whether digital adherence tools can improve care retention among breastfeeding women and treatment	Digital Adherence Technologies (DATs), using a medication box (Wisepill) that sends daily SMS messages and

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
		breastfeeding women, children, and adolescents living with HIV in Tanzania: a mixed-methods study followed by clinical trials		and their children	adherence among children and adolescents. Result: Positive impact on ARV adherence for children and adolescents	feedback upon opening
2	Ahinkhai, A et all (2023), Nigeria [11]	*Successful Implementation Strategies in iCARE Nigeria—A Pilot Intervention with Text Message Reminders and Peer Navigation for Youth Living with HIV*	Mix methods Pilot Study	40 adolescents aged 15–24	Objective: To address poor outcomes among adolescents and young adults living with HIV. Result: High success of initial text reminder implementation (99.9%), 95% of participants and 90% of peer navigators found reminders non-intrusive. Significant increase in ARV adherence and viral suppression by week 48.	iCARE Text Message Reminders and Peer Navigation The iCARE Nigeria treatment intervention combines peer support with tailored, bidirectional daily SMS medication reminders for adolescents living with HIV.
3	Msosa, T.C et all (2023), Malawi [12]	*The effect of a customised digital adherence tool on HIV treatment outcomes in young people living with HIV (YPLHIV) in Blantyre, Malawi: a protocol for a randomised controlled trial*	RCT	Adolescents aged 15–24	Objective: To determine the efficacy of a customized tool in improving ART adherence and viral suppression. Result: Effective in improving ART adherence and virological suppression	Digital Adherence Tool (DAT) based on Real-Time Medication Monitoring (RTMM) RTMM is a medication box developed by Wisepill™ that contains a Subscriber Identity Module (SIM) card, enabling it to transmit data to a central server via the General Packet Radio Service (GPRS) network.
4	Kizito et all (2022), Afrika[13]	*Monitoring adherence to antiretroviral*	RCT	702 adolescents aged 10–16	Objective**:** To monitor ARV adherence and	Self-report (SR) and Wisepill Electronic

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
		therapy among adolescents in Southern Uganda: comparing Wisepill to Self-report in predicting viral suppression in a cluster-randomized trial.			compare the performance of Self-Report (SR) and Wisepill Electronic Monitoring (EM) in measuring ARV treatment adherence and predicting viral suppression Result**:** Good ARV treatment adherence, at 79.2% and 97%, was associated with viral load suppression overall. There was a high level of agreement (78%) between SR and EM in monitoring ARV treatment adherence.	Monitoring (EM). The Wisepill adherence monitoring device is connected to the mobile telecommunications network. Each time the patient opens the device, it sends a signal to the central server, which is recorded as a "dose taken." If the device is not opened, it also sends a signal, indicating a missed dose..
5	MacCarthy et all (2020) Uganda[14]	*A randomized controlled trial study of the acceptability, feasibility, and preliminary impact of SITA (SMS as an Incentive To Adhere): a mobile technology-based intervention informed by behavioral economics to improve ART adherence among youth in Uganda*	RCT	Adolescents aged 15–24	Objective: To assess ARV adherence among adolescents using a text-based (SMS) intervention that provided weekly feedback. Result: Sending text messages containing adherence-related information improved adolescents' adherence to ARV treatment. Group-based information delivery proved effective in enhancing health behaviors among adolescents, including increased physical activity, healthier food choices, reduced alcohol	Adherence SMS using Mobile/Cell Phone-Based Technology

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
					use, and improved sexual health.	
6	Dulli (2020) Nigeria[15]	*A Social Media–Based Support Group for Youth Living With HIV in Nigeria (SMART Connections): Randomized Controlled TrialA Social Media–Based Support Group for Youth Living With HIV in Nigeria (SMART Connections): Randomized Controlled Trial*	RCT	Adolescents aged 15–24	Objective: To evaluate the effectiveness of the Social Media to Promote Adherence and Retention in Treatment (SMART) intervention Result**:** The use of SMART Connections may contribute to improvements in HIV knowledge, ARV treatment adherence, and social support. HIV-related knowledge was high in both groups. However, no statistically significant differences were observed between the study groups in terms of ARV adherence, social support, social isolation, HIV-related stigma, or depression.	Social media–based support to promote adherence and retention in treatment (SMART Connections), delivered through social media platforms, for improving HIV treatment retention among adolescents
7	Fatimatuzahro (2023), Indonesia[9]	Model Pengembangan Aplikasi "Ingat Minum Obat ARV" Berbasis Android Sebagai Pengingat Minum Obat Pada ODHA	Research and development (R&D)	Adolescents to adults aged 10–59	Objective: To explore the needs of people living with HIV/AIDS (PLWHA) for a medication reminder application and to develop an Android-based app Result: The "Ingat Minum Obat ARV" application, abbreviated as "IMUT ARV," was found to be highly feasible and needed by PLWHA as a tool to help	The "IMUT ARV" Android-based application is designed to explore the medication reminder needs of people living with HIV (PLHIV)

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
					remind them to take their antiretroviral (ARV) medication.	
8	[7],Mimiaga MJ, et all (2019), Massachusetts [7]	*Positive Strategies to Enhance Problem-Solving Skills (STEPS): A Pilot Randomized, Controlled Trial of a Multicomponent, Technology-Enhanced, Customizable Antiretroviral Adherence Intervention for HIV-Infected Adolescents and Young Adults*	Pilot Study RCT	Adolescents aged 16–24 (average age 19)	Objective: To develop a multicomponent intervention focused on adolescents living with HIV by integrating technological aspects Result: Over a 4-month assessment period, changes in ARV adherence among the intervention group [mean change score = 13%, standard deviation (SD) = 29.5] were significantly higher compared to the standard care group (mean change score = -26%, SD = 26.0; effect size = 1.43, confidence interval = 0.17–2.49, p = 0.02)	Incorporating technological aspects such as short message services (SMS), text messages, and video sketches, the "Positive Steps" strategy aims to enhance problem-solving skills by combining five individual counseling sessions with daily text message reminders.
9	Akankunda et all (2022) Uganda [16]	*The Role of Mass Media Campaigns in Improving Adherence to Antiretroviral Therapy Among Adolescents Living with HIV in Southwestern Uganda*	Qualitative phenomenology	Adolescents aged 10–19	Objective: To explore the impact of mass media campaigns in promoting adherence to antiretroviral therapy (ART) among adolescents. Result: Three main themes emerged: (1) awareness of HIV campaigns in mass media promoting ART adherence, (2) the influence of mass media campaigns on adherence to antiretroviral	Mass media campaigns include messages on ARV adherence, stigma, family planning, condom use, circumcision, abstinence, counseling and testing, positive living, and antenatal care services. These messages are broadcast through print media, broadcast media, and

No	Author, Year, Location	Research Title	Method	Sample and Population	Research Objectives and Results	Tools
					therapy, and (3) preferred modes of media delivery among adolescents living with HIV.	community-based media.

DISCUSSION

Various research findings show that the utilization of technology can help improve adherence to antiretroviral (ARV) treatment among children living with HIV. This can be in the form of technology-based medication reminder models, such as the use of smartphones, the development of Android-based applications, electronic monitoring, Short Message Service (SMS), social media-based support, and mass media campaigns. The purpose of utilizing such technologies is to improve ARV treatment adherence in children with HIV, thereby helping to inhibit or slow the replication and spread of the HIV virus in the body.

A study conducted by Kizito et al. aimed to monitor ARV treatment adherence and compare the performance of self-report (SR) and electronic monitoring (EM) in measuring ARV adherence and predicting viral suppression among adolescents living with HIV [13]. Digital Adherence Technologies (DAT) in this case used Wisepill, which is connected to a cellular telecommunications network. Every time a patient opens the device, it sends a signal to a central server indicating a dose has been taken. If the device is not opened, it emits a different signal. The results showed a relatively high coverage in assessing ARV adherence among children with HIV. In relation to that study, Boer et al. also reported positive outcomes in ARV treatment adherence among children and adolescents [10]. The digital adherence tool (DAT), based on real-time medication monitoring (RTMM), contains a SIM card that enables data transmission from the mobile device to a central server via the global GPRS network. The results proved effective in improving ARV adherence and virological suppression in adolescents living with HIV [12].

MacCarthy et al. stated that improving ARV adherence in adolescents could be achieved using mobile-based technology, namely incentive-based SMS, which provides weekly feedback [14]. Text message delivery containing adherence information can enhance adolescents' ARV treatment adherence and has proven effective in improving adolescent health behaviors, such as increased physical activity, healthier food choices, reduced alcohol use, and better sexual health. Another study found that text message reminders and peer navigation could address adverse outcomes among adolescents and young adults living with HIV. The implementation of initial text message reminders had a success rate of 99.9%. Most participants (95%) and peer navigators (90%) found the text reminders non-intrusive. Thus, the study showed a significant improvement

in ARV adherence and viral suppression at week 48 [11]. A study developed by Mimiaga et al. (2019) created a multicomponent intervention focused on adolescents with HIV by integrating technological aspects. This intervention combined short messaging services, text messages, and video sketches. Over a four-month assessment visit, ARV adherence improved significantly in the intervention group compared to the standard care group.

In a study by Dulli et al improving ARV adherence among children was achieved through social media–based support (SMART Connections) delivered via social media platforms [15]. This intervention was designed to promote retention in HIV care by leveraging social support and enhancing HIV knowledge and treatment literacy. It involved group support and positive connections and was delivered via a private Facebook group. The results showed high levels of HIV knowledge in both groups at the end of the study, although it was significantly higher in the intervention group. There were no statistically significant differences between the groups in terms of ARV adherence, social support, social isolation, HIV-related stigma, or depression.

Research by Fatimatuzahro et al designed and developed an Android-based medication reminder application called "IMUT ARV" (an acronym for "Ingat Minum Obat ARV" or “Remember to Take ARV Medication”)[9]. This technology-based application was developed to meet the needs of people living with HIV/AIDS (PLWHA) in taking ARV medication. This is supported by mobile technology's ability to reach patients anywhere and anytime Maloney et al. The validation test results showed that the model was highly feasible and greatly needed by PLWHA as a tool to remind them to take their ARV medication.

A study by Akankunda et al explored the impact of mass media campaigns in promoting ARV therapy adherence among adolescents living with HIV [16]. The campaign messages included topics on ARV adherence, stigma, family planning, condom use, circumcision, abstinence, counseling and testing, positive living, and antenatal care services. These messages were broadcast through print media, broadcasting, and community media. The results of the study indicated that mass media campaigns had an influence on adherence to antiretroviral therapy and highlighted the preferred delivery methods of these messages among adolescents living with HIV.

CONCLUSION

Adherence to ARV treatment in children living with HIV requires serious attention. The utilization of technology through various models of medication reminder applications, such as the use of smartphones, development of Android-based applications, electronic monitoring, Short Message Service (SMS), social media–based support, and mass media campaigns, can significantly contribute to improving treatment adherence.

DECLARATIONS

Ethics approval

The data used in this research were obtained from a systematic review, not directly from human subjects. Therefore, it does not require ethical clearance.

Conflict of interest.

The authors declare no conflict of interest.

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not for profit sectors.

Acknowledgments

None.

REFERENCES

[1] World Health Organization. Adherence to long term therapies. 2003. https://doi.org/10.4028/www.scientific.net/AMM.321-324.1779.

[2] RI K. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/Menkes/413/2020 Tentang Pedoman Pencegahan dan Pengendalian Coronavirus Disease 2019 (COVID-19). Indonesia: 2020.

[3] GebreEyesus F, Mitku D, Tarekegn T, Temere B, Terefe T, Belete A, et al. Levels of adherence and associated factors among children on ART over time in Northwest, Ethiopia: evidence from a multicenter follow-up study. HIV/AIDS-Research Palliat Care 2021:829–38.

[4] Martelli G, Antonucci R, Mukurasi A, Zepherine H, Nöstlinger C. Adherence to antiretroviral treatment among children and adolescents in Tanzania: comparison between pill count and viral load outcomes in a rural context of Mwanza region. PLoS One 2019;14:e0214014.

[5] Tuot S, Sim JW, Nagashima-Hayashi M, Chhoun P, Teo AKJ, Prem K, et al. What are the determinants of antiretroviral therapy adherence among stable people living with HIV? A cross-sectional study in Cambodia. AIDS Res Ther 2023;20:47.

[6] Kemenkes RI. Pedoman penerapan terapi HIV pada anak. Kementeri Kesehat RI Jakarta 2014.

[7] Mimiaga MJ, Bogart LM, Thurston IB, Santostefano CM, Closson EF, Skeer MR, et al. Positive strategies to enhance problem-solving skills (STEPS): a pilot randomized, controlled trial of a multicomponent, technology-enhanced, customizable antiretroviral adherence intervention for HIV-infected adolescents and young adults. AIDS Patient Care STDS 2019;33:21–4.

[8] Pierce LJ, Were MC, Amaral S, Aliyu MH, Ezechi O, David A, et al. PEERNaija—a mobile health platform incentivizing medication adherence among youth living with HIV in Nigeria: study protocol for a randomized controlled trial. Pilot Feasibility Stud 2023;9:179.

[9] Fatimatuzahro, Widjanarko B SZ. MODEL PENGEMBANGAN APLIKASI" INGAT MINUM OBAT ARV" BERBASIS ANDROID SEBAGAI PENGINGAT MINUM OBAT PADA ODHA. J Keperawatan Silampari 2023;6:1479–91.

[10] Sumari-de Boer IM, Ngowi KM, Swai IU, Masika L V, Maro RA, Mtenga AE, et al. Effect of a customized digital adherence tool on retention in care and adherence to antiretroviral treatment in breastfeeding women, children and adolescents living with HIV in Tanzania: a mixed-methods study followed by clinical trials. Trials 2023;24:285.

[11] Ahonkhai AA, Kuti KM, Hirschhorn LR, Kuhns LM, Garofalo R, Johnson AK, et al. Successful implementation strategies in iCARE Nigeria—a pilot intervention with text message

reminders and peer navigation for youth living with HIV. Trop Med Infect Dis 2023;8:498.
[12] Msosa TC, Swai I, Sumari-de Boer M, Ngowi K, F. Rinke de Wit T, Aarnoutse R, et al. The effect of a customised digital adherence tool on HIV treatment outcomes in young people living with HIV (YPLHIV) in Blantyre, Malawi: a protocol for a randomised controlled trial. Trials 2023;24:535.
[13] Kizito S, Namuwonge F, Brathwaite R, Neilands TB, Nabunya P, Bahar OS, et al. Monitoring adherence to antiretroviral therapy among adolescents in Southern Uganda: comparing Wisepill to Self-report in predicting viral suppression in a cluster-randomized trial. J Int AIDS Soc 2022;25:e25990.
[14] MacCarthy S, Wagner Z, Mendoza-Graf A, Gutierrez CI, Samba C, Birungi J, et al. A randomized controlled trial study of the acceptability, feasibility, and preliminary impact of SITA (SMS as an Incentive To Adhere): a mobile technology-based intervention informed by behavioral economics to improve ART adherence among youth in Uganda. BMC Infect Dis 2020;20:1–10.
[15] Dulli L, Ridgeway K, Packer C, Murray KR, Mumuni T, Plourde KF, et al. A social media–based support group for youth living with HIV in Nigeria (SMART Connections): randomized controlled trial. J Med Internet Res 2020;22:e18343.
[16] Akankunda S, Najjuma JN, Tayebwa S, Byamugisha B, Ariho S, Bahati R. The role of mass media campaigns in improving adherence to antiretroviral therapy among adolescents living with HIV in Southwestern Uganda. HIV/AIDS (Auckland, NZ) 2022;14:397.