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Meta-analysis

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The Effectiveness of Mobile Phone Text Messages on the Adherence to Antiretroviral Drug Taking in Patients Living with HIV/AIDS: A Meta-Analysis

Fara Aristya Prisma[1)], Hanung Prasetya[2)], Burhannudin Ichsan[3)]

[1)]Master's Program in Public Health, Universitas Sebelas Maret, Indonesia
[2)]Study Program of Acupuncture, Health Polytechnics, Ministry of Health Surakarta, Indonesia
[3)]Faculty of Medicine, Universitas Muhammadiyah Surakarta, Indonesia

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ABSTRACT

Background: The use of antiretroviral (ARV) therapy has been shown to reduce the mortality and morbidity of people living with HIV (PLHIV). The characteristic factor of the PLHIV health care system is a key factor as well as how health workers and services synergize to improve patient adherence to adherence to taking ARVs.
Subjects and Method: This research was conducted using a systematic review and meta-analysis with PICO namely, Population: PLHIV. Intervention; mobile phone text message. Comparison: not given a mobile phone text message. Outcome: obediently taking ARVs. By searching articles in 4 databases namely PubMed, Google Scholar, Science Direct, and ProQuest published from 2012 to 2022, entering the following keywords ("Mobile phone text messages" OR mHealth) AND anti-retroviral AND (HIV or AIDS) AND "Randomized controlled trials". Articles were selected using PRISMA flow and data analysis using the Review Manager 5.3 application.
Results: There are a total of 9 articles using the RCT study design with a total sample of 2,762 PLHIV from China, Estonia, Nigeria, Cameroon, Kenya, and Mozambique which have been subject to systematic review and meta-analysis. The data that has been processed shows that mobile phone text messages are effective in increasing PLWHA adherence in taking ARVs, and are statistically close to significant. PLHIV who receive mobile phone text messages are more likely to comply with taking ARVs 1.12 times than those who do not receive mobile phone text messages (RR= 1.12; 95% CI= 1.00 to 1.26; p= 0.050).
Conclusion: Mobile phone text messages are effective in increasing PLWHA compliance in taking ARVs.

Keywords: HIV/AIDS, people living with HIV, ARV, mobile phone text messages.

Correspondence:
Fara Aristya Prisma. Master's Program in Public Health, Universitas Sebelas Maret. Jl. Ir. Sutami 36A, Surakarta, 57126, Central Java, Indonesia. Email: fara.aristya@gmail.com. Mobile: +6285697129819.

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BACKGROUND

Acquired Immune Deficiency Syndrome or more often abbreviated as AIDS is a collection of symptoms of a disease caused by the Human Immunodeficiency Virus or commonly known as HIV. Patients infected with this virus (HIV) are declared AIDS sufferers when they show certain symptoms as a result of decreased body immunity (Srikartika et al., 2019). HIV/AIDS has an increasing number of cases every year, both nationally and globally. In 2021, as many as 650,000 people died from this disease, around 38.4 million people living with HIV/AIDS (PLWHA), at the end of 2021 with 1.5 million people newly infected with HIV (WHO, 2022).

In Indonesia, the estimated number of people with HIV in 2020 is 543,100 people with a total of 29,557 new infections and 30,137 deaths. HIV positive cases reported from year to year tend to increase, but in 2021 the number of HIV positive cases will be the lowest since the last four years, namely 36,902 cases. The number of AIDS cases in Indonesia tends to decrease and in 2021 there are reported to be 5,750 cases (RI Ministry of Health, 2022). Ironically, the decline in HIV/AIDS cases in 2021 and 2022 is due to the Covid-19 pandemic where many health workers in services are helping to handle Covid-19, while in 2021 health workers in services will be diverted to help provide Covid-19 vaccinations to the community (RI Ministry of Health, 2021).

The study conducted by Yé et al. (2018) through the intervention of mobile phone text messages offers potential benefits for disseminating health information to the wider community. Mobile phone technology can generally be used to overcome geographic barriers and improve communication, this technology allows it to be used in marginalized rural areas where health services are often difficult to access or people who do not have time to go to health services to get their health information. The spread of mobile devices is also critical in disease prevention and management by promoting changes in health behavior in the community.

Based on the effects of failing to comply with taking ARVs for PLWHA, a way is needed to address the failure rate of ARV therapy. In addition, comprehensive research is needed from various studies and previous literature on the effectiveness of mobile phone text messages on adherence to taking ARVs in PLHIV.

SUBJECTS AND METHOD

1. Study Design

This research uses systematic review and meta-analysis with PICO namely, Population: PLHIV, Intervention: mobile phone text messages, Comparison: not given mobile phone text messages, Outcome: adherence to taking ARVs. By searching articles in 4 databases namely PubMed, Google Scholar, Science Direct, and ProQuest, entering the following keywords ("Mobile phone text messages" OR mHealth) AND antiretroviral AND (HIV or AIDS) AND "Randomized controlled trials".
using the PRISMA flow diagram.

2. Step of Meta-Analysis

The meta-analysis was carried out in five steps as follows:

1) Formulate research questions in the PICO format (Population, Intervention, Comparison, Outcome).
2) Search for primary study articles from various electronic and non-electronic databases.
3) Conduct screening and critical assessment of primary research articles.
4) Perform data extraction and synthesize effect estimates into RevMan 5.3.
5) Interpret and conclude the results

3. Inclusion Criteria

The inclusion criteria of this study were full-text English articles and an RCT research design, the subject of the study was PLHIV, and the outcome of the study was adherence to taking ARVs.

4. Exclusion Criteria

Exclusion criteria from this study were the size of the results of the study were not complete or did not clearly describe the results, the year of publication was more than 10 years from the time this study was conducted, the intervention and study population were different.

5. Operational Definition of Variables

Mobile phone text messages are text messages via cell phones that aim to increase PLHIV compliance in consuming ARVs which contain information regarding drug use, side effects, reasons why it is important to consume ARVs, reminders, and social support for PLWHA. The measurement scale is categorical.

Adherence to taking ARVs themselves is defined as PLWHA taking ARVs in the right dose, time, and method according to what has been recommended. This compliance greatly affects the success of ARV therapy. The measurement scale is categorical.

6. Instruments

This systematic review was carried out following the PRISMA flow diagram guidelines, with an assessment of the quality of the articles using the Critical Appraisal checklist for Randomized controlled study (CEBMa, 2014).

7. Data Analysis

The data in this study were analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots are used to determine the effect size and heterogeneity of the data. Data processing is carried out based on variations between studies by determining the use of an analysis model, namely the fixed effect model or the random effect model.

RESULTS

The process of screening articles according to the research criteria can be seen in the PRISMA flow diagram (Figure 1).

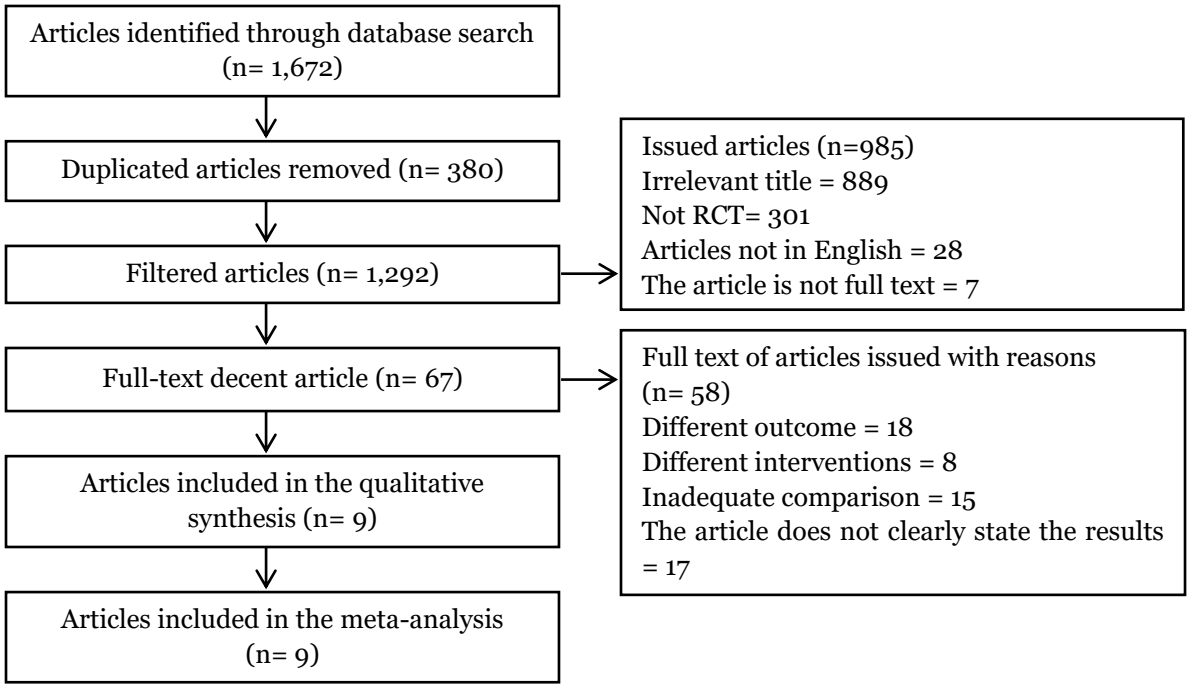

Figure 1. Results of Prisma Flow Diagrams

The initial search process obtained 1,627 then after going through the screening process, 1,292 articles were obtained which were considered as primary articles of this study, and 9 articles were include in this meta-analysis. The articles obtained came from 4 continents, namely Asia (China), Africa (Cameroon, Kenya, Nigeria, and Mozambique), and Europe (Estonia).

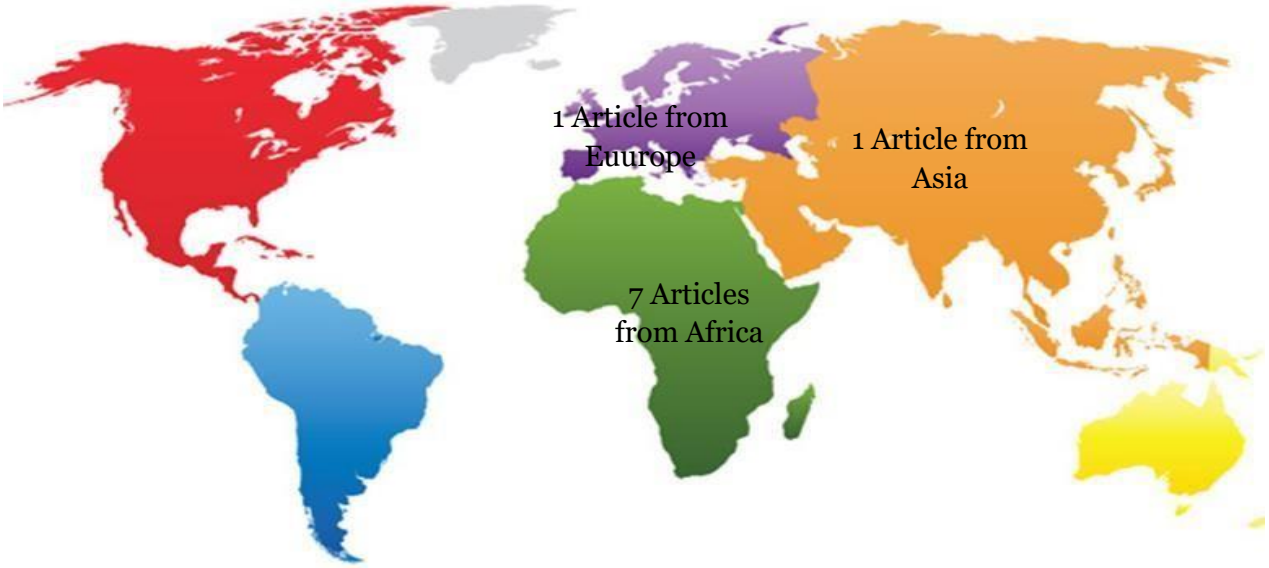

Figure 2. Resarch Distribution Map

Table 1. Critical Appraisal using CEBM

Primary Study	Criteria												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Patel et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Maduka et al. (2013)	2	2	2	2	2	2	2	2	2	2	2	2	24
Sabin et al. (2015)	2	2	2	2	2	2	2	2	2	2	2	2	24
Mbuagbaw et al. (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Davey et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Kibu et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	24
Uuskula et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Atukunda et al. (2017)	2	2	2	2	0	2	0	2	2	2	2	2	20
Kassaye et al. (2016)	2	2	2	2	2	2	2	2	2	2	2	2	24

Description of the question criteria:

1. Do the research objectives clearly address the focus/problem of the research?
2. Is the research method (research design) suitable for answering the research question?
3. Is the research subject selection method clearly written?
4. Does the sampling method give rise to bias (selection)?
5. Does the research sample take represent the designated population?
6. Was the sample size based on pre-study considerations?
7. Is the measurement method achievable?
8. Are the research instruments valid and reliable?
9. Was statistical significance assessed?
10. Was a confidence interval given for the main outcome?

11. Are there any confounding factors that have not been taken into account?
12. Are the results applicable to your research?

Description of scoring:
Yes = 2;
Hesitate=1;
No =0

Study quality assessment was carried out quantitatively, where this study used study quality assessment for a randomized controlled trial design based on the Center for Evidence-Based Management (CEBMa) in 2014. The results of the study quality assessment based on CEBMa can be seen in Table 1.

Table 2 contains brief descriptions of 9 articles relating to the effectiveness of mobile phone text messages on the adherence of antiretroviral drug taking in patients living with HIV/AIDS.

The forest plot in figure 3 showed that mobile phone text messages are effective in increasing PLWHA compliance in taking ARVs, and are statistically close to significant. PLHIV who receive mobile phone text messages are more likely to comply with taking ARVs 1.12 times than those who do not receive mobile phone text messages (RR= 1.12; 95% CI= 1.00 to 1.26; p= 0.050).

The forets plot in figure 3 also showed the effect estimates between studies with high heterogeneity (I^2= 81%), thus calculating the effect estimates using the Random Effect Model (REM) approach.

The funnel plot in figure 4 showed that the distribution of effect estimates is more to the right of the average vertical line, indicating publication bias. Because there are more effect estimates in the funnel plot to the right of the vertical line which is the same as the average effect estimate (•) in the forest plot on the right, publication bias tends to overestimate the effects.

DISCUSSION

This systematic study and meta-analysis research raised the effectiveness of mobile phone text messages on adherence to taking ARVs in PLHIV. This research is considered important because the intervention of mobile phone text messages can increase PLHIV's adherence to taking ARVs by sending text messages via mobile phones containing reminders to take medication until social support is assessed to be able to increase ARV consumption in PLWHA.

The results of a meta-analysis of 9 articles showed that mobile phone text messages were effective in increasing PLWHA adherence in taking ARVs, and were statistically close to significant. PLHIV who receive mobile phone text messages are more likely to comply with taking ARVs 1.12 times than those who do not receive mobile phone text messages (RR= 1.12; 95% CI= 1.00 to 1.26; p= 0.050).

Table 2. Summary of Articles the Influence of Smoking Parents on Teenagers' Smoking Habits.

Author (Year)	Country	Sample	Study Design	Population	Intervention	Comparison	Outcome
Patel et al. (2017)	Nairobi, Kenya	180	RCT	Kenyans living with HIV/AIDS who have started ARV treat-ment have cell phones.	Get text messages to take ARVs appropriately.	Not getting text messages.	Increasing adherence to taking ARVs.
Maduka et al. (2013)	Port Harcout, Nigeria	104	RCT	HIV/AIDS positive patients currently undergoing ARV therapy.	Get text messages of social support and reminders to take ARVs.	Not getting text messages of social support and reminders to take ARVs.	Patients experienced increased consumption of ARVs.
Sabin et al. (2015)	Nanning, China	120	RCT	Adult patient (18 years and over) tested positive for HIV/AIDS at a clinic in Guangxi, China.	Get text messages for medication reminders.	Not getting text messages for medication reminders.	Compliance with taking ARVs has increased.
Mbuagbaw et al. (2012)	Yaounde, Kamerun	200	RCT	Adults infected with HIV/AIDS aged 21 years and over.	Get motivational text messages to take ARV drugs.	Did not get moti-vational text messages to take ARV drugs.	Increasing patient compliance in taking ARVs.
Davey et al. (2018)	Maputo, Mozambik	830	RCT	Patients infected with HIV/AIDS who are taking ARV therapy who have cell phones.	Receive text message reminders to take your ARVs regularly.	Not receiving text message reminders.	Increasing adherence to taking ARVs.
Kibu et al. (2022)	Kumba, Kamerun	210	RCT	Adult patients (18 years and over) in the Buea Regional Hospital who are HIV/AIDS positive and are undergoing ARV therapy.	Receive reminders and motivational text messages to comply with taking ARVs.	Not receiving reminders and motivational text messages to comply with taking ARVs.	Patients experienced an increase in adherence to taking ARVs.

Author (Year)	Country	Sample	Study Design	Population	Intervention	Comparison	Outcome
Uuskula et al. (2017)	Tallin, Estonia	512	RCT	People with HIV/ AIDS over 18 years who are not pregnant and are being treated in an Estonian regional hospital who are undergoing ARV therapy.	Get counseling related to ARV treatment via text message.	Did not receive counseling related to ARV treatment via text message.	There was an increase in adherence to ARV consumption.
Atukunda et al. (2017)	Mbarara, Uganda	103	RCT	Patients infected with HIV/AIDS who are receiving ARV therapy are aged 20 years and over.	Get reminders via text message to take ARVs.	Not getting reminders via text messages to take ARVs.	Increasing adherence to taking ARVs in patients.
Kassaye et al. (2016)	Nyanza, Kenya	503	RCT	Pregnant women with HIV/AIDS who are taking ARVs.	Get text messages regarding motivation to take ARVs to prevent transmission from mother to baby.	Did not get text messages regarding motivation to take ARVs.	Motivation through text messages increases ARV consumption.

Table 4. Adherence behaviors among study participant

(Author, year)	Intervention			Control			RR (95% CI)
	A	NA	Total sample	A	NA	Total Sample	
Patel et al. (2017)	81	9	90	63	27	90	1.29 (1.10-1.50)
Maduka et al. (2013)	40	12	52	29	23	52	1.38 (1.04-1.83)
Sabin et al. (2015)	52	11	63	29	28	57	1.62 (1.23-2.14)
Mbuagbaw et al. (2012)	72	29	101	66	33	99	1.07 (0.89-1.29)
Davey et al. (2018)	272	144	416	269	145	414	1.01 (0.91-1.11)
Kibu et al. (2022)	55	27	82	45	37	82	1.22 (0.95-1.57)
Uuskula et al. (2017)	177	77	254	167	89	256	1.08 (0.95-1.22)
Atukunda et al. (2017)	32	30	62	25	16	41	0.85 (0.60-1.19)
Kassaye et al. (2016)	234	27	261	229	13	242	0.95 (0.90-1.00)

Note: A= Adherence; NA= Non-Adherence

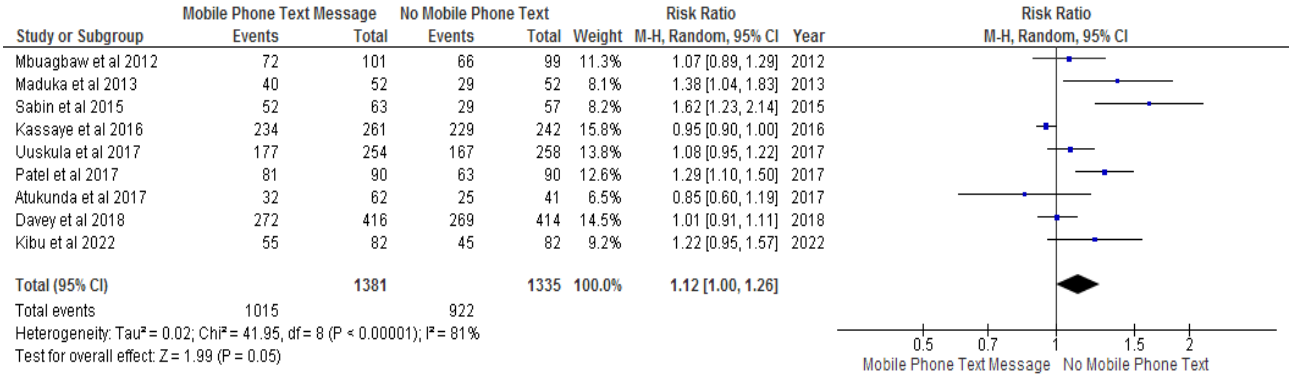

Figure 3. Forest plot of the effectiveness of mobile phone text messages on adherence to taking ARVs in PLHIV

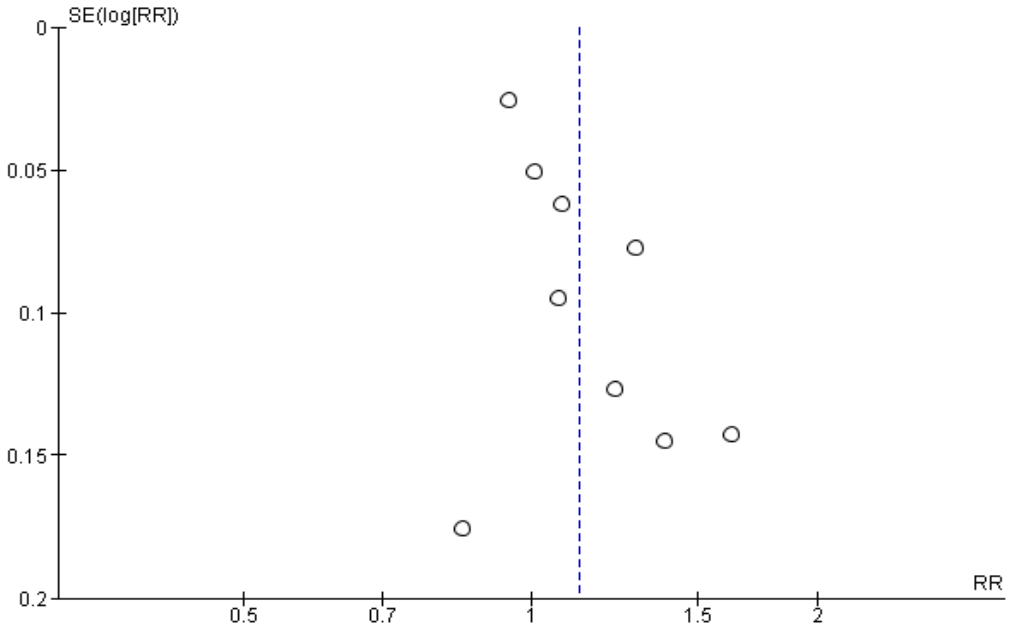

Figure 4. Funnel plot of the effectiveness of mobile phone text messages on adherence to taking ARVs in PLHIV

Several studies have shown the effect of mobile phone text messages on adherence to taking ARVs in PLHIV, one of which is the study by Maduka et al. (2013) with a total of 52 people in the intervention group and 52 people in the control group with a total of 104 people. The investigators were responsible for sending reminder messages to the intervention group, to ensure that the text messages were received by the patients then two-way messaging was carried out. The researchers operated these mobile phones to provide medication reminders and provide counseling support based on the patient's needs. The intervention was carried out for a full 6 months and evaluation was carried out at each return visit of the patient at the health clinic and at the end of the intervention.

Another study by Sabin et al. (2015), this study involved 120 PLWHA taking ARVs, for a full 6 months the intervention group received reminder messages via cell phones and counseling via cellular text messages. All subjects were checked monthly and all received electronic compliance monitoring throughout the study. Counselors in this study were trained to use supportive counseling methods, received special training to communicate with subjects via cell phones such as how to review reported adherence, explore reasons why they missed taking medication, inquire about possible barriers that patients go through in taking medication, as well as develop a strategic approach to the patient to overcome them. With the conclusion that reminders when taking medication via mobile phone text messages significantly increased adherence in taking ARVs (RR= 1.62; 95% CI= 1.23 to 2.14; p< 0.039).

In the treatment of HIV infection, routine patient control and adherence to ARV treatment are very important for the evaluation of the disease. Various methods have been tried to increase adherence includeing text message reminders via mobile phones, clinical studies on HIV conducted in urban areas of the United States that patients have cell phones and will use them to increase adherence to ARV therapy (Belzer et al., 2018). The activity of exchanging text messages is also increasingly varied in various applications. In this case world health encourages the use of technology to assist the delivery of health services, UNAIDS also encourages the use of wireless communication technology to address morbidity and mortality related to HIV infection, both in promotive, preventive and curative (Patel et al., 2017).

The support received by HIV/AIDS patients through mobile phone text messages is able to increase patient compliance in taking ARV drugs. In this intervention, text messages are sent daily so that patients say that the text messages are very helpful in reminding them to take the drug correctly, both in terms of method, time and dosage. By reading text messages that have been sent, patients understand that taking ARV drugs must be done regularly according to what is recommended for their own health and for a healthier quality of life (Liu et al., 2019).

In a study conducted by Nhavoto et al. (2017) 95% of health workers strongly agree that a text message system via mobile phone helps in increasing adherence to taking ARVs in HIV/AIDS patients, especially where the text message is in the context of receiving reminders to take ARVs. Patients also feel motivated to live a healthier life and the desire to recover is high so that adherence to taking the therapy increases. In this study, patients thought that the text message system via cell phone helped in reminding them to take the drug on time, taking the recommended dose, as well as timely control at health services. Patients

also admit that patients feel happy when they get the text message because they feel cared for so that the patient's self-motivation increases.

In Fairbanks et al. (2018) there is limited understanding of the contents of text messages sent with what the patient wants, or the messaging mechanism that can affect patient compliance in taking ARVs, especially in the context of pregnancy and the postpartum period. The design of the text messaging intervention for adherence to taking ARVs can take lessons from previous HIV-infected studies and populations. It is necessary to pay attention to what kind of population to target in implementing the text messaging intervention via mobile phone because each patient has different needs and must be adapted to the patient's circumstances to achieve treatment success.

In addition, obstacles are also felt towards the use of mobile phone services. Perceptions of individuals or groups about obstacles in carrying out health behaviors, namely individuals who feel ashamed, lazy, afraid of being ridiculed by others and afraid of being the subject of gossip by health workers. Other problems encountered include low HIV risk and privacy issues from patients (Nindiyastuti et al., 2018).

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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