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Meta-Analysis

Effectiveness of Telemedicine to Improve Drug Taking Adherence in Tuberculosis Patients: Meta-Analysis

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ABSTRACT

Background: Tuberculosis is a disease caused by a bacterium called Mycobacterium tuberculosis which usually attacks the lungs, but TB bacteria can attack any part of the body such as the kidneys, spine and brain. TB treatment must be carried out regularly so that it can be declared cured so it is necessary to monitor the patient's medication intake, namely by using telemedicine. This study aims to analyze the effectiveness of the use of telemedicine in tuberculosis patients to increase treatment adherence.

Subjects and Method: Meta-analysis was carried out using PICO as follows: The population in this study was tuberculosis patients. Intervention in the form of the use of telemedicine. Comparison is not using telemedicine. The outcome is an increase in medication adherence. A meta-analytic study was applied to this study with electronic data sources: Google Scholar, MEDLINE/PubMed, Science Direct and web of science. The article used is a full-text article with a Randomized Control Trial (RCT) study design. There are 6 articles used in this study which were analyzed using the Review Manager 5.3 application.

Results: A total of 6 articles with Randomized Control Trial (RCT) studies from Malaysia, Peru, Cameroon, China and Ethiopia showed that the use of telemedicine is effective for increasing treatment adherence in tuberculosis patients, and the effect is statistically significant (aOR = 1.98; 95% CI = 1.53 to 2.55; p<0.001).

Conclusion: The provision of high salaries and supervision increases the job satisfaction of health workers.

Keywords: telemedicine, tuberculosis, medication adherence

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BACKGROUND

Tuberculosis (TB) is caused by a bacterium called Mycobacterium tuberculosis. Bacteria usually attack the lungs, but TB bacteria can attack any part of the body such as the kidneys, spine and brain (Kemsetneg, 2021).

Mycobacterium tuberculosis is transmitted through the air, not through contact from surfaces. Transmission occurs when a person inhales droplet nuclei containing Mycobacterium tuberculosis, and the droplet nuclei enter through the mouth or nose, then into the upper respiratory tract, and continue to the bronchi and reach the alveoli of the lungs (CDC, 2013).

Tuberculosis is currently still a public health problem both in Indonesia and internationally so that it becomes one of the goals of sustainable health development (SDGs). TB is one of the 10 main causes of death worldwide (RI Ministry of Health, 2021).

In 2020, an estimated 9.9 million (8.9-10.9 million) people will fall ill with TB worldwide, of which 5.5 million are men, 3.3 million women and 1.1 million children. Eight countries account for two-thirds of the global total: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa (WHO, 2021).

It is estimated that 10 million people will suffer from Tuberculosis (TB) in 2019. In 2015 – 2019 the cumulative decrease in TB cases was only 9% (WHO, 2020). Globally, TB incidence rates fell by 11% between 2015 and 2020 (from 142 to 127 new cases per 100,000 population), including a 1.9% decrease compared to 2019 (WHO, 2021).

The number of deaths from TB in 2019 was 1.4 million, while in 2020 there were 1.5 million people including 214,000 people living with HIV. The cumulative number of deaths between 2015 – 2019 is 14%, which is less than half of the set target (WHO, 2020).

Data collected from over 200 countries has shown a significant reduction in TB case notifications, with a 25-30% decrease reported in the 3 high burden countries – India, Indonesia, Philippines – between January and June 2020 compared to the 6-month period in 2020. 2019. This reduction in case notifications could lead to a dramatic increase in additional TB deaths (WHO, 2020).

The reduction in TB cases is due to the COVID-19 pandemic. In many countries, human, financial and other resources have been shifted from TB to the COVID-19 response. TB patients do not want to go to health services for fear of contracting COVID-19. The reluctance of TB patients has an impact on the patient's treatment process. In fact, to be able to recover, TB patients who have shown symptoms must undergo continuous treatment ranging from six months to two years, depending on the severity of the disease. In addition, it has an impact on the TB case data collection and reporting system (Baturaja Research and Development Center, 2021).

One of the efforts made in optimizing TB services during the pandemic, both in dealing with a decrease in the number of case findings and monitoring taking medication, is by using Telemedicine. Telemedicine is defined as the use in the field of information and communication technology that is carried out electronically with the aim of providing and supporting patient health care without any separation. This is in accordance with Circular No. HK.02.01/MENKES/303/2020 concerning Provision of Health Services Through Utilization of Information and Communication Technology in the Context of Preventing the Spread of COVID-19. The circular letter explains that health services during a pandemic can be carried out through telemedicine services (Ministry of Health, 2020).

During the COVID-19 pandemic, TB handling efforts were hampered, so efforts to treat TB were needed, one of which could be done by utilizing digital technology, namely by using telemedicine. The telemedicine used can be in the form of SOBAT TB and EMPATI Client applications. These two applications are very useful with the advantages they have such as being effective and efficient in tackling TB during a pandemic because people do not need physical contact with health services and the public can get information through this application, applications that are easy to operate are also the main attraction in their use, besides In addition, this application is also useful in monitoring, recording and reporting TB cases (Septiani, 2022).

Prolonged TB treatment puts patients at risk of discontinuing treatment with various underlying causes of discontinuation of treatment. The use of mHealth technology can be an alternative to increase TB patient compliance in treatment with medication reminder methods, regular visit schedules, education, and social support (Pampalia and Waluyo, 2019).

There are several previous systematic review articles that have been published discussing the effectiveness of the use of telemedicine on tuberculosis patient adherence. The author is interested in using meta-analysis techniques in this study so that it is easier to obtain evidence-based research results with a large number of samples for the effectiveness of using telemedicine in tuberculosis patients and can be taken into consideration by health workers in its use. The purpose of this study was to analyze the use of telemedicine in tuberculosis patients to improve treatment adherence.

SUBJECTS AND METHOD

1. Study Design

This research is a systematic review and meta-analysis involving various databases of appropriate electronic journals including: MEDLINE/ PubMed, Science Direct, Google Scholar, and Web of Science. With keywords including: (mobile OR telemedicine OR "video directly observed therapy") AND tuberculosis AND ("patients adherence" OR "treatment adherence" OR conformity OR obedience) AND "Randomized Controlled Trial".

2. Steps of Meta-Analysis

1) Formulate research questions in PICO (Population, Intervention, Comparison, Outcome).
2) Search for articles from various databases including Google Scholar, Pubmed, and Science Direct.
3) Conduct screening and critical appraisal of primary studies using the Critical Appraisal Checklist for Cross-sectional Studies from the Center for Evidence Management
4) Perform data extraction and enter the effect size of each primary study into the RevMan 5.3 application
5) Interpret the results of the research analysis and draw conclusions

3. Inclusion Criteria

The article used is full-text in English, the study design is Randomized Controlled Trial (RCT) which lists the number of compliance for each group. The research subjects were tuberculosis patients. With intervention in the form of the use of telemedicine. The research outcome is medication adherence.

4. Exclusion Criteria

Articles not in English and articles published before 2013.

5. Operational Definition

Telemedicine is a form of utilizing health information technology with the aim of diagnosing, treating and preventing disease and injury to improve the quality of health services and improve effective and efficient work processes.

Compliance with taking medication is a form of behavior in taking medication according to the schedule and the right dose of medication.

6. Research Instruments

The instrument used in this study was the Critical Appraisal Checklist Center for Evidence Based Management (CEBMa).

7. Data Analysis

The instrument used in this research is critical appraisal for a randomized controlled trial (RCT) study published by the Center for Evidence Based Management.

RESULTS

The article selection process was carried out using the Mendeley application. In the initial

search process, 1054 articles were obtained. After the selection process, 171 similar articles were found. The same article was deleted so that a total of 883 articles were obtained. Of the 883 articles, 859 articles were excluded because they did not meet the inclusion criteria. The remaining 24 articles were then filtered again, obtaining 15 articles that were not appropriate. The remaining 9 articles were subjected to qualitative synthesis with the results of 3 articles being excluded because there was no number of adherent patients in each group. 6 articles included in the meta-analysis process can be seen in (Figure 1).

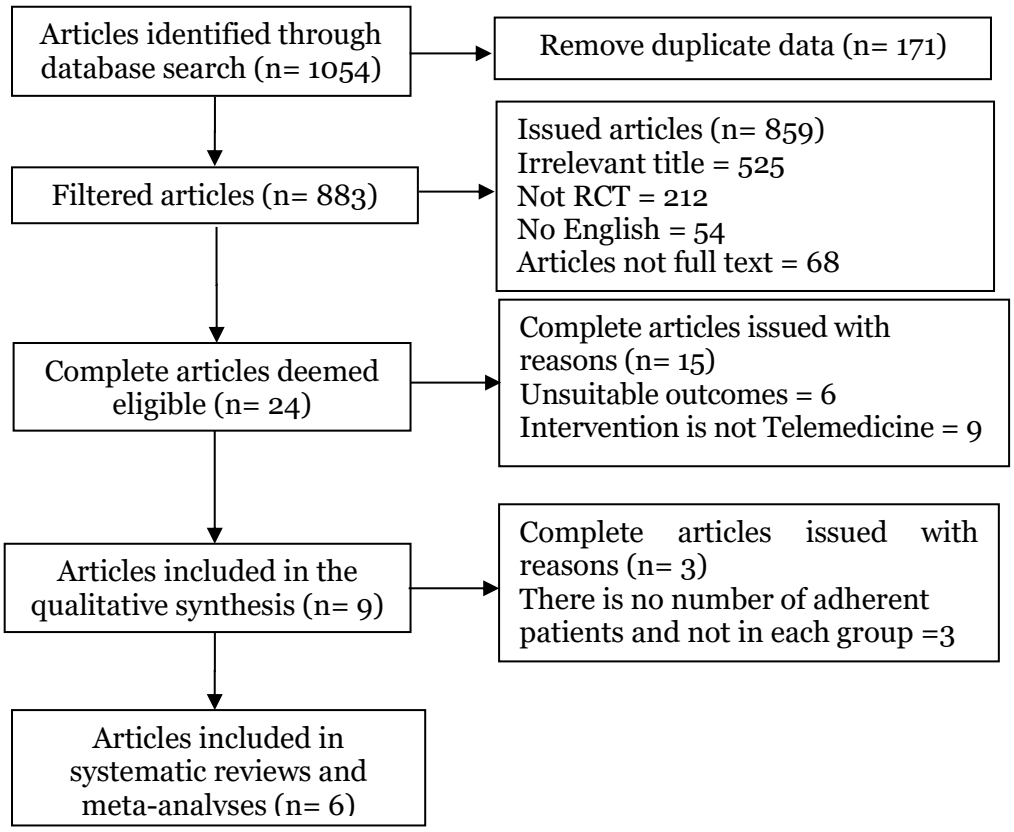

Figure 1. Prisma flow diagram

Figure 2. Map of the effectiveness of using telemedicine

in TB patients to improve treatment adherence

Table 1. Critical appraisal checklist for randomized controlled trial studies in a meta-analysis

Author (Year)	Question of Checklist												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Abdulrahman et al. (2017)	1	1	1	1	1	1	1	1	1	1	1	1	12
Acosta et al. (2022)	1	1	1	1	1	1	1	1	1	1	1	1	12
Bediang et al. (2014)	1	1	1	1	1	1	1	1	1	1	1	1	12
Fang et al. (2017)	1	1	1	1	1	1	1	1	1	1	1	1	12
Gashu et al. (2021)	1	1	1	1	1	1	1	1	1	1	1	1	12
Guo et al. (2020)	1	1	1	1	1	1	1	1	1	1	1	1	12

Question Criteria Description:

1= Does this study address a clear research focus?

2= Is the Randomized Controlled Trial research method suitable for answering the research questions?

3= Were there enough subjects in the study to establish that the findings were not coincidental?

4= Were the subjects randomly allocated to the experimental and control groups?

5= Were inclusion/exclusion criteria used?

6= Were the two groups comparable at the start of the study?

7= Were objective and unbiased outcome criteria used?

8= Were objective and validated measurement methods used to measure the results?

9= Is the effect size practically relevant?

10= How precise is the estimated effect? Are there confidence intervals?

11= Could there be confounding factors that haven't been taken into account?

12= Are the results applicable to your research?

Answer score description:

0= No

1= Yes

Table 2 Description of the primary studies included in the primary study meta-analysis

Author (Year)	Sample	P	I	C	O
Abdulrahman et al. (2017)	242	Patients Tuberculosis	Telemedicine using Mobile phone reminders	Direct consultation	Tuberculosis patient treatment adherence
Acosta et al. (2022)	112	Patients Tuberculosis	Telemedicine using a medication event reminder monitor system (MERM)	Direct consultation	Tuberculosis patient treatment adherence
Bediang et al. (2014)	279	Patients Tuberculosis	Telemedicine using TB-SMS Cameroon	Direct consultation	Tuberculosis patient treatment adherence
Fang et al. (2017)	350	Patients Tuberculosis	Telemedicine using the ShortMessage Service of Pulmonary Tuberculosis	Direct consultation	Tuberculosis patient treatment adherence

Author (Year)	Sample	P	I	C	O
Gashu et al. (2021)	306	Patients Tuberculosis	Telemedicine using a phone reminder system	Direct consultation	Tuberculosis patient treatment adherence
Guo et al. (2020)	405	Patients Tuberculosis	Telemedicine using video directly observed therapy (VDOT)	Direct consultation or directly observed therapy (DOT)	Tuberculosis patient treatment adherence

Table 3 Number of primary study adherence included in the primary study meta-analysis

Author (Year)	Telemedicine		Non telemedicine	
	Event	Non-event	Event	Non-event
Abdulrahman et al. (2017)	107	9	59	17
Acosta et al. (2022)	38	11	33	53
Bediang et al. (2014)	65	23	69	21
Fang et al. (2017)	154	30	165	87
Gashu et al. (2021)	110	29	95	48
Guo et al. (2020)	185	14	171	25

The forest plot in Figure 3 shows that telemedicine is effective in increasing medication adherence in tuberculosis patients, and the effect is statistically significant. TB patients using telemedicine were 1.98 times more likely to comply with treatment than those not using telemedicine (aOR= 1.98; 95% CI = 1.53 to 2.55; p<0.001).

The forest plot also shows low heterogeneity effect size (I^2=46%; P=0.100). Thus the calculation of the average effect estimate is carried out using the Fixed Effect Model (FEM) approach.

The funnel plot in Figure 4 shows that the distribution of effects between studies is symmetrically located to the right and left of the estimated mean vertical line. Thus the funnel plot does not identify publication bias.

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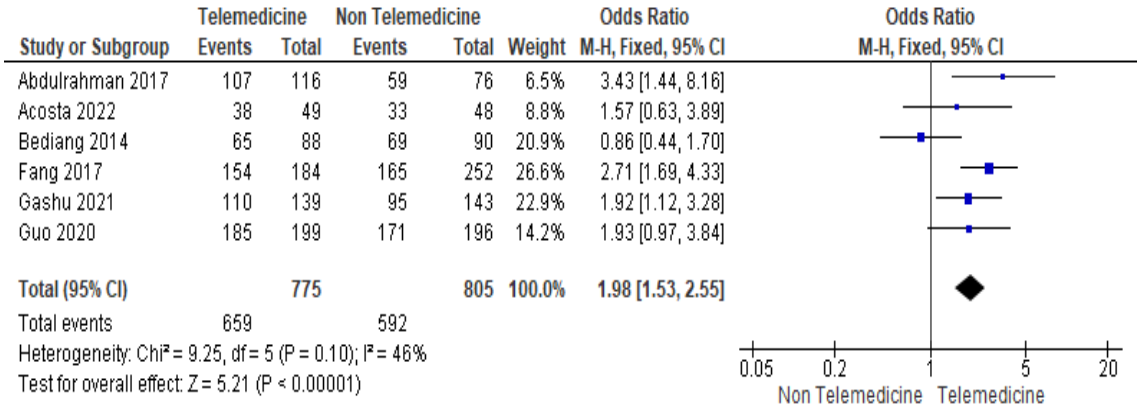

Figure 3. Forest plot on the effectiveness of using telemedicine in TB patients to improve treatment adherence

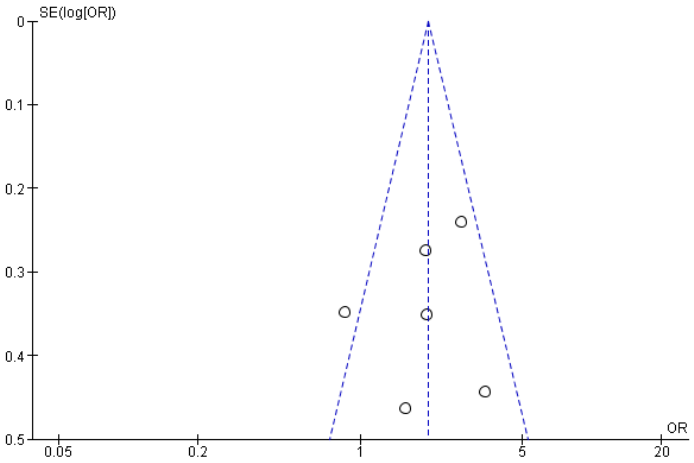

Figure 4. Funnel plot on the effectiveness of using telemedicine in TB patients to improve treatment adherence

DISCUSSION

Telemedicine is the provision of health services remotely by health professionals using information and communication technology. The provision of telemedicine services consists of teleradiology, teleelectrocardiography, tele-ultrasonography, clinical teleconsultation and other consulting services in accordance with developments in science and technology (Ministry of Health, 2019).

The terms "telemedicine" and "telehealth" have been defined separately over time but are often used interchangeably with overlapping scopes. The definition of telemedicine from the Guidelines for Strengthening Health Systems is as follows: “the provision of remote health services with communications made between health care providers seeking clinical guidance and support from other health care providers (provider-to-provider telemedicine); or conducted between remote healthcare users seeking health services and healthcare providers (client-to-provider telemedicine)” (WHO, 2020).

Dwi et al's research (2019) aims to determine the effectiveness of sending SMS reminders on increasing adherence to pulmonary TB treatment and to find out how to operate the SMS Gateway software and to find out the response of TB sufferers to sending SMS. This type of research is quasi-experimental in the form of a posttest only control group design involving 2 groups of subjects, 1 of which is given treatment (experimental group) and the other is given nothing (control group). Sampling used is the total sampling method. The population was all new TB patients (positive smear) who had been diagnosed in November 2016 and underwent treatment at the puskesmas for 2 months (advanced treatment) and met the inclusion and exclusion criteria. The results of this study can be concluded statistically that there is a significant relationship between sending SMS reminders on medication adherence in pulmonary TB patients. (OR=31.26; 95% CI= 1.54 to 634.64; p=0.025). The conclusion of this study is that sending SMS reminders increases adherence to pulmonary TB treatment at the Palangka Raya health center.

The aim of the study by Doltu et al (2021) was to compare adherence and short-term and long-term TB treatment outcomes for TB patients who underwent asynchronous Video Observed Treatment (aVOT) during three months of outpatient treatment compared to Directly Observed Treatment (DOT) in operational conditions in 2016-2017 in Chisinau. The results from this study

indicate that aVOT improves adherence to TB treatment convenience and operational terms in terms of short-term and long-term treatment outcomes.

Tuberculosis is TB or Tuberculosis is an infectious disease caused by the bacterium mycobacterium tuberculosis which can attack the lungs and other organs (Kemsetnag, 2021).

Mycobacterium tuberculosis is transmitted through the air, not through contact from surfaces. Transmission occurs when a person inhales droplet nuclei containing Mycobacterium tuberculosis, and the droplet nuclei enter through the mouth or nose, then into the upper respiratory tract, and continue to the bronchi and reach the alveoli of the lungs (CDC, 2013)

Based on SITB (TB Information System Software) TB cases in Indonesia as of April 2021 recorded 357,199. One of the factors for TB treatment problems is treatment adherence, based on data from the Ministry of Health, the success rate for TB treatment has decreased since 2016. The success of treating TB patients for 10 years was the highest in 2010 at 89.2%, while in 2020 treatment success experienced the lowest decline at 82.7%. and in 2021 it will be 83% (RI Ministry of Health, 2020a).

Support from various parties is needed to increase the success of TB treatment. One of the supports in the national strategy for tackling tuberculosis in Indonesia 2020-2024 is good drug side effect management to increase the success of treatment for drug-sensitive and drug-resistant tuberculosis patients, one of which is by utilizing new technology such as video observed treatment (VOT), support from health workers, and support from the community/former patients (Kemenkes RI, 2020b)

The government has made efforts to increase the success rate of TB treatment by issuing Presidential Decree number 67 of 2021 concerning tuberculosis control. This Presidential Regulation is intended to provide a reference for ministries/agencies, provincial regional governments, district/city regional governments, village governments, and other stakeholders in implementing TB control. With the target of eliminating TB by 2030, namely reducing the incidence of TB to 65 per 100,000 population and reducing the death rate from TB to 6 per 100,000 population (Kemsetnag, 2021).

This study takes the topic of the effectiveness of the use of telemedicine in tuberculosis patients, where the independent variable in this study is the use of telemedicine and the dependent variable in this study is adherence to treatment of tuberculosis patients.

Confounding factors are things that cannot be avoided in a study, but can be controlled. Confounding factors affect the relationship or effect of exposure to disease incidence which is estimated (estimated) by the study is not the same as the relationship or effect that actually occurs in the target population (target population), aka the study results are invalid (incorrect) (Murti, 2018a).

This study uses research that controls confounding factors. This can be seen from the inclusion and exclusion requirements required in this study, so that it can control confounding factors that can make the research invalid. There were 6 articles that met the inclusion and exclusion requirements from a number of primary studies that were included in this systematic review and meta-analysis. Then the number of adherent and non-adherent patients in the telemedicine group and the control group were combined and processed using the RevMan 5.3 application.

The results of data processing using the RevMan 5.3 application on 6 articles originating from Malaysia, Peru, Cameroon, China

and Ethiopia resulted in the following conclusions: Tuberculosis patients who use telemedicine have the possibility to adhere to treatment 1.98 times compared to tuberculosis patients who do not use telemedicine (aOR = 1.98; 95% CI = 1.53 to 2.55; p<0.001)

This is in line with previous research by Abdulrahman et al., (2017) which stated that cell phone reminders in the form of SMS and phone call reminders increased TB patient treatment adherence compared to peer counseling. After 6 months of follow-up, mean adherence was significantly higher in the intervention group (mean=95.68; 95% CI= 94.39 to 96.97) compared to the control group (mean=87.5; 95% CI= 86.14 to 88.81). The proportion of study subjects who had good adherence (>95%) was significantly higher in the intervention group (92.2%) compared to the control group (54.6%).

The results from the research by Acosta et al. (2022) The use of the Medication event reminder driver system (MERM) in the second phase of treatment showed a significant increase in the success rate of treatment in drug-susceptible pulmonary TB patients. Treatment success was significantly more common in the MERM group (RR=1.15; 95% CI = 1.02 to 1.30; P=0.032). There was no significant difference in adherence outcomes, but the percentage of patients who missed at least one dose and patients with more than 10% of the total dose missed was lower in the intervention group.

The results of the study by Bediang et al (2014) stated that there were 87 recovered patients (63.5%) in the intervention group and 88 patients (62%) in the control group. The results of this study are that SMS reminders have the possibility to adhere to treatment 1.06 times compared to those who do not use SMS reminders (OR = 1.06; 95% CI = 0.65 to 1.73; p = 0.791).

Research conducted by Fang et al (2017) with the results of managing pulmonary TB patients through SMS can effectively strengthen the complete treatment rate of pulmonary TB patients and reduce missed dose rates and interrupted treatment rates, and further increase their awareness of re-examination. The treatment completion rate in the SMS group (96.25%) was significantly higher than in the control group (86.84%).

Research conducted by Gashu et al (2021) stated that adherence to patient-centered TB treatment was 79% (110/139) in the intervention and 66.4% (95/143) in the control group. The results of this study showed that patients using a reminder system were able to improve TB treatment adherence (RR=1.632; 95% CI= 1.162 to ∞ ; p= 0.018).

Guo et al (2020) The results of this study indicate that video directly observed therapy (VDOT) for tuberculosis patients using VDOT may be able to improve treatment adherence compared to patients using directly observed therapy (DOT)

The treatment completion rate of patients with VDOT was 96.1% while tuberculosis patients with DOT was 94.6% Patients in the VDOT group had a better experience compared to the DOT group.

AUTHOR CONTRIBUTION

Lilik Anggar Sri Rahayuningsih as the main researcher who selects topics, conducts research, collects research data, formulates research articles, and data processing. Didik Gunawan Tamtomo helped formulate a framework and analyze research data. Bhisma Murti played a role in formulating the background and discussion of the research.

CONFLICT OF INTEREST

There was no conflict of interest in the study.

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