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Factors Associated with Pulmonary Tuberculosis Prevention Behavior among Students at Al-Ikhsan Beji Islamic Boarding School, Banyumas, Indonesia

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Abstract

Background: Pulmonary tuberculosis (TB) is an infectious disease, and one of the risk factors is low levels of community preventive behavior. TB prevention efforts are important in community groups in high-risk places, such as Islamic boarding schools, which have dense occupancy and intense interactions among students. This study aimed to identify the determinants of TB prevention behavior among students.

Methods: This study used a quantitative, cross-sectional design. The sampling procedure applied proportional stratification and obtained 81 students from the Al-Ikhsan Beji Islamic Boarding School. Data were collected through questionnaires and interviews. Data were analyzed using chi-square tests and logistic regression analysis.

Results: Most respondents exhibited poor TB prevention behavior (51.9%). Bivariate analysis revealed that knowledge (p=0.026), perceived benefits (p=0.005), and perceived barriers (p=0.013) were related to TB prevention behaviors. Multivariate analysis indicated that knowledge (p=0.049), perceived benefits (p=0.018), and perceived barriers (p=0.043) were significantly associated with TB prevention behaviors. Knowledge was the strongest predictor, with an odds ratio (OR) of 3.615, indicating that students with low knowledge had 3.615 times higher odds of poor TB prevention behavior.

Conclusion: Perceived vulnerability, perceived seriousness, and cues to action did not determine TB prevention behaviors among students. Increasing educational messages on TB prevention and collaboration between community health centers, Islamic boarding school caregivers, and Islamic boarding school health posts are needed.

Keywords: Health belief model, Islamic boarding school, students, tuberculosis

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Introduction

Pulmonary tuberculosis (TB) remains a serious global health problem. The World Health Organization (WHO) estimates that 10.6 million people suffer from TB.[1] The ease of TB transmission has made it the second most infectious killer disease after COVID-19[2] and placed Indonesia second in the world with the highest TB cases after India.[3] There are 345 people out of 100.000 Indonesians who suffer from TB. The distribution of TB cases in Indonesia is quite even across all provinces, with Central Java as the second-highest province after West Java.[4] The number of TB cases found in Central Java Province in 2021 was 114.60 per 100,000 population, placing Banyumas Regency in 4th place for the highest number of TB cases.[5]

One of the factors causing the high number of TB cases in Indonesia is the lack of preventive community behavior. Poor behavior is associated with TB transmission, with a risk of 4.21 times.[6] Indarto et al. stated that behaviors associated with TB sufferers include a lack of exercise, smoking, poor diet, and low compliance with TB treatment.[7] The government has made various efforts to prevent TB transmission, as stated in Presidential Regulation Number 67 of 2021 concerning TB Prevention and Control Efforts, which states that one of the efforts is through finding TB cases in community groups in high-risk places, such as Islamic boarding schools.[8] Islamic boarding schools are educational institutions that are filled with many productive-age students. According to the National Health Profile, the highest incidence of TB occurs among the productive age group (15-34 years), which is 34%, with 16.9% of cases occurring in the 15-24 years age range.[9] The Tuberculosis Information System (SITB) recorded the discovery of 127 TB cases in boarding school students in 2021. In Central Java Province, there are 5,087 institutions with 620,958 students.[10] Islamic boarding schools become a population at risk for TB because they have characteristics of dense housing, intense interaction between students, and communal boarding school life, which has the potential to be a place for TB transmission.[11,12]

Considering that TB is a preventable disease, it is important for the Islamic boarding school community to have good TB prevention behavior. However, preventive behavior can be formed because it is influenced by the determinant factors that could form it. In this case, the health belief model (HBM) introduced by Lewin (1954) can explain preventive behavior and individual responses to disease. When individuals act to fight or treat their disease, there are 4 key variables, namely perception of vulnerability, perception of seriousness, perception of benefits and barriers, and cues to action.[13] Based on Lawrence Green's theory, behavior is influenced by predisposing, enabling, and reinforcing factors.[14]

According to the research results of Asfiya et al. (2021), knowledge is related to the practice of PHBS to prevent pulmonary TB in students at the Attholibiyah Bumijawa Islamic Boarding School.[15] Marhamah et al. (2019) also found that knowledge influences the behavior of preventing the transmission of Pulmonary Tuberculosis.[16] A good understanding of TB raises patient awareness to change detrimental behaviors such as spitting carelessly, not practicing proper cough etiquette, and not maintaining a clean home environment. A poor perception of seriousness is 4.07 times more likely to experience pulmonary tuberculosis than a good perception of seriousness.[17] Furthermore, the study also found that a poor perception of vulnerability is 1.36 times more likely to experience tuberculosis. Ali et al. (2020) stated that the perception of benefits influences the behavior of preventing TB transmission.[18] Sari et al. (2022) found that there was a significant relationship between the perception of barriers in implementing Poskestren and the behavior of students in forming healthy students in Islamic boarding schools in Batanghari District.[19] Bad cues in action also have a 1.37 times greater risk of experiencing pulmonary tuberculosis than the perception of good cues in action.

Kedungbanteng Subdistrict, Banyumas District, is included in the category of TB locus areas. According to the Banyumas District Health Office, Beji Village has the highest number of TB cases in the Kedungbanteng area. To prevent and control TB, the Kedungbanteng Health Center also makes Islamic boarding schools a place to implement community-based health efforts, also known as Islamic Boarding School Health Posts (Poskestren). Six out of 19 Islamic boarding schools have been integrated with Poskestren, one of which is the Al-Ikhsan Beji Islamic Boarding School (AIBS). According to information from two boarding school administrators, the Al-Ikhsan Beji Islamic Boarding School has approximately 540 students. The boarding school has male and female dormitories

with a fairly dense number of occupants in each room, approximately 10-25 students. The positive activities of the students are very busy from morning to night, which are filled with school activities, reciting the Quran, language classes, self-development, and so forth. Daily routines, such as studying, sleeping, eating, bathing, washing, and using the toilet are performed together.

The results of a preliminary study conducted on five students found that their knowledge of TB was not excellent. They knew little about the symptoms of TB and did not fully understand its causes, treatment, or prevention. They felt that TB was a serious disease but did not feel susceptible to it. Students received information about TB only from health centers. The activities of the Health Post there provided more curative services because promotive and preventive activities were still followed by the activities of the Kedungbanteng Health Center. Efforts to handle TB in Islamic boarding schools were in the form of screening and education from the Health Center for students, which was conducted approximately once a year. There were no data on TB incidence in the boarding school, but the researcher assumed that TB prevention efforts were important, considering that students also lived in the Beji village community, where many TB cases were found. Therefore, based on the problems and results of previous studies, the researcher was interested in examining the determinant factors that influenced TB prevention behavior in students at the Al-Ikhsan Beji Islamic Boarding School in the Kedungbanteng Subdistrict.

Methods

This study used a quantitative research design and a cross-sectional approach. This study was conducted at the Al-Ikhsan Beji Islamic Boarding School in the Kedungbanteng Subdistrict of Banyumas District. The research was conducted from September 2023 to January 2024 after obtaining ethical research approval from the Health Research Ethical Commission of Jenderal Soedirman University (number 1258/EC/KEPK/X/2023). The population in this study were all students at the Al-Ikhsan Beji Islamic Boarding School, totaling 540 students, consisting of 340 MTs students, 123 MA students, and 77 students at the college level. A sample of 81 respondents was obtained through a proportional stratified sampling procedure consisting of two strata: MTs and MA. The sample size was calculated using a *two-proportion hypothesis* test formula. The sample inclusion criteria were as follows: respondents were mukim (permanently living) students registered at the Al-Ikhsan Islamic Boarding School and were willing to become respondents and participate in the research until it was completed. The exclusion criteria were respondents who were over 19 years old, were sick, were not at the research location, and respondents who did not complete the questionnaire.

The independent variables were knowledge, seriousness of the disease, vulnerability to the disease, benefits of the vaccine, barriers to vaccination, and cues to action. The dependent variable in this study was the pulmonary tuberculosis (TB) prevention behavior. The data sources consisted of primary and secondary data sources. Primary data sources were obtained through interviews with the Kedungbanteng Health Center, caregivers, and administrators of the Al-Ikhsan Beji Islamic Boarding School. Interviews were also conducted by distributing questionnaires to students to obtain data related to the determinants of TB prevention behavior at the Al-Ikhsan Beji Islamic Boarding School. Secondary data in data collection used in this study, namely Indonesian Health Profile Data, Provincial/Subdistrict Health Profile Data, Kedungbanteng Health Center Profile Data, Al-Ikhsan Beji Islamic Boarding School Profile Data, books, and previous research, were also used. Data were collected using questionnaires through interviews. The questionnaire development was tested for validity using Pearson product-moment correlation and for reliability using Cronbach's alpha formula for 30 respondents at the Anwaarul Hidayah Islamic boarding school. Question items were considered valid if the calculated r-value ≥ r-Table (0,361). Data

analysis was performed using univariate, bivariate (chi-square), and multivariate (multiple logistic regression) analyses. This study was conducted in accordance with ethical rules and the basic principles of research. The determination of research subjects was carried out with prior informed consent after receiving an explanation of the study. Subjects who met the requirements as respondents were included in the study with a guarantee of the right to confidentiality and privacy.

Results

Based on Table 1, 42 respondents (51.9%) of students at Al-Ikhsan Beji Islamic Boarding School in Kedungbanteng Subdistrict had poor TB prevention behavior. Most of them were in the middle adolescence category, with a total of 46 respondents (56.8%), while 50 respondents (61.7%) were female, and as many as 60 respondents (74.1%) were studying in middle school (MTs). The majority of respondents had good knowledge, accounting for 63 (77.8%) respondents. Of the respondents, 50 (61.7%) had a positive perception of vulnerability, and 51 (63.0%) had a positive perception of seriousness. The number of respondents with positive perceived benefits was 42 (51.9%), while 50 respondents (61.7%) had low perceived barriers, and most had positive cues to action (44 respondents [54.3%]).

Based on Table 2, it is known that students with poor TB prevention behavior, 14 (77.8%) have fairly good and poor knowledge, while 28 (44.4%) have good knowledge. The results of the chi-square test analysis showed a p-value of 0.026 (p-value <0.05); thus, it can be concluded that there is a relationship between TB knowledge and TB prevention behavior. Furthermore, among students with poor pulmonary TB prevention behavior, 19 (61.3%) had a negative perception of vulnerability and 23 (46.0%) had a positive perception of vulnerability. The results showed a p-value of 0.267 (p-value ≥ 0.05), indicating no association between perceived vulnerability and TB prevention behavior among students. In terms of perceived seriousness, 19 (63.3%) respondents with poor TB prevention behavior had a negative perception of seriousness, whereas 23 (45.1%) respondents with good TB prevention behavior had a positive perception of seriousness. The results of the analysis showed a p-value of 0.175 (p-value ≥ 0.05), which means that there was no relationship between perceived seriousness and TB prevention behavior in students.

There was a relationship between perceived benefits and TB prevention behavior (p = 0.005), where among respondents with poor TB prevention behavior, 27 (69.2%) had negative perceived benefits, and 15 (35.7%) had positive perceived benefits. The same results were also obtained for perceived barriers, where it was found that respondents who had poor TB prevention behavior, 22 (71.0%) had high perceived barriers, while 20 (40.0%) had low perceived barriers. The results showed a p-value of 0.013, indicating a relationship between perceived barriers and TB prevention behavior among students. Furthermore, the results showed that 20 (54.1%) respondents with negative cues to action had poor TB prevention behavior, while 22 (50.0%) respondents with positive cues to action had poor TB prevention behavior. The results of the analysis showed a p-value of 0.888; therefore, there was no relationship between cues to act and TB prevention behavior in students.

Multivariate analysis was used to determine the effect of the independent variables on the dependent variable, namely, the tuberculosis prevention behavior of students at Al-Ikhsan Beji Islamic Boarding School. This multivariate analysis used a multiple logistic regression test with the enter method. The variables included in the multivariate testing were those with a p-value ≤ 0.25, namely, knowledge, perceived susceptibility, perceived seriousness, perceived benefits, and perceived barriers.

Table 1. Characteristic Respondent

Variables	Frequency	Percentage (%)
Age		
Early Adolescents (10-12 years)	15	18.5
Middle Adolescents (13-15 years)	46	56.8
Late Adolescents (16-19 years	20	24.7
Gender		
Male	31	38.3
Female	50	61.7
Education		
Middle School (SMP/MTs)	60	74.1
High School (SMA/SMK/MA)	21	25.9
Knowledge		
Good	63	77.8
Fairly Good	16	19.8
Poor	2	2.5
Perceived Vulnerability		
Positive	50	61.7
Negative	31	38.3
Perceived Seriousness		
Positive	51	63.0
Negative	30	37.0
Perceived Benefits		
Positive	42	51.9
Negative	39	48.1
Perceived Barriers		
High	31	38.3
Low	50	61.7
Cues to Action		
Positive	44	54.3
Negative	37	45.7
TB Prevention Behavior		
Good	39	48.1
Poor	42	51.9

Table 2. Crosstab between the Determinants and TB Prevention Behavior among Students

Category	TB Prevention Behavior				Total		*p-value*
	Poor		Good				
	n	%	n	%	n	%	
Knowledge							
Fairly Good and Poor	14	77.8	4	22.2	18	100.0	0.026
Good	28	44.4	35	55.6	63	100.0	
Perceived Vulnerability							
Positive	19	61.3	12	38.7	31	100.0	0.267
Negative	23	46.0	27	54.0	50	100.0	
Perceived Seriousness							
Positive	19	63.3	11	36.7	30	100.0	0.175
Negative	23	45.1	28	54.9	51	100.0	
Perceived Benefits							
Positive	27	69.2	12	30.8	39	100.0	0.005
Negative	15	35.7	27	64.3	42	100.0	
Perceived Barriers							
High	22	71.0	9	29.0	31	100.0	0.013
Low	20	40.0	30	60.0	50	100.0	
Cues to Action							
Positive	20	54.1	17	45.9	37	100.0	0.888
Negative	22	50.0	22	50.0	44	100.0	

Subsequently, gradual elimination was performed on variables with a p-value ≥ 0.05, and the final results were obtained, as shown in Table 3. Based on Table 3, the knowledge variable has a significance value of 0.049 ($p < 0.05$). The perceived benefit variable had a significance value of 0.018 ($p < 0.05$). Furthermore, the

perceived barriers variable had a significance value of 0.043 (p <0.05). This means that Ho on the three variables is rejected, or there is an influence between knowledge, perceived benefits, and perceived barriers to tuberculosis prevention behavior among students at Al-Ikhsan Beji Islamic Boarding School

Table 3. Multivariate Logistic Regression Modeling Result

Variable	*Sig.*	α	Exp (B)	95% CI for Exp (B)	
				Lower	Upper
Knowledge	0.049	0.05	3.615	1.000	13.063
Perceived Benefits	0.018	0.05	3.297	1.227	8.861
Perceived Barriers	0.043	0.05	2.892	1.034	8.091

Discussion

Knowledge

The multivariate analysis results showed that knowledge influences the behavior of preventing pulmonary TB among students at the Al-Ikhsan Beji Islamic Boarding School. The results of this study are in line with the research of Asfiya et al. (2021), who found a relationship between knowledge and the practice of PHBS for preventing pulmonary TB in students (p-value=0.002).[20] Students with good knowledge can distinguish between good and bad, so they will carry out PHBS for preventing pulmonary TB according to their understanding. Yun (2020) also stated that knowledge is the main factor influencing TB prevention behavior in students in six regions of Korea (p-value = 0.025).[21]

According to Green (1980) in Pakpahan et al. (2022), knowledge is a facilitating factor because it is a trigger, basis, or motivation to act; thus, individuals with good knowledge will act based on what they know and understand.[22] After someone knows the stimulus or health object, then he makes an assessment or responds to what is known and the next process is expected that he will practice what he has known and responded to Notoatmodjo (2014).[13]

Based on the results of this study, respondents who were well-informed showed good preventive behaviors, such as covering their mouths or noses when coughing or sneezing and washing their hands with soap and running water. The majority of respondents did not know that sweating at night is also a symptom of TB (58.0%), considered TB to be a hereditary disease (70.4%), and did not know that patients who had recovered from TB could get it again (81.5%). Information needs to be given to someone who can then increase their knowledge and raise awareness to behave according to the knowledge they have.[13] The researcher argues that the low knowledge of students regarding the symptoms and transmission of pulmonary TB can have implications for students' lack of awareness of factors that can influence the transmission of pulmonary TB.

Perception Benefits

The perception of benefits significantly influenced TB prevention behaviors among students. Based on the results of this study, it is in line with the research of Ali et al. (2020) which shows that the perception of benefits influences the behavior of preventing TB transmission (p = 0.045).[23] Someone who has a good perception of the benefits of a disease tends to be more likely to carry out preventive behavior for pulmonary tuberculosis.[24] Perception of benefits is an important factor that influences respondents to be more compliant in TB treatment in Iran.[25] If an individual feels vulnerable to diseases that are considered serious, then he will take certain actions that depend on the benefits he feels.[13] Perception of benefits refers to a person's perception of the effectiveness of various actions available to reduce the threat of disease.[26]

Based on the results, the researchers argue that when students perceive the benefits of preventing TB, the tendency to adopt TB prevention measures will be greater. As many as 64.3% of respondents

who had a positive perception of benefits showed good TB prevention behavior, such as often and always opening the window/ventilation of the room every morning (81.5%) and covering their mouth or nose when coughing or sneezing (76.6%). According to researchers, the perception of benefits among these students can be influenced by their knowledge of TB infection. When they already know the benefits of TB prevention behavior, they will feel effective benefits in preventing TB. In some cases, respondents with a positive perception of benefits showed poor TB prevention behavior, such as rarely exercising regularly (85.2%) and never or rarely getting enough rest (82.7%). Researchers assume that this can happen because of the perception of barriers that will reduce their chances of engaging in pulmonary TB prevention behaviors.

Perception of Barriers

The multivariate analysis showed that perceptions of barriers to preventing pulmonary tuberculosis among students influenced the results. This study is in line with Sari et al. (2022) which showed that there was an influence between perceptions of barriers to the behavior of healthy students in Islamic boarding schools in Batanghari District.[27] Perception of barriers is the potential negative side of certain health actions that are considered as barriers to carrying out recommended behaviors.[28] This study is in line with the Health Belief Model (HBM) theory which states that actions depend on the obstacles found in taking those actions.[13]

This study shows some of the biggest obstacles for students at the Al-Ikhsan Islamic Boarding School in carrying out TB prevention behavior, namely, in terms of time and social emotion. In the midst of quite dense activities at the boarding school, students also have different habits regarding cleanliness and health issues. In this study, 71.0% of respondents with high perceptions of obstacles showed poor TB prevention behavior, such as rarely exercising regularly (85.2%) and rarely resting (45.7%). The researcher argues that a high perception of obstacles may be a barrier for students to engage in pulmonary tuberculosis prevention behavior.

Perception of Vulnerability

Perceived vulnerability had no significant effect on the behavior of preventing pulmonary tuberculosis in students ($p = 0.842$). This study is in contrast to the study by Ali et al. (2020), which showed that there is a relationship between perceived vulnerability and behavior to prevent pulmonary TB transmission.[23] There is a relationship between perceived vulnerability and TB prevention behavior.[29,30] Respondents who have a poor perception of vulnerability, such as feeling that pulmonary TB cannot be transmitted through the air, will have poor prevention behaviors. This study is not in line with the HBM theory, which states that preventive measures against a disease will arise if he or his family are susceptible to the disease.[13] Someone who has a negative perception of vulnerability tends to feel that they have a low risk of contracting the disease and is passive in health maintenance behavior.[31]

The results of this study indicate that 23 out of 42 students had poor TB prevention behavior but had positive perceptions of vulnerability. This means that even though students have a positive perception of vulnerability, it is not necessarily true that their preventive behavior is good, and vice versa. The researcher argues that most of the respondents feel vulnerable to pulmonary TB, but there are other factors that inhibit (perceived obstacles) the implementation of pulmonary TB prevention behavior. For example, students felt vulnerable, as seen from the number of students who agreed and strongly agreed that being near someone who sneezes or coughs makes them more at risk of contracting TB (91.3%), that the densely populated boarding school environment facilitates TB transmission (80.2%), and that they are vulnerable to TB if they have friends who have a history of TB in the boarding school (63.0%). However, the results of this study show that they also have perceptions of obstacles, namely, feeling uncomfortable if

they have to keep their distance from sufferers. Students also cannot be separated from daily activities or activities carried out together, so that pulmonary TB prevention behavior cannot be fully implemented.

Perception of Seriousness

Based on the results of the multivariate analysis, it was found that the variable of perception of seriousness had no influence on the behavior of preventing pulmonary tuberculosis in students (p = 0.804). This study contrasts with the study by Ali et al. (2020), which showed that the perception of seriousness influenced the behavior of preventing pulmonary TB.[23] In this study, respondents felt that pulmonary TB was a harmless disease and not a fatal disease; therefore, respondents tended not to carry out good TB prevention behavior. The results of this study are not in line with the HBM theory, which states that individual actions to prevent disease will be driven by the perception of the seriousness of the disease.[13] When someone has a high perception of the seriousness of the threat of disease, their prevention behavior is also good.[23,24,32]

In the results of this study, most students had a positive perception of the seriousness of gambling (63.0%). This could be because most students also have good knowledge. The results showed that 23 out of 42 students had poor TB prevention behavior but had a positive perception of seriousness. This means that even though students have a positive perception of seriousness, their preventive behavior is not necessarily good. According to the researchers, most respondents felt that pulmonary TB is a serious disease, but there are other factors that inhibit pulmonary TB prevention behavior. For example, many students assumed that TB is a highly contagious disease (85.2%) and that exposure to TB can reduce their learning productivity (88.9%). However, the results of this study also show that there are perceptions of obstacles that make TB prevention less effective.

Cues to Action

Based on the results of the bivariate test, there was no relationship between cues to action and TB prevention behavior in students (p = 0.888). The results of this study contradict the research of Yoshitake et al. (2019) in Japan, which found that cues to action are related to pulmonary TB prevention behavior.[33] Anything that drives decisions to change behavior is called cues to action.[34] This study is not in line with the HBM theory and the hypothesis that positive cues to action will affect good pulmonary TB prevention behavior.

In this study, there were 22 respondents who had positive action cues among the 42 respondents with poor TB prevention behavior. This means that respondents with positive action cues do not necessarily have good pulmonary TB prevention behavior. Most respondents agreed or strongly agreed that they had received an explanation of TB prevention from health workers (65.5%) and that their families encouraged them to engage in TB prevention behavior (53.1%). However, the researcher believes that there may be a lack of information retention related to TB prevention behavior. Retention is one of the definitions of remembering and forgetting or providing information that needs to be repeated to reach the proportion of being remembered. This is evident from the 46.9% of respondents who did not agree that they had received information from the Poskestren administrators (46.9%). Poskestren administrators are the parties who should be closer to the students and are expected to always remind them of the value of living a clean and healthy life, including efforts to prevent pulmonary TB.

Conclusion

This study found that the factors associated with pulmonary tuberculosis prevention behavior were knowledge), perception of benefits, and perception of obstacles. Knowledge was the strongest predictor, with an odds ratio (OR) of 3.615, indicating that students with low knowledge had 3.615 times higher odds of poor TB prevention behavior. The limitations of this

study are that it was conducted through a questionnaire, so it relied on the honesty of the respondents' answers. This can be overcome by a recall approach or by memory. The data collection for the research respondents was carried out in the afternoon on weekdays, so that there were some respondents who were in a hurry when answering questions because they would continue their activities at Maghrib time. This can be overcome by changing the data collection schedule to the weekend, when students have free time.

The Kedungbanteng Health Center can foster and empower cadres of Islamic boarding school health posts (Poskestren) to provide promotive and preventive efforts to students and collaborate with Islamic boarding school supervisors in terms of data updates and monitoring students who are indicated to have TB. The management of the Al-Ikhsan Beji Islamic Boarding School and the Islamic boarding school health post (Poskestren) should provide more intensive health messages to students regarding the implementation of clean and healthy living behavior (PHBS). Islamic boarding school management can enforce and control mandatory PHBS regulations, such as creating checklist cards. . Future researchers conducting similar research can explore further how the perception and behavior of TB prevention in Islamic boarding school students are qualitative in nature. Further research is needed to develop research instruments on the variable of TB prevention behavior to be more applicable to groups of adolescents and Islamic boarding school students.

Ethics Approval

Ethical approval for this study was granted by the Health Research Ethics Committee of the Faculty of Health Sciences, Universitas Jenderal Soedirman (approval no. 1258/EC/KEPK/X/2023).

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available because of a privacy protection agreement between the authors and the respondents.

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Author Contribution

AE was responsible for the study design, data collection, statistical analysis, interpretation of the results and writing of the manuscript. EG and WL corrected all analyses and helped interpret the data. All authors contributed to the critical revision of the manuscript and approved its final version.

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