

META-ANALYSIS STUDY: ENVIRONMENTAL RISK FACTORS OF TUBERCULOSIS (TB)

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Abstract

Introduction: Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* and is a major cause of global health problems. Therefore, this study aims to analyze the risk factors of the physical environment in terms of ventilation, home density, and lighting, as well as to test their sensitivity to TB. **Methods:** The Meta-Analysis method was used with the PICOS technique, and a total of 11 articles were obtained through Google Scholar and Science Direct. **Results and Discussions:** The meta-analysis showed that home density posed the highest risk among the physical environment variables with a pooled PR = $e1.33 = 3.781$ (95% CI 1.10 – 1.56). Furthermore, the results were relatively on the variable of ownership and home density, and unstable on the lighting. **Conclusion:** Based on the results, home density had the highest risk among the physical environment variable. Therefore, the community is advised to improve promotive services by providing information related to TB, such as healthy homes and fulfilling requirements.

INTRODUCTION

Tuberculosis (TB) is a communicable disease caused by *Mycobacterium tuberculosis*, which is responsible for global health. *Mycobacterium tuberculosis* often attacks the lungs but also attacks other body organs, such as the lymph nodes, pleura, bones, and extra lungs (1). Furthermore, in the early phase of TB infection, alveolar macrophages can inhibit its proliferation through granuloma formation in the lungs and phagocytosis (2). The World Health Organization (WHO) in 2019 estimated that there were 3.3% (95% CI 2.3–4.3%) new and 18% (95% CI 9.7–27%) previously treated TB cases worldwide (3).

After HIV/AIDS, TB is one of the top 10 causes of death and is estimated to have infected one-third of the world's population. The World Tuberculosis Report showed that there are a total of 10 million incidents and

12 million general cases (4). Global tuberculosis report revealed that after India, Indonesia has the second-highest number of TB cases. Furthermore, Indonesia's health profile data showed that the number of people with the disease increased by 330,729 and 351,893 in 2015 and 2016, respectively. The country also has a TB rate of 0.4%, indicating that a total of 400 positive pulmonary TB cases are obtained out of every 100,000 people. According to the 2018 basic health research, the prevalence was 321 per 100,000 people (5). This increase was caused by the increasing population in developing countries and the spread of HIV (6).

Environmentally-based disease pathogenesis can be drawn into a model or paradigm, which describes the relationship between environmental components with the potential to harm human disease. A previous study revealed that this association is essentially an

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environmental health paradigm (7), and one of the environmental-based conditions is TB. The emergence of disease is not only caused by germs but is also influenced by external factors from the environment (8).

From an epidemiological perspective, disease events are caused by the interactions between 3 components, namely the host, agent, and environment (9). Several studies revealed that environmental factors are the main transmission medium for TB, especially in an area where people interact daily as social beings. Furthermore, epidemiology believes the incidence of pulmonary TB is due to the interaction between three components, including the host, agent, and environment. The agent factor that influences the transmission of pulmonary TB disease is the bacterium *Mycobacterium tuberculosis* (10). The home environment is a physical structure that people use as shelter (11). Several studies revealed that physical environmental factors, such as the level of lighting, density of the house, ventilation area, and type of floor greatly affect the presence of this causal bacterium. The resistance of *Mycobacterium tuberculosis* in the house depends on the presence or absence of sunlight, the type of floor, as well as the house density (10).

Living or working in an environment with a high incidence, dense population, and poor ventilation can the risk of *Mycobacterium tuberculosis* exposure. Factors that delay diagnosis can also increase the length of exposure in infectious TB patients. Furthermore, patients who live in houses without windows or one are two times more at risk of developing TB compared to people whose houses have many windows (12).

One of the indicators used to assess the success of the pulmonary TB program is the Case Detection Rate (CDR). Based on previous reports, the global CDR achieved is still below the set target of >70%. The 2014 Indonesian Health Profile data revealed the rate in Indonesia was 70.08%. A low case detection rate indicates that TB cases in the community have not yet been identified and treated adequately, and the transmission of the disease is still continuous (13).

Therefore, this study aims to analyze the risk factors for the physical environment, namely the ventilation, home density, and lighting, as well as to test their sensitivity to TB.

METHODS

A meta-analysis method was used in this study with the PICOS technique, which combines two or more similar study results to obtain a combination of quantitative data with the same hypothesis to reach a

conclusion (14). Furthermore, meta-analysis is quantitative in nature because it uses numerical and statistical calculations for practical purposes, namely gathering and extracting information from large data volume (15). A total of 11 major library source journals were used in the compilation of this study. The articles were obtained from a search process on Google scholar and Science Direct with the keywords: risk factors, physical environment, and TB. All the papers collected have a complete article structure with full text. The search results were then filtered based on the established criteria, namely published between 2015-2021, available in full text, has statistical data of sectional cross, the independent variables include ventilation, home density, and lighting, while consumption serves as the dependent variable.

Meta-analysis is often carried out in 5 steps, and the first involves the formulation of a study problem, followed by the collection of literature based on the expected goal, as well as an evaluation. The process is then continued with analysis and interpretation of the acquired literature, followed by the presentation in the form of an article (16).

First, Search for Journals and Articles

The first step was to select journals based on the inclusion criteria. The choice of journals is those related to the physical environmental risk factor of TB. Furthermore, the search process involved the combination of keywords on Google Scholar and Science Direct, including risk factors, physical environment, and TB until 2021. After the search, the next step was to filter out the results based on the abstract reviews. The process was then continued with re-screening to select articles with a cross-sectional study design.

Second, Adjusting to the Selected Data Types

The secondary data used were obtained from selected articles and journals that have been filtered. The bound variables include the incidence of TB, while the free variables are ventilation, densities, and lighting. The meta-analysis methods were similar to swift and systematic reviews, while the workline was identical to the library review. Furthermore, the first step was to formulate questions and determine the purpose of the study, followed by relevant literature identification, strategy, and screening of the relevant journals. The process was continued with the extraction of data, calculation of relevant journal sizes, and evaluation of heterogeneity. The fourth step was to synthesize the data and calculate the confidence interval, followed by exploration, analysis of results, and recommendations.

Third, Data Analysis Techniques

The first stage was data abstraction, where each journal was changed and inputted with the same table, including presentation, location, study design, year of publication, and results. The next step was to use JASP

software to analyze the data using a fixed or random effect model. The process was then continued with bias and sensitivity tests, followed by journal extraction based on the study objectives. Furthermore, the flow diagram (prism) of data collection is presented in Figure 1.

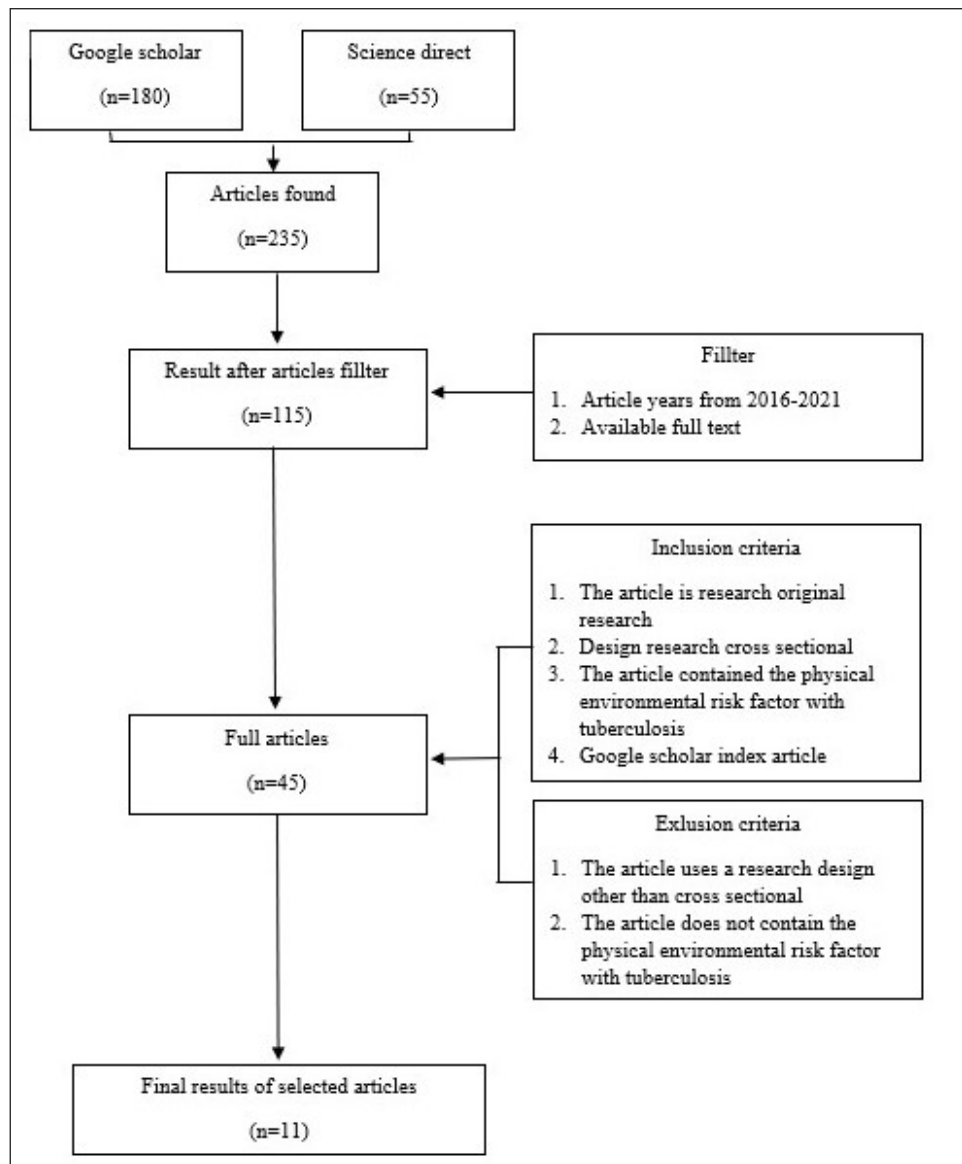


Figure 1. Prism Flow Diagram of The Framework Analysis of Physical Environmental Risk Factors with TB

RESULTS

Meta-Analysis of Ventilation Factor with Tuberculosis

Figure 2 shows that the estimated Prevalence Ratio (PR) based on the Fixed Effect (FE) model was 95% CI of 0.92 with a range of impact of -2.55 – 4.39. Furthermore, the forest plot results showed pooled PR = $e^{0.92} = 2.509$, indicating that the intensity of unqualified ventilation increased the risk of TB by 2.509 times compared to qualified ventilation.

The heterogeneity test of the ventilation factor obtained a p-value >0.05 with $p = 1,000$, as shown in Table 1. This finding indicates that the variations between studies are homogeneous, hence, the analysis was carried out with a fixed effect.

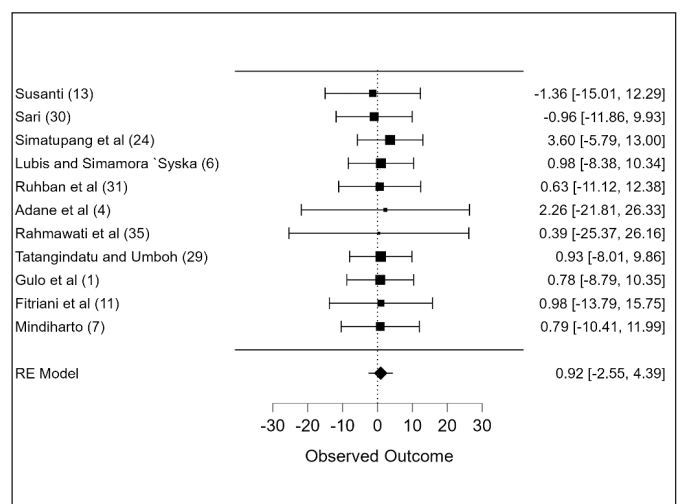


Figure 2. Forest Plot Risk Ventilation Factor with TB

Table 1. Heterogeneity Test Ventilation Meta Analysis with TB Fixed Effect Models

| | Q | df | p |
|------------------------------------|-------|----|-------|
| Omnibus test of Model Coefficients | 0.272 | 1 | 0.602 |
| Test of Residual Heterogeneity | 0.553 | 10 | 1.000 |

Note. p-values are approximate

The funnel plot of ventilation with TB shows the absence of bias because the symmetrical model of the dark circle was not available in the triangular area, as shown in Figure 3. Furthermore, based on Egger's test, the p-value was >0.05, namely 0.898, indicating an unregistered publication bias, as shown in Table 2.

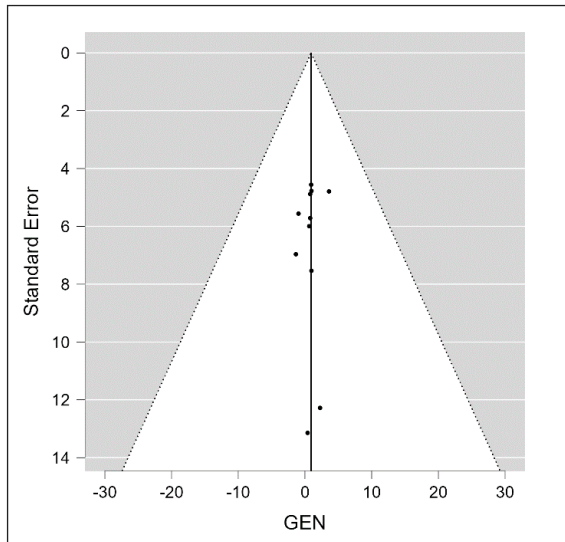


Figure 3. Funnel Plot Risk Ventilation Factor with TB

Table 2. Egger's Test Bar Test Meta Analysis of Ventilation Risk Factors with TB

| | z | p |
|--------------|--------|-------|
| Egger's Test | -0.129 | 0.898 |

Meta-Analysis of Home Density Factor with Tuberculosis

Figure 4 shows that the estimated PR value based on the FE model was 95% CI of 1.33 with a range of impact of 1.10 – 1.56. Furthermore, the forest plot results showed pooled PR = $e^{1.33} = 3.781$, as shown in Figure 3. This finding indicates that unqualified home density increases the risk of TB by >3.781 times compared to qualified home density.

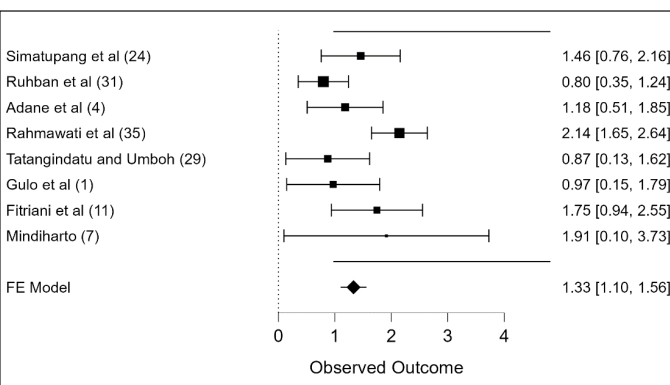


Figure 4. Forest Plot Home Density Factor with TB

Table 3. Heterogeneity Test Home Density Meta Analysis with TB Fixed Effect Models

| | Q | df | p |
|------------------------------------|---------|----|--------|
| Omnibus test of Model Coefficients | 125.954 | 1 | < .001 |
| Test of Residual Heterogeneity | 19.835 | 7 | 0.006 |

Note. p-values are approximate.

The meta heterogeneity test of the home density obtained a p-value >0.05 with p = 0006, as shown in Table 3. This shows that the value variation between the studies was homogeneous, hence, the analysis was carried out with a fixed effect. Furthermore, in the habit-density and lighting variables, there was no bias test because the amount of data in the meta-analysis was less than 10 studies.

Meta-Analysis of Lighting Factor with Tuberculosis

Based on Figure 5, the estimated PR value based on the FE Model was 95% CI of 1.08 with a range of impact of 0.27 – 1.88. Furthermore, the forest plot results obtained pooled PR = $e^{1.08} = 2.944$, as shown in Figure 4. This indicates that the intensity of unqualified lighting increased the risk of TB by 2.944 times compared to qualified lighting.

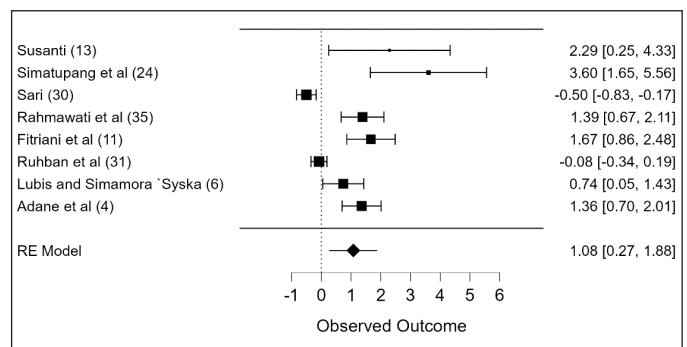


Figure 5. Forest Plot Lighting Factor with TB

Table 4. Heterogeneity Test Lighting Meta-Analysis with TB Fixed Effect Models

| | Q | df | p |
|------------------------------------|--------|----|--------|
| Omnibus test of Model Coefficients | 6.896 | 1 | 0.009 |
| Test of Residual Heterogeneity | 74.582 | 7 | < .001 |

Note. p-values are approximate.

The meta heterogeneity test of lighting factor obtained a p-value value <0.05, namely 0.001, as shown in Table 4. This finding shows that the variation between the studies was heterogeneous, hence, the analysis was carried out using the Random Effect Model.

Sensitivity Test Environmental Risk Factor with Tuberculosis

Based on the comparative sensitivity test, it is evident that the variable of ventilation and lighting shows the value of pooled PR between the fixed and random model, as shown in Table 5. In the habit-density variable, the pooling value between both models was similar.

Tabel 5. Comparative Sensitivity Test Pooled Prevalence Ratio Fixed Model and Random Mode

| Research Variable | n | p-Value | Fixed Effect Models | | Random Effect Models | |
|--------------------------------------|----|---------|---------------------|--------------|----------------------|--------------|
| | | | PR | CI 95% | PR | CI 95% |
| Ventilation faktor with tuberculosis | 12 | 1.000 | 2.509 | -2.55 – 4.39 | 2.509 | -2.55 – 4.39 |
| Densities faktor with tuberculosis | 8 | 0.006 | 3.781 | 1.10 – 1.56 | 3.819 | 0.95 – 1.74 |
| Lighting faktor with tuberculosis | 8 | <0.001 | 2.944 | 0.00 – 0.36 | 2.994 | 0.27 – 1.88 |

DISCUSSION

People who have insufficient ventilation are 2.509 times more at risk of developing TB compared to others with adequate ventilation. The Regulation of the Minister of Health of the Republic of Indonesia No.1077 of 2011 revealed that air exchange that does not meet the requirements can cause the growth of microorganisms to thrive, thereby disrupting human health (17). Furthermore, ventilation is an air exchange between indoors and external fresh, which is intended to replace pollutant air that is harmful to humans. Previous studies revealed that a poorly ventilated room is characterized by stale odors, lack of oxygen, as well as increased room air temperature, CO₂ gas levels, and humidity (18).

One of the main functions of ventilation is to keep the room fresh and maintain an adequate amount of oxygen (19). The size of a good design can be measured using the formula 1/10 x the area of the room. Furthermore, it is better to use a height of about 20 cm to 50 cm (20) when placing the ventilation together with the door and window frames. TB germs with a small size of 50 microns, which are transmitted through droplet nuclei can float in the air (21). The absence of lighting in a poorly ventilated house causes the multiplication of germs, thereby leading to an increase in humidity and temperature. Outdoor temperature, as well as window and door conditions are factors that can affect the ventilation in the house space (19).

Collagen growth caused by inadequate air exchange can lead to the disruption of human health. Ventilation rate is the rate of air exchange through vents or permanent air outlets apart from windows and doors. A house can be ventilated by using an exhaust fan, arranging the room layout, equipping at least 10% of the floor area with a cross-aeration system, and opening the window in the morning regularly (22). Ventilation also serves as an opening for ultraviolet light, which is important in the room. A poorly ventilated room can cause uncomfortable air, which leads to stuffiness, bronchitis, asthma relapse, and colds. This condition also increases the production of dirty air and this facilitates the transmission of respiratory tract diseases (23).

Apart from affecting oxygen and carbon monoxide levels, ventilation is also related to room temperature and humidity. A previous study revealed that it affects the air dilution process due to its ability to dilute the concentration of TB bacteria (24). Ventilation that circulates air can reduce the amount of phlegm splashing, and the presence of direct sunlight in the room helps to kill bacteria. Furthermore, the bacteria contained in the sprinkling of phlegm can survive for several hours in dark and damp conditions. This indicates that a healthy home environment is achievable by providing adequate sunlight and ventilation, thereby reducing the spread of TB (25).

Communities whose residential density does not meet the requirements are 3.781 times more at risk of developing TB compared to those that meet the standard. TB can increasingly be dangerous due to poor housing conditions, especially in dense communities (26). The home density is the ratio of the number of occupants to the area of the house occupied in square meters (m²), and the minimum requirement is 8 m²/patient (22). The increasing number of occupants can affect the oxygen levels in a room, as well as the moisture content and air temperature. Furthermore, increased CO₂ levels in the air can provide more opportunities for *Mycobacterium tuberculosis* to grow and reproduce, thereby increasing exposure to germs (27). A previous study revealed that the rate of transmission of TB among families living with high density is very high (28).

Density is a prerequisite for the process of transmitting a disease (29), and the lack of oxygen consumption in the house makes it easier for household members to get infected (30). The higher the number of occupants, the faster the rate of air pollution, and this can affect the development of disease germs (31). Microorganisms spread through the air when a TB patient coughs, talks, sneezes, or splashes saliva containing germs. Infected droplets can reach a distance of 1 m, hence, dense residential densities can increase the risk of transmission (32). In one house, the presence of more than 4 people increases the risk of infection by three times compared to other homes with less than 4 members due to the crowdedness of the room (33). These findings are in line with the WHO theory that a house is a physical structure used by humans for shelter. The structural environment includes equipment that is useful for physical health, necessary facilities, and services, as well as good social conditions for families and individuals (34).

People who have lighting intensity that does not meet the requirement are 2.944 times more at risk of developing TB compared to those who meet the standard.

Furthermore, each room must have a light or ventilation hole that allows radiation to enter directly or indirectly, especially natural light. Furthermore, natural light can be obtained from sunlight, which has germicidal effects. Sufficient sun radiation is also one of the requirements for a healthy home. A previous study revealed that the lack of sunlight entering the home or the neighborhood causes the environment to become unstable, moist, and become a breeding ground for various diseases. Natural light sources can enter the house through windows or doors, but excess radiation causes discomfort. The need for lighting in a home must match the standard for vision and reading, namely a minimum light intensity requirement of 60 lux (18). Several studies revealed that TB germs can survive for years, and they die when exposed to sunlight, Lysol, and carbolic acid. Houses that are not exposed to the sun are 3-7 times more at risk of developing TB compared to others with sufficient exposure (28). *Mycobacterium tuberculosis* germs often die within 2 hours of being exposed to sunlight. They can also die within 5 minutes, 24 hours, and 2-10 minutes of exposure to tinctura iodii, 5% phenol, and 80% ethanol, respectively (23).

The results showed that one of the factors causing the lack of lighting in the respondent's house is the absence of glass tiles and proper ventilation. Similar condition was observed in the Pekalongan Health Center work area, where house lighting does not meet the requirements. This was because sunlight cannot enter the house due to the very limited number of ventilation source as well as large number of thick trees. Therefore, the community need to provide clear glass tiles in homes without lighting to prevent low humidity (35).

Based on the meta-analysis results, habit density has the highest risk of TB with a pooled PR value = $e^{1.33} = 3.781$ (95% CI 1.10 – 1.56). This indicates that unqualified home density increases the risk of the disease by 3.781 times more compared to others that meet the standard. Microorganisms disperse in the air as people with TB cough, talk, sneeze, spray, and spatter while breathing. The infected droplet can reach a distance of 1 m, hence, high home density tends to increase the risk of contamination (32). Furthermore, people who live in one house with more than four members are three times more likely to develop TB compared to others living with less than four members in the household. This is probably because crowded spaces increase the risk of disease transmission (33).

Previous studies revealed that occupancy density is closely related to other home environmental factors, such as air ventilation, humidity, and lighting. The increasing number of residents in urban settlements

causes the density of buildings and makes it difficult to build houses that comply with health standards (36). Narrow houses with a large number of family members also cause an imbalance between the number of occupants and the area. Furthermore, the interaction and frequency of contact between occupants of the house with each other are high, and this leads to increased temperature. A previous study revealed that oxygen exchange in a crowded room is limited. Bacteria and viruses that are spread through the air enter through breathing from one occupant to another (37).

The condition of the home environment is closely related to the transmission of TB due to the nature of germs that have very strong and long durability. The density of occupancy is a possible factor causing disease transmission and a breeding ground for TB disease. Therefore, the number of occupants in the house must be appropriate and sufficient for the existing floor area (38).

CONCLUSION

Based on the meta-analysis result, home density is the highest risk factor for TB with PR value = $e^{1.33} = 3.781$ (95% CI 1.10 – 1.56). This indicates that unqualified home density increases the risk of the disease by 3.781 times compared to others. Furthermore, the sensitivity test by comparing the pooled prevalence ratio of the fixed and random models showed that the meta-analysis results were relatively stable and unstable. Stability was obtained in the ventilation and home density variables, while instability was recorded in the exposure variable.

The effort that can be made to minimize the risk factors of home density is by ensuring the area of the floor and the number of people in the house meet the standard requirements. It is also advisable to increase promotional services by providing information on TB, such as healthcare through social media, leaflets, and other media. Environmental worthiness is associated with the family economic condition, hence, there is a need to increase income by training local entrepreneurs.

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