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Meta-Analysis and Systematic Review: Risk Factors of Measles Incidence in Indonesia (2012 – 2021)

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Abstract

Measles is a highly contagious disease caused by the morbillivirus. According to WHO data, measles is one of the worldwide leading causes of death in children and infants. Indonesia is one of the ten countries with the most significant measles cases worldwide. Cases in Indonesia have increased due to a decrease in immunization coverage in Indonesia during the pandemic. Besides low immunization coverage, other factors that influence the incidence of measles in Indonesia are nutritional status, mother's knowledge, and occupancy density. This study aims to analyze the risk factors of immunization status, nutritional status, Mother's knowledge, and occupancy density for measles in Indonesia. This study used a meta-analysis method. The data sources used are Google Scholar, Pubmed, and Science Direct, from 2012-2021. The research articles found in this study are 148 articles. The report is then selected by screening to choose the year and research method and continued selection using inclusion criteria. Thus, the articles analyzed in this article are 23 research articles. The results showed that the variable immunization status, nutritional status, Mother knowledge, and occupancy density have risk factors for the incidence of measles in Indonesia. The result of measuring the pooled OR value sequentially from immunization status, nutritional status, mother's knowledge, and occupancy density is e1.26=3.53; e0.72= 2.05; e1.36= 3.82; e1.34= 3.89. The variable with the highest risk factor value for measles incidence in Indonesia is the occupancy density, followed by the Mother's knowledge; immunization status; and nutritional status.

Introduction

Measles is a highly contagious disease caused by the morbillivirus. The virus begins to infect when the measles virus uses the H-protein to infect the cell target (Rasool et al., 2018). The measles virus genome is a single chain of unsegmented RNA. The incubation time of measles is 7 – 12 days. Symptoms of the disease are fever, rash on maculopapular erythematous, cough, and conjunctivitis. Complications commonly occur in people with measles are pneumonia, otitis media, platelets, diarrhea, and brain inflammation (Donadel et al., 2021).

In 2018 WHO reported that there were 140,000 deaths globally from measles. Most of the deaths occurred in children under the age of 5 years. Indonesia is one of the 10 countries with the highest number of measles cases worldwide. The number of measles cases in Indonesia is 1,211 until October 12, 2022 (CDC), and it occupies the 9th country with the

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most measles cases worldwide.

The spread of measles in the community through coughing, sneezing, and personal contact with sufferers. The measles virus is still active and contagious even though it is in the air or on the surface of objects for up to 2 hours. The CDC (2022) says that about 9 out of 10 unprotected people will be infected with people who get measles. According to WHO, the COVID-19 pandemic has caused many countries to forget about measles programs. Data from CDC shows that nearly 41 countries have forgotten about measles and other diseases during the pandemic. It leads to a greater risk of spreading worldwide, including in Indonesia. The laboratory results of the Ministry of Health in Indonesia stated that there was a 15-fold increase in cases of measles confirmed in 2022 compared to 2021. This data was followed by a decrease in the achievement of measles-rubella immunization in Indonesia in 2020 and 2021, namely 65.3% and 58.5%. Indonesia was unable to achieve its predetermined immunization targets, even achieving lower than the previous two years in 2018 and 2019.

Risk factors that influence the incidence of measles in an area are immunization coverage and contact between communities (Nguyen et al., 2022). Until now, immunization is still a matter of debate in the community. People's hesitancy to immunization is influenced by many things the fear of the risk of immunization, religious beliefs, or values that contradict those of the individual or society. Measles immunization is carried out when the child is 9 months – 15 years old (Kementerian Kesehatan Indonesia, 2022). At this age, the child does not yet have the ability and authority to control his health and body. Therefore, parents have a vital role in the immunization status of their children. Parents must have sufficient knowledge about immunization and the risks that can be obtained if the child does not get a complete immunization (Conis, 2019). Mother is one of the key factors in a child vaccination coverage (Harapan et al., 2021). Contact between exposed individuals to healthy individuals can increase the risk of measles transmission (Qin et al., 2019). Transmission of measles spreads through the air, so human density somewhere becomes one of the vital factors in the spread of the measles virus. Therefore, people affected by measles must self-isolate (Torner et al., 2021).

Nutritional status influences the incidence of measles. There is a complex relationship between nutritional status and pain in humans. Malnutrition increased the mortality rate of measles disease(Salman et al., 2022). Nutritional status is always associated with the incidence of disease in the human body. The illness causes humans to cause a decrease in nutritional status, but on the contrary, it is also the same if humans lack nutritional status, it will be easy to get the disease (Schneider, 2022). The risk factors causing measles are very diverse, especially in Indonesia, an archipelagic country with a large population. The purpose of this study was to analyze the risk factors for immunization status, nutritional status, Mother knowledge, and occupancy density for the occurrence of measles in Indonesia. This study analyzes research articles discussing the risk factors for measles in Indonesia.

Method

This research is quantitative research with the Meta-analysis method. This method analyzes several research data in articles combined into one. The data is then summarized and analyzed to give rise to the effect size value (Hari Basuki Notobroto, 2019). The research article used in this study is an article that discusses the risk factors for measles in Indonesia. Data sources from this study used Google Scholar (2012 – 2021), Pubmed (2012 – 2021), and Science Direct (2012 – 2021). The selection of keywords used in this study used the PICO (Population, Intervention, Comparison/Control, Outcome) method (Methley et al., 2014 & Pollock & Berge, 2018). The keyword population used is "Indonesia" to describe Indonesians affected by measles. The intervention keyword used is "risk factor" to find variables that are risk factors for measles. The control and outcome keywords used in this study were "measles" and "no measles" or "measles" and "non-measles". The combination of keywords used in this study was "risk factors" and "measles" and "Indonesia"; "risk factor" and "measles" and "Indonesia". Then the article is screened and sorted again using inclusion criteria. The PRISMA flow chart in this study showed in Figure 1.

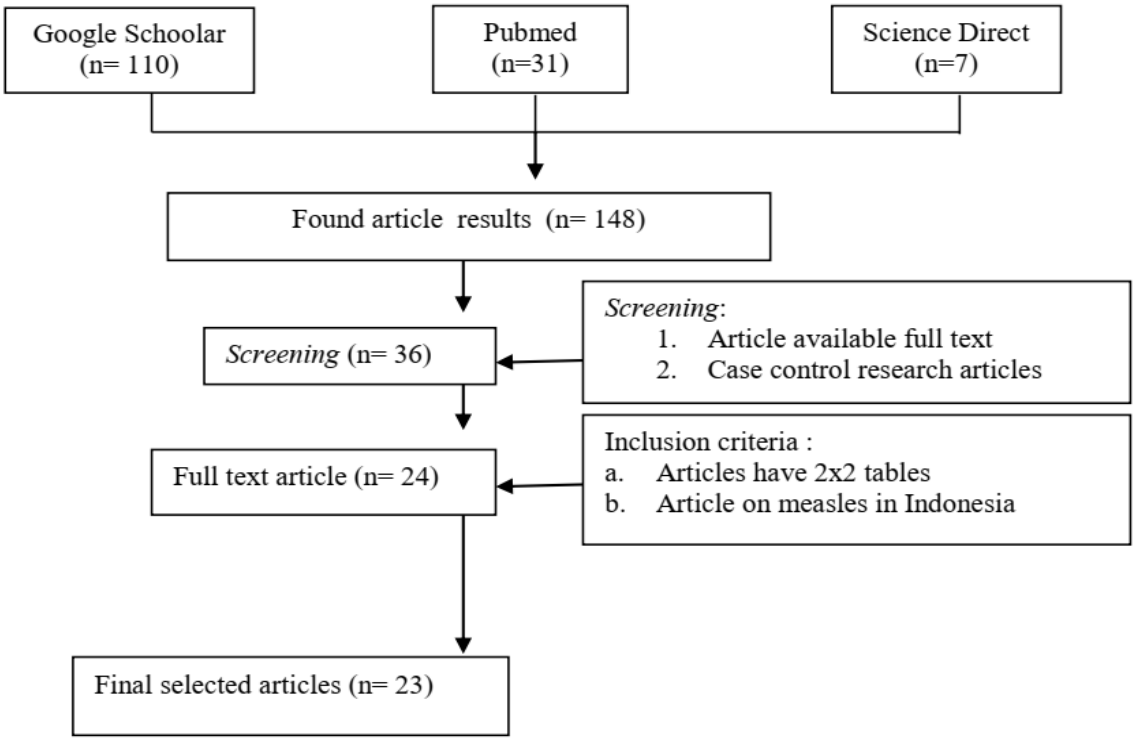

Figure 1. PRISMA Flow Chart Risk Factors for Immunization Status, Nutritional Status, Mother Knowledge, and Occupancy Density for the Incidence of Measles in Indonesia

The collected data is then analyzed using classic meta-analysis and processed with the JASP application. The technical stages of data analysis used at first are data collection/ abstraction. Data is collected in the state-of-the-art table for screening. Then the selected data is entered into Comma Separated Values (CSV) and then entered into the application. Data analysis was performed in JASP Version 0.16.3.0 application. Data is collected in the state-of-the-art table for screening. Then the selected data is entered into Comma Separated Values (CSV) and the application. Egger or Bias Tests are analyzed with the same application. This data analysis was used to look at biases in the study. Data can be analyzed in Egger's test and funnel plot tables. After that, the data was analyzed using a sensitivity test with the same application. This test is used to see if the data is relatively stable to changes. This study compared the data using fixed effect models and random effect models.

This study uses pooled odd ratio analysis with the Mentel – Heaenszel method with two methods. Namely for fixed effect models using Mentel-Haesnzel and for analysis with random effect models using DerSimonian-land. The alpha (α) value used is 0.05. In the determination of homogeneous and heterogeneous variation, it is determined by p analysis and compared with α values. The data of the research article is declared homogeneous if the p-value is > α, then the opposite is the case that the data is heterogeneous if the p-value is < α. Homogeneous data will be analyzed with fixed effect models, and heterogeneous data will be analyzed using random effect models. The interpretation of the OR value is expressed in the following statement: Variables with an estimated OR > 1 with a Confident Interval (CI) not passing the number 1, can be interpreted that these variables are risk factors for measles in Indonesia; Variables with an estimate of OR < 1 and Confident Interval (CI) do not pass the number 1, so it is stated that these variables are a protective factor of each variable related to the incidence of measles in Indonesia; and Variables with an estimate of OR = 1 and Confidence Interval (CI) do not pass the number 1 then the variables have no relationship with the incidence of measles in Indonesia

Result and Discussion

The number of articles found in the study

was 148 articles. Articles that are not available are full text and not researched using case-control and then carried out elimination. After that, another elimination was carried out for articles that did not meet the inclusion criteria of this study. The results of searching the research article literature from the data source came from predetermined keywords, and the data found as many as 148 research articles. After the screening stage, the data were eliminated into 36 research articles. Furthermore, a selection was made with inclusion criteria so that the final result of the articles used was 23 research articles. The research article is then analyzed to find its statistical value. The result of the Meta-Analysis and Eggers Test in Tables 1 and 2, respectively, are as follows.

Table 1. Meta-Analysis of Risk Factors for Immunization Status, Nutritional Status, Occupancy Density, and Mother Knowledge of the Incidence of Measles in Indonesia

Research Variables	N	p-value
Immunization Status	25	< 0.01
Nutritional Status	11	< 0.01
Mother's Knowledge	10	0.015
Occupancy Density	9	0.187

Based on the results in Table 1, the p-value of the heterogeneity test is smaller than the α value (0.05), which is p= < 0.001. These results suggest that the variation of the research articles used is heterogeneous. Therefore, this analysis uses the Restricted ML method. Same as for immunization status, the p-value for variable nutritional status of this analysis is greater than the α value (0.05), where p= < 0.001. Based on these results, it can be concluded that the research articles used in this analysis are heterogeneous. Therefore, the analysis used is a restricted ML method too. Similar to the two variables before, the p-value of the mother's knowledge of the heterogeneity test is smaller than the α value which is p= 0.015. These results suggest that variations in research are used in heterogeneous Mother knowledge analysis. Therefore, the study uses the Restricted ML method too. Meanwhile, the results of the analysis heterogeneity of occupancy density data in Table 1 show that the data need to use a homogeneous model. The p-value of this heterogynous analysis is 0.187, which means that the data is more than the α value of 0.05. So data analysis on residential density variables uses the Fixed Effects Method.

Table 2. Egger's Test Variabel Immunization Status, Nutritional Status, Occupancy Density, and Mother Knowledge of the Incidence of Measles in Indonesia

Research Variables	N	z	p-value
Immunization Status	25	0.33	0.74
Nutritional Status	11	-0.86	0.39
Mother's Knowledge	10	-0.29	0.78
Occupancy Density	9	2.03	0.04

The Egger's test in Table 2 shows that the p-value of variable immunization is 0.744. This value is greater than the α value (0.05), so it can be said that there is no research bias in this analysis. If it is figured on illustrated, there will be seen from the symmetrical effect size around the mean. Same as before, the results of egger's test of variable nutritional status showed that the p-value is higher than α (0.05), i.e. p= 0.39. Based on these results, there is no bias in this analysis. It means that the distribution of effect size is symmetrical to the mean. The p Egger's test value of the Mother knowledge variable is 0.775. The value is more than α (0.05), so we can conclude no publication bias in this analysis. The result can give us an illustration that the distribution effect size is symmetrical with the research mean. Unlike other variables, the value of Egger's test in Table 2 indicates that the p-value is greater than the < α value (0.05) which is 0.043. So it can be concluded that there is a research bias in this analysis. If the plot effect size distribution is figured in an illustration, the plot will not be symmetrical to the mean value.

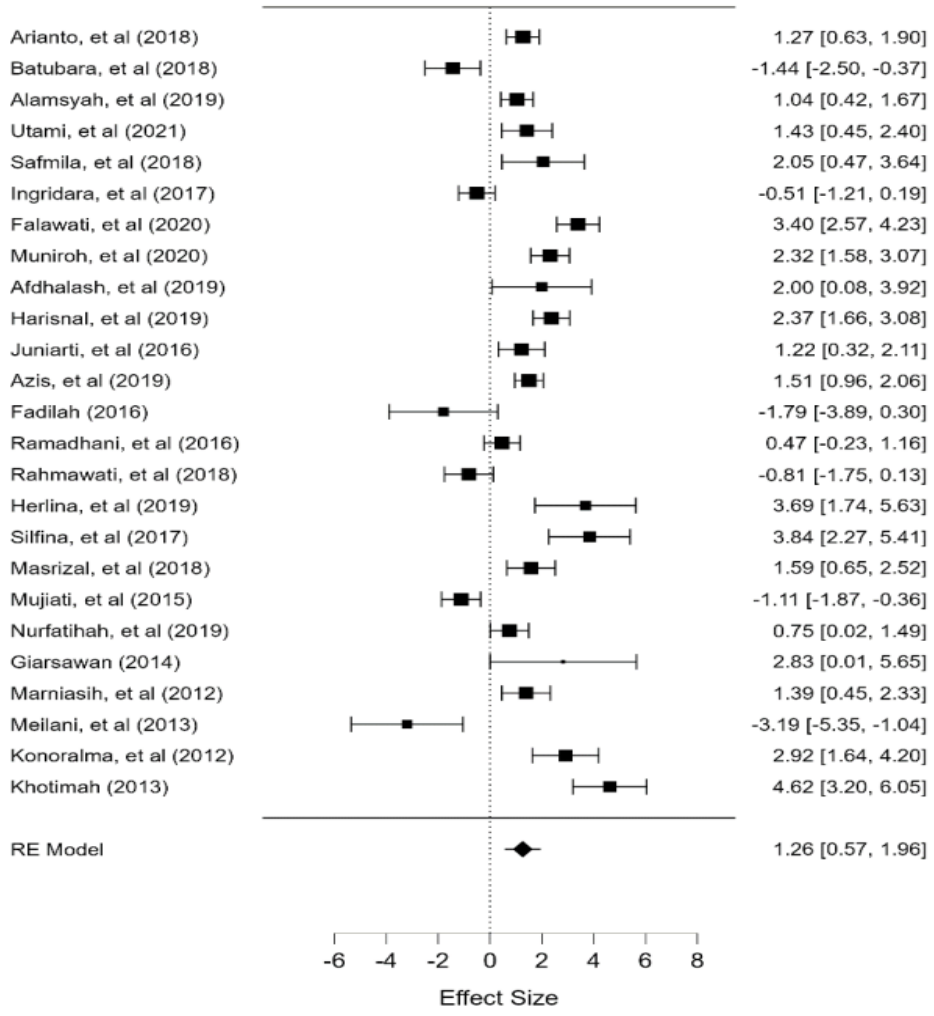

Figure 2. Forest plot Risk Factors for Immunization Status for Measles Disease Incidence in Indonesia

The results from the forest plot shown in Figure 2 show that the Odd Ratio (OR) value depicted in the model's Restricted ML (RE) value is 1.26 with a 95% Confident Interval (CI) range of 0.57 – 1.96. The result is then entered into the equation of the pooled OR value, and a result of e1.26=3.53 is obtained. Based on these results, we concluded that immunization status has a risk influence of 3.53 times on the incidence of measles in Indonesia. The value of this risk is higher than previous research conducted by Morgan, et al. in 2016. In the study, the pooled OR value found was 0.58 (Morgan et al., 2016). Immunization status affects the incidence of measles in Indonesia. The results of this meta-analysis measurement show that the immunization variable has a 3.53 times risk of measles in Indonesia. Measles immunization is one of the preventive efforts to avoid measles. The immunization status is closely related to the incidence of measles in Indonesia. Immunization is one of the efforts to increase immunity. Immunization is effective to decrease measles cases (Bose et al., 2022). Before vaccination, measles fatalities significantly increased pediatric mortality, especially for children under five. Around 95% of children who receive the vaccine at 12 months of age and 98% who receive it at 15 months of age generate anti-measles antibodies (Peart Akindele, 2022). Indonesians who do not get immunization are proven to have higher risk factors for developing measles. This study is per the meta-analysis research conducted by Morgan et. al (2016), which states that immunization is at risk of measles. Immunization affects immunoglobin G (IgG) (Ichimura et al., 2022). Antibody IgG is an antiviral against the measles virus, and its

titers were affected by immunization (Bose et al., 2022).

Socioeconomic status plays a vital role in immunization status in Indonesia (Hope et al., 2021). Measles immunization in Indonesia is provided free of charge by the Indonesian government to the general public. However, even though it is given free of charge, immunization is usually obtained for free at the Puskesmas, while the Puskesmas have limited working hours. Parents with low socioeconomic status tend to be more reluctant to vaccinate a child. It is related to the pattern of working hours of parents with low economic status who tend to have a more busy work schedule and do not match the puskesmas schedule, so they do not have time to take children to the health center. Parents with sufficient income, despite having a busy schedule, still have a high probability of having a caregiver for their child who can deliver the child to get the vaccine or they will go to a paid immunization location that has flexible time.

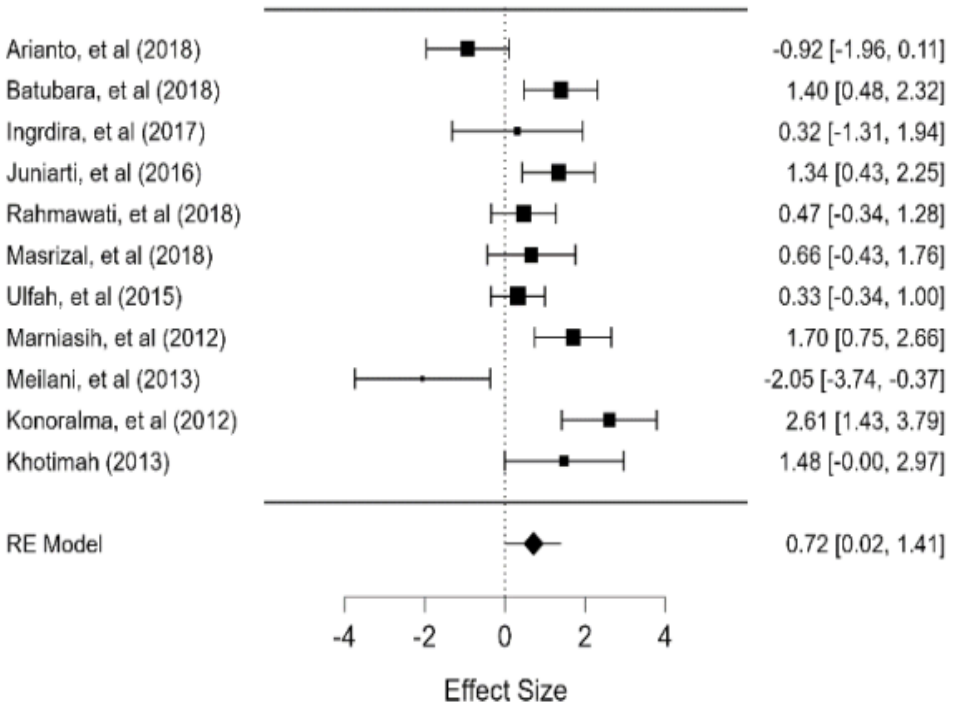

Figure 3. Forest plot Risk Factors for Nutritional Status for the Incidence of Measles in Indonesia

The forest plot image shown in Figure 3 shows that the RE (OR) number in this analysis is 0.72 with a 95% CI range of 0.02 – 1.41. Based on these results, the pooled OR score of this analysis is e0.72= 2.05. Based on these results, nutritional status has a risk influence of 2.05 times on the incidence of measles in Indonesia. The results of the analysis of this study prove that nutritional status is one of the risk factors for the incidence of measles, with a risk value of 2.05 times. Research by Rahmawati, et. Al (2018) mentioned that nutritional status has a risk of 2.11 for measles. This result is linear with the analysis results obtained in this analysis. Several other research articles show results that align with this study, which shows that nutritional status influences the incidence of measles in Indonesia (Rahmawati et al., 2018). The study in the Republic Democratic of Chongo also shows that chlid with malnutrition has a significant association with measles. It may be a sign of past low nutritional status, linked to a decline in cell-mediated immunity, and is known to affect children's vulnerability to infectious infections (Ashbaugh et al., 2020). Nutritional status is an indirect factor in the occurrence of measles. Immunity after immunization is influenced by nutritional status. In addition to affecting post-immunization immunity, nutritional status also plays a vital role in forming immunity. Aside crucial for preserving healthy and regular bodily functions, nutrients are also needed to boost

immunity and protect against viral infections (Thirumdas et al., 2021). Almost all immune systems are impacted by protein-energy deficiency. An effective immune response depends on micronutrients, and immune function is reduced by deficits in one or more micronutrients (Calder & Yaqoob, 2020). The study on Sub-sahara Africa showed that the vast majority of those impacted are pastoralists, whose food instability results in widespread malnutrition. To combat measles, it is essential to enhance nutritional conditions (Nchasi et al., 2022). There are still few international articles that discuss the risk factors for nutritional status with the incidence of measles, and there is not even a meta-analysis that discusses this. Based on the analysis in this study, nutritional status has a considerable risk factor for the incidence of measles in Indonesia.

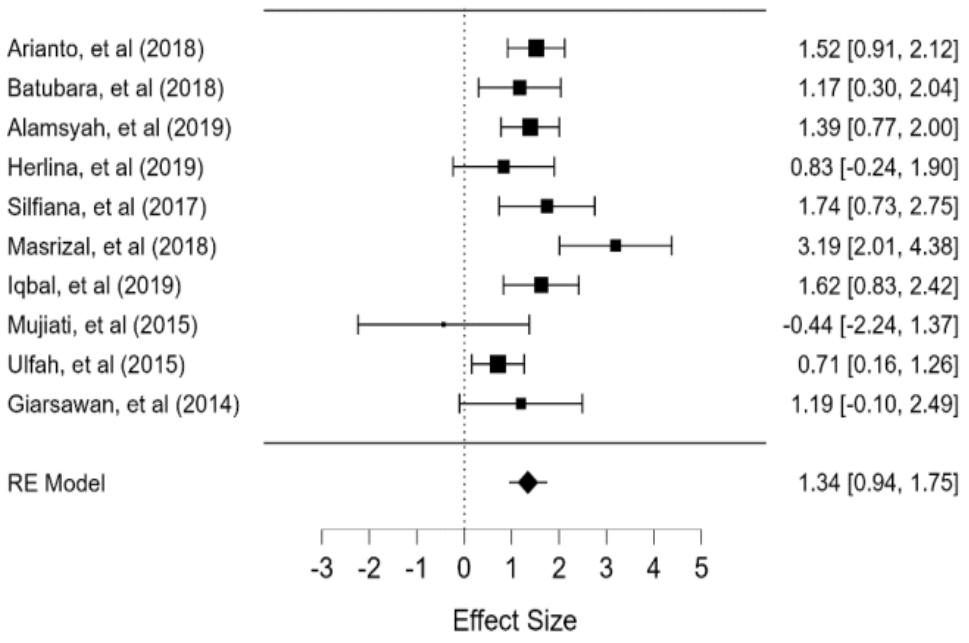

Figure 4. Forest Plot Risk Factors for Mother Knowledge on the Incidence of Measles in Indonesia

The RE value in Figure 4 showed that the OR estimation from the Mother knowledge risk factor analysis of measles incidence was 1.34 with a 95% CI range of 0.94 – 1.75. Based on these results, the pooled OR value obtained is e1.34 = 3.82. These results mean that the Mother knowledge variable has a risk influence of 3.82 on the incidence of measles in Indonesia.

The results of this study show that Mother knowledge affects the incidence of measles and has a risk of 3.82 times the incidence of measles in Indonesia. Knowledge is a condition in which a person knows and has a sensitivity to an event. Knowledge or cognitive's factors is the dominant factor in the determination of attitudes and behaviors. Knowledge affects things. The higher the mother's knowledge of a disease, will be accompanied by the increase in the mother's behavior and attitude in efforts to prevent and control the disease. The study from the Philippines found that mothers with a high degree of knowledge had a favorable attitude and appropriate behaviors toward children's vaccination (Arceo et al., 2021). The results of this study are in line with research conducted by Muluneh (2022), which states that there is a relationship between mothers' knowledge of measles incidence. Four risk factors make infants suffer from measles, and one of them is a mother with no maternal education (Bettampadi et al., 2021).

Mother knowledge is closely related to the level of education of mothers and their age (Yufika et al., 2020) Mothers without educational background or just primary education had fewer children with a second dose vaccine than a mother who has higher education level (Goshu Muluneh et al., 2022). Mothers with a

higher level of education, such as a diploma, tend to be more courageous and not afraid of immunization compared to mothers with low education. Meanwhile, mothers with higher education have better analytical skills. On the contrary, mothers with low education tend to be easily influenced by others (Mohd Azizi et al., 2017). It can be understood that mothers with higher education are more likely to be exposed to knowledge about immunization than mothers with low education. In addition, Mothers who have received more education are more likely to actively seek medical attention, adhere to nutritional guidelines, and use health services. They are also better able to identify serious conditions affecting children's health, follow immunization requirements, actively seek prenatal care, and receive postnatal care services that increase the likelihood of their child's health (Amoah & Asamoah, 2022).

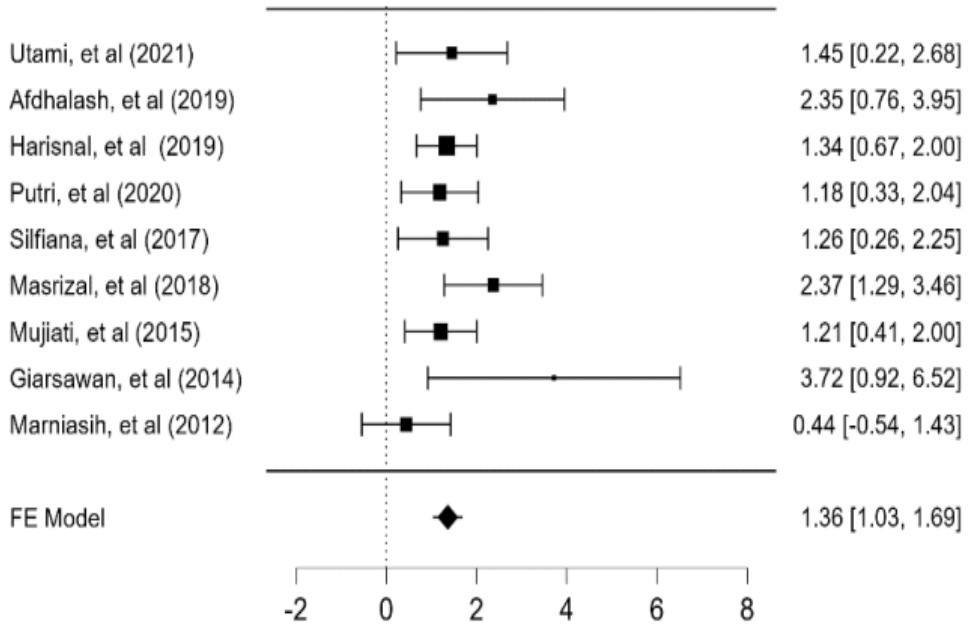

Figure 5. Forest Plot Risk Factors for Occupancy Density for Measles Disease Incidence in Indonesia

The analysis results with the forest plot in Figure 5 showed that the Fixed Effect Model value was 1.36 with a 95% Confident Interval (CI) value of 1.03-1.69. The pooled OR value from the forest plot analysis results is e1.36= 3.89. Based on the pooled OR analysis, occupancy density has a 3.89 times risk of measles incidence. This analysis can also mean that people who have houses with poor occupancy density or do not comply with regulations set by the government have a 3.89 times risk of being infected with measles.

Measles is one of the infectious diseases through air transmission (Nardell & Nathavitharana, 2023). Occupancy density is one of the factors that affect the air quality in the home space. The ideal condition of a house is when the size of the house meets the Indonesian standard of 8 m2 / person. So that when the house does not meet the standard standards, it is said to have poor occupancy density. In the analysis, the results were obtained that there was a significant relationship between the variable occupancy density and the incidence of measles in Indonesia, with a pooled OR risk value of 3.40. Otherwise, the analysis in this study had shortcomings, namely that there was a research bias described in the funnel plot and Egger's test. This bias is likely because the articles used are homogeneous and less varied.

Indonesia is one of the most populous countries in the world. Although it has a large area, the population distribution is still uneven and is still centered in the Java region. Urban areas in Java have a very dense population, so the land houses are limited. People with lower-middle-class socioeconomic conditions are forced to live in narrow locations. This condition

causes occupancy density, so it is not suitable for habitation. The presence of good ventilation can minimize this condition. Good ventilation is proven to reduce the risk of airborne disease infection. These two factors, occupancy density and ventilation, when combined well, can be one of the solutions to control the spread of airborne disease (Zhang et al., 2021).

A healthy building is a building built to promote and serve the well-being of occupants. A good strategy in building management is the key to provide good indoor air quality (Vergerio & Becchio, 2022). One of the ways is to pay attention to manage the occupancy density. A building must ensure that the building area is following the number of occupants of the house in one room. A study from a hospital in China showed that occupancy density highly affects indoor PM25 concentrations, and it shows how crucial the number of people inside is to the interior atmosphere (Zhou & Yang, 2022). We need to increase our knowledge of how buildings affect occupant health as well as the elements that support occupant health in buildings. We need to understand the health effects of building design, construction, usage, operation, and maintenance is crucial given that we spend the majority of our time inside our homes, schools, workplaces, and other indoor spaces (Nardell & Nathavitharana, 2023).

Conclusions

Measles is still a challenge for Indonesia, especially in the post-pandemic period. This research analyses some of the risk factors faced by Indonesians to be free from measles. The result shows that the variable with the highest risk factor for measles incidence in Indonesia is the variable occupancy density, followed by Mother knowledge; immunization status; and nutritional status. The disadvantage of this study is that there is one variable that has a research bias, namely the occupancy density variable. In contrast, the other variable does not have a research bias. More research needs to be done on the influence of risk factors for residential density on the incidence of measles in Indonesia. In addition, it is necessary to increase the coverage of measles immunization and nutrition in the community. Parents, especially mothers, need to increase their knowledge of measles and support government programs called measles-rubella immunization to avoid infection with measles. One of the way is enhancing primary health care facilities to improve the proportion of moms who are well-versed in immunization and address other concerns surrounding childhood vaccination

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