



## Risk Analysis of Pesticide Exposure Associated with Reduced Cholinesterase Levels in Indonesian Farm Workers: A Meta-Analysis

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### ABSTRACT

Pesticide exposure remains a major occupational health problem, with the World Health Organization (WHO) reporting between 1 and 5 million cases of pesticide poisoning annually among agricultural workers. This study aimed to analyze the risk factors associated with pesticide poisoning by conducting a meta-analysis of published research. The meta-analysis was performed in four stages: data abstraction, statistical analysis using JASP Version 0.18.3, heterogeneity testing, and publication bias assessment. The random-effects model was applied to the variables of Personal Protective Equipment (PPE) use and length of work, as the heterogeneity test indicated significant variation between studies ( $p = 0.001$ ). In contrast, the fixed-effects model was used for individual hygiene ( $p = 0.006$ ). Egger's test showed no indication of publication bias for PPE use ( $p = 0.356$ ) and length of work ( $p = 0.395$ ). The results revealed that PPE use increased the risk of decreased cholinesterase levels by 1.584 times, poor individual hygiene by 1.954 times, and working more than 5 hours by 1.665 times. In conclusion, individual hygiene was identified as the most significant risk factor. Farmers who neglect personal hygiene practices, such as bathing after spraying or changing clothes immediately, face a substantially greater risk of reduced cholinesterase levels due to pesticide poisoning.

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## INTRODUCTION

Pesticides are toxic chemicals used to control the growth of pests and weeds. According to WHO data, every year, there are 1 to 5 million cases of pesticide poisoning among agricultural workers, causing 220,000 deaths. Most poisoning cases, about 80%, occur in developing countries. The impact of this event can continue to be felt for another 30 years, with an increasing number of congenital disabilities and incidences of organ failure. Although mild poisoning in the short term only irritates the eyes or skin, mild poisoning in the long term can have serious health consequences, such as hormonal disorders, organ failure, and even death.<sup>1</sup>

Pesticide poisoning is one of the health problems arising from exposure to pesticide substances. One impact of this poisoning is abnormal blood pressure disorders triggered by repeated exposure to pesticide chemicals.<sup>2</sup> Pesticides such as carbamates and organophosphates are often used. The body can absorb organophosphate molecules through the skin, inhalation, or the digestive tract. Once these molecules enter the body, they combine with acetylcholinesterase molecules in red blood cells, causing the enzyme to lose activity. As a result, there is an increase in acetylcholine at synapses and neuromuscular connections.<sup>3</sup> Pesticides are extremely harmful to aquatic life, including fish species and other aquatic organisms that are part of the tropical food web. Pesticides are used to manage destructive and invasive pests in agriculture, forestry, and landscapes. The same topic of pesticide toxicology was the emphasis of the previous study, which also addressed some important chronic toxicology-induced effects of pesticides on fish and their bioaccumulation rates in fish tissues.<sup>4</sup>

Various factors, including internal ones such as age, nutritional status, gender, and knowledge, can affect cholinesterase enzyme levels. On the other hand, external factors derived from pesticide exposure include dosage, duration of spraying, wind direction during spraying, spraying time, personal hygiene, frequency of spraying, type of pesticide used, and use of personal protective equipment.<sup>5</sup> Many farmers in Indonesia are knowledgeable about pesticides, but they often ignore the risks they pose. Many people use pesticides without wearing personal protective equipment, such as masks,

hats, clothes that cover the body, and so on. According to the findings of the previous study, there is a need for monitoring, risk assessment, and regulation for dichlorvos and dimethoate. In addition, users should ensure strict compliance with all practices, such as Acceptable Agricultural Practices, Effective Storage Practices, and Effective Hygienic Practices, among other safety practices, when handling pesticide products.<sup>6</sup>

This condition is very detrimental because it can increase farmers risk of pesticide poisoning. Many farmers consider handling pesticides to be impractical and troublesome. The length of spraying is also affected by how often farmers spray pesticides and whether they use personal protective equipment. However, most farmers do not attach importance to personal protective equipment. They only wear hats, long sleeves, and trousers. Additionally, farmers who smoked while spraying pesticides reported did not use personal protective equipment, such as masks.<sup>7</sup>

Long-term exposure to pesticides increases the risk of pesticide-related health issues for pest sprayers. The WHO requires that the length of work in risky situations, such as pesticide use, is limited to 5 hours per day or 30 hours per week. Many workers are exposed to pesticides for over 5 hours daily.<sup>8</sup> Length of work and length of service have a positive correlation, where the longer the working period, the greater the exposure experienced by workers. This should be a concern for employers to set working hours according to applicable regulations to reduce exposure to workers or farmers. The government has regulated the use of pesticides through established rules. Government Regulation No. 6 of 1995 concerning Plant Protection, which is an elaboration of Law No. 12 of 1992, guides the use of pesticides effectively, efficiently, and minimizes negative impacts on human health and the environment.

One of the factors that causes pesticide poisoning is the lack of attention farmers pay to personal hygiene after spraying pesticides. Farmers can potentially prevent harmful pesticide substances from entering their bodies by maintaining personal hygiene. Farmers should follow Personal hygiene measures after spraying, including washing hands with soap, changing unique clothing used when spraying,

cleaning atomizers in places away from water and food sources, and other measures.<sup>9</sup>

However, most existing studies on pesticide exposure and cholinesterase reduction among Indonesian farm workers are fragmented and limited to small-scale observational designs. To date, no comprehensive quantitative synthesis using meta-analysis has specifically evaluated the combined risks of personal using protective equipment, personal hygiene, and length of work. This research gap highlights the importance and novelty of the present study.

Indonesia is a densely populated country consisting of 34 provinces with diverse climatic conditions, despite its location in the tropical region.<sup>10</sup> Temperature and environmental characteristics vary across regions, influence air quality and public health. Therefore, monitoring air quality and implementing effective environmental management are essential preventive measures to maintain ecosystem balance.<sup>11</sup> The Indonesian Ministry of Health recommends the complete use of Personal Protective Equipment (PPE) as a precaution against environmental risks.<sup>12</sup> Environmental health plays a crucial role in determining the quality of life and community well-being, as it is influenced by environmental, socio-cultural, and economic factors, as well as exposure to hazardous substances such as organochlorine compounds and the quality of clean water consumed.<sup>13,14,15</sup>

Based on the description above, the general objective of this study is to analyze the risk of pesticide exposure that can cause a decrease in cholinesterase levels in agricultural workers in Indonesia. The particular aim is to explore the risks of using Personal Protective Equipment (PPE), personal hygiene, and length of work to reduce cholinesterase levels among agricultural workers in Indonesia.

## MATERIAL AND METHOD

This study employed a meta-analysis design, a statistical approach that synthesizes findings from multiple similar studies to provide more comprehensive quantitative evidence and stronger conclusions. The review process was conducted in accordance with the PRISMA guidelines.

**Data Sources and Search Strategy**  
A systematic literature search was conducted to

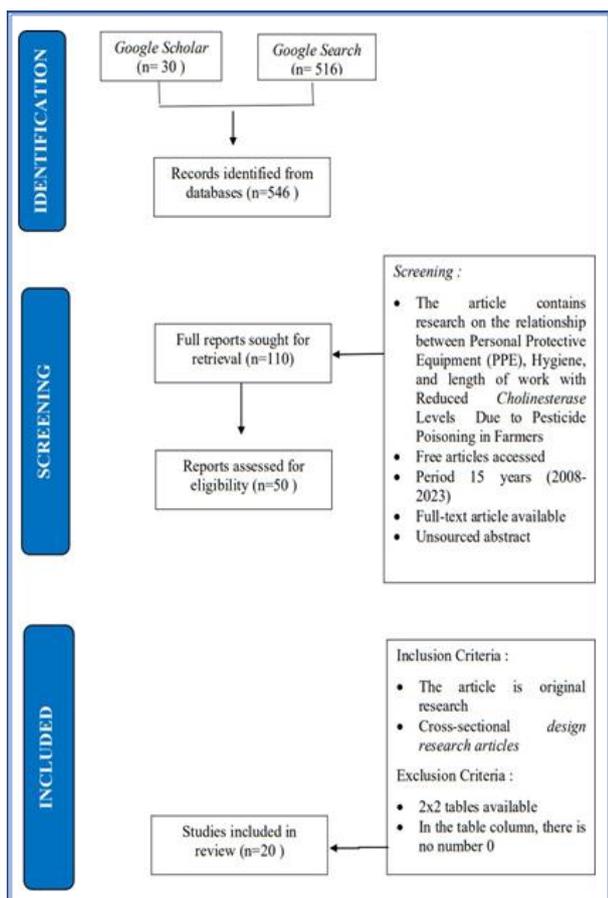
identify relevant studies published between 2008 and 2023. The time frame (2008–2023) was chosen to capture the most recent two decades of evidence relevant to pesticide exposure and health outcomes. The primary databases used were Google Scholar and Google Search, which were also employed to capture grey literature (e.g., theses, proceedings). However, reliance on these sources may limit comprehensiveness. This study acknowledges its reliance on non-academic databases as a limitation.

The keywords applied included: “reduced cholinesterase levels due to pesticide poisoning in farmers,” “Personal Protective Equipment (PPE),” “personal hygiene,” and “length of work.” Eligibility criteria and study selection the initial search yielded 546 records (30 from Google Scholar and 516 from Google Search). After removing duplicates and screening titles and abstracts, 110 articles were retained for further review. Of these, 50 full-text articles were assessed for eligibility. Finally, 20 studies met the inclusion criteria and were included in the quantitative synthesis (Figure 1).

The inclusion criteria were as follows: (1) original research articles, (2) studies involving pesticide exposure among farm workers, (3) outcomes related to cholinesterase enzyme activity, and (4) availability of sufficient data (2x2 tables or effect sizes) for meta-analysis. Studies were excluded if they lacked extractable data, were duplicates, or involved populations not relevant to the research question.

Data extraction and analysis from each eligible study were systematically extracted into a standardized table, including information on publication year, sample size, type of exposure, and reported outcomes. Pooled effect sizes were calculated using either fixed-effect or random-effect models, depending on heterogeneity. Heterogeneity was assessed using the Q-test; if significant ( $p < 0.05$ ), a random-effects model was applied; otherwise, a fixed-effects model was used.

All statistical analyses were conducted using JASP Version 0.18.3. Results were presented as forest plots and funnel plots. Publication bias was assessed using Egger’s test, applied when at least ten studies were available for a given variable.



Source: Primary Data, 2024

**Figure 1. Prisma Flow Diagram Risk Analysis of Pesticide Exposure Associated with Reduced Cholinesterase Levels in Indonesian Farm Workers: A Meta-Analysis**

**RESULTS**

**Heterogeneity Test for the Use of Personal Protective Equipment (PPE), Individual**

**Hygiene and Length of Work with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

Based on Table 1, Personal Protective Equipment (PPE), it is known that the p in the heterogeneity test is smaller than 0.05, namely  $p=0.001$ , which means that the variation between studies is heterogeneous, so in this analysis, using a random effect model. Individual hygiene is known to have a p in the heterogeneity test greater than 0.05, namely,  $p = 0.006$ , which means that variations between studies are homogeneous. Hence, this analysis uses a fixed effect model. The length of work is known to be the p in the heterogeneity test is smaller than 0.05, namely,  $p = 0.001$ , which means that variations between studies are heterogeneous, so in this analysis, using a random effect model.

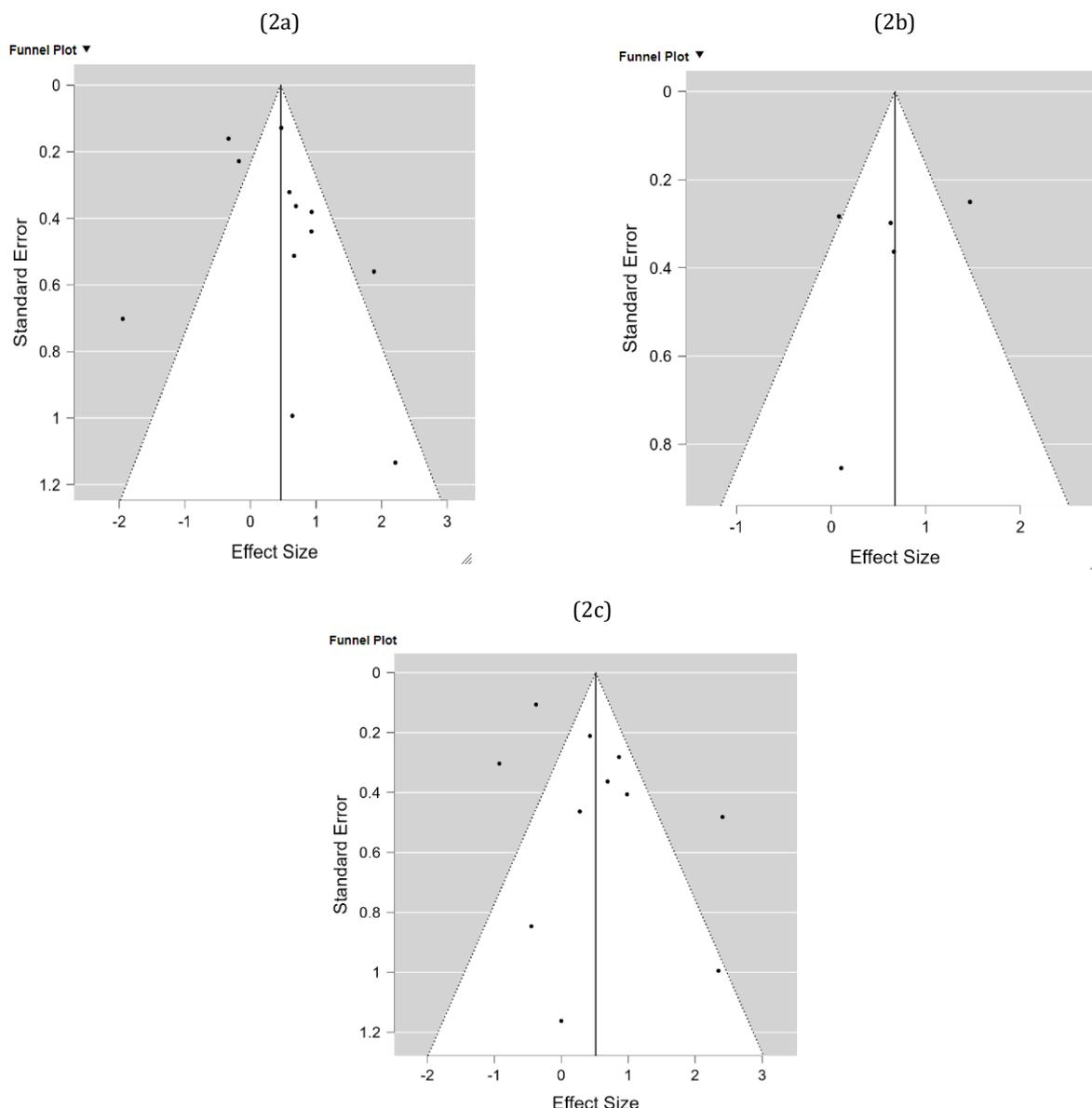
**The Funnel Plot Illustrates The Risk Factors Associated with Personal Protective Equipment (PPE), Length of Work, and Individual Hygiene in Relation to Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

Figure 2a. Funnel Plot Risk Analysis of Personal Protective Equipment (PPE) Use, Figure 2b. Funnel Plot of Individual Hygiene Risk Analysis and Figure 2c. Funnel Plot Risk Analysis of Working Time with Reduced Cholinesterase Levels Due to Pesticide Poisoning among Farmers. There is an indication of Publication bias because the model formed is not symmetrical. Specifically, the dark circles extend beyond the triangular area.

**Table 1. Meta-Analysis of Heterogeneity Test of Personal Protective Equipment (PPE), Individual Hygiene and Length of Work with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

Variable	Q	Df	p
<b>Personal Protective Equipment</b>			
Omnibus test of Model Coefficients	3.683	1	0.055
Test of Residual Heterogeneity	49.890	11	< 0.001
<b>Individual Hygiene</b>			
Omnibus test of Model Coefficients	5.815	1	0.016
Test of Residual Heterogeneity	14.579	4	0.006
<b>Length of Work</b>			
Omnibus test of Model Coefficients	2.838	1	0.092
Test of Residual Heterogeneity	75.845	10	< 0.001

Source: Primary Data, 2024



Source: Primary Data, 2024

**Figure 2. (2a) Funnel Plot of Risk Factors for Personal Protective Equipment (PPE) Use, (2b) Funnel Plot Hygiene Individuals and (2c) Funnel Old Plot Work with Decreased Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

**Test Egger's Test (Test Publication Bias) The Personal Protective Equipment (PPE) and The Duration of Work**

The variables of Personal Protective Equipment (PPE) use and length of work were tested for publication bias due to the amount of data in the meta-analysis of more than ten studies. In comparison, individual hygiene variables were not carried out in the publication bias tests because the amount of data in the meta-analysis

was less than ten studies. In the variable use of PPE, the Publication test is proven by the p on Egger's test, which is more significant than 0.05, namely  $p = 0.356$ , which means there is no indication of Publication bias. In the variable length of work, after further tests with the p in Egger's test greater than 0.05, namely  $p = 0.395$ , there is no indication of Publication bias (Table 2).

### Forest Plot Risk Factors for Personal Protective Equipment (PPE), Length of Work, and Individual Hygiene with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers

The forest plot Figure (3a) result obtained a pooled value  $PR = e0.46 = 1.584$  (95% CI -0.01 – 0.93). Thereby, it can be concluded that farmers without using complete Personal Protective Equipment (PPE) risk a 1,584 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning. The forest plot Figure (3b) result obtained a pooled value  $PR = e0.67 = 1.954$  (95% CI 0.13–1.22). Thereby, it can be concluded that farmers who ignore personal hygiene, namely not bathing after spraying and not immediately changing clothes, are at risk of having a 1.954 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning compared to farmers who do not have a risk with a value of 95% CI not exceeding number 1. The forest plot figure (3c) results obtained pooled value  $PR = e0.51 = 1.665$  (95% CI 0.08–1.11). Thereby, it can be concluded that farmers with a working period of >5 hours have

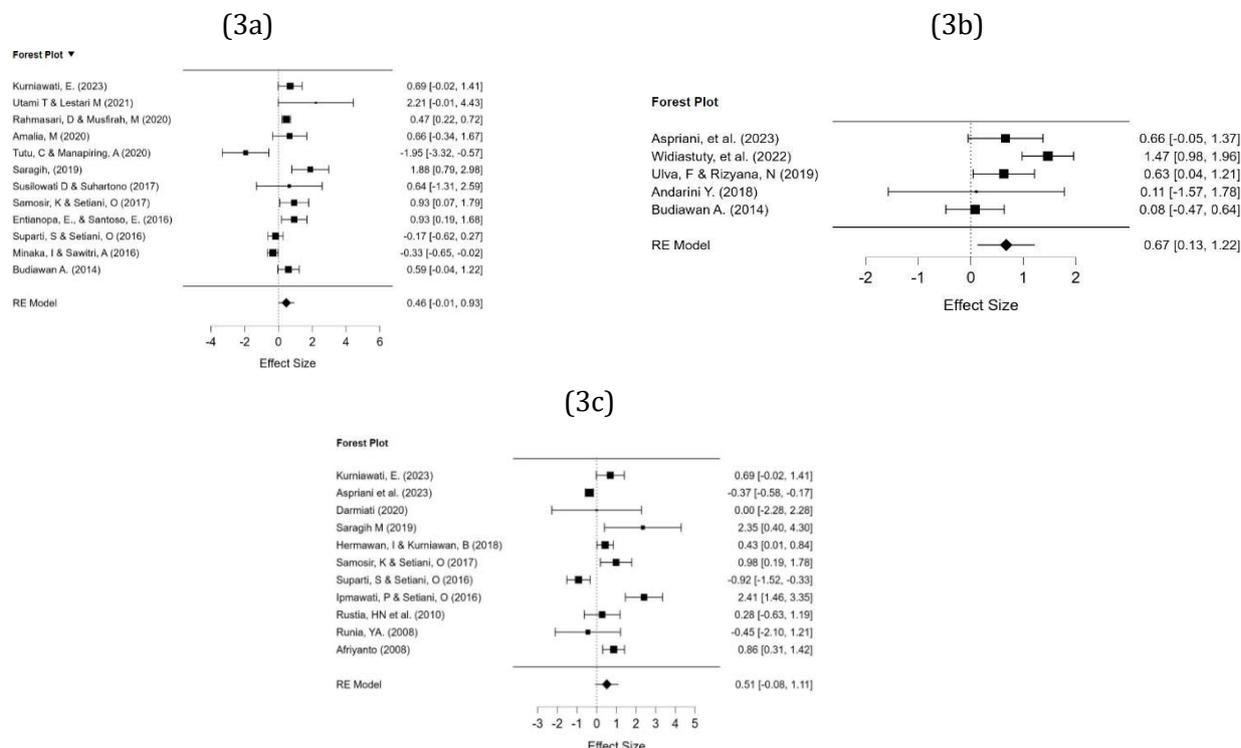
a risk of having a 1.665 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning compared to farmers who have working hours of <5 hours and have no risk with a value of 95% CI not exceeding number 1.

Individual hygiene is the highest risk factor for reducing cholinesterase levels due to pesticide poisoning in farmers, with a pooled value of  $PR = e0.67 = 1.954$  (95% CI 0.13–1.22). Thereby, it can be concluded that farmers who ignore personal hygiene, namely not bathing after spraying and not immediately changing clothes, are at 1.954 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning (Table 3).

**Table 2. Test Table of Egger's test Meta-Analysis of Personal Protective Equipment (PPE) Risk and Length of Work with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

Egger's Test	Z	p
Personal Protective Equipment (PPE)	0.923	0.356
Length of Work	0.851	0.395

Source: Primary Data, 2024



Source: Primary Data, 2024

**Figure 3. (3a) Forest Plot Risk Factors for Personal Protective Equipment (PPE), (3b) Individual Forest Plot Hygiene, and (3c) Long Working Forest Plot with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

**Table 3. Risk Factors for the Use of Personal Protective Equipment (PPE), Length of Work and Individual Hygiene with Reduced Cholinesterase Levels Due to Pesticide Poisoning among Farmers**

Variable	Pooled PR Value	95% CI
Individual Hygiene	$e^{0.67} = 1.954$	0.13–1.22
Length of Work	$e^{0.51} = 1.665$	-0.08–1.11
Personal Protective Equipment (PPE)	$e^{0.46} = 1.584$	-0.01–0.93

Source: Primary Data, 2024

## DISCUSSION

### Meta-analysis Risk Analysis of Personal Protective Equipment Use with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers

In Table 1. It was found that the results of the heterogeneity test of the meta-analysis were known that the use of personal protective equipment ( $p = 0.001 < 0.05$ ), which means variation between heterogeneous studies, so it was analyzed using a random effect model that resulted in a pooled odd ratio value of 1.584 (95% CI -0.01–0.93). It is interpreted that farmers who do not have the habit of using personal protective equipment have a 1,584 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning. According to the results of the research conducted, the use of Personal Protective Equipment (PPE) was found to correlate with the risk of organophosphate poisoning in farmers, which was also influenced by factors such as age, level of knowledge, smoking habits, and duration of spraying activities).<sup>16</sup> PPE is essential for farmers because it can prevent various health problems such as pesticide poisoning, respiratory and skin irritation, and the potential for cancer. Farmers with access to complete PPE, adequate knowledge of PPE, and a positive attitude tend to be more likely to use PPE correctly when spraying pesticides.<sup>17</sup>

According to the theory, farmers generally consider using PPE impractical and inconvenient when handling pesticides.<sup>18</sup> Pesticides can enter the body through the skin and respiratory system without PPE. The results of a study that included more than ten articles discussing the use of PPE showed a significant relationship between the habits of farmers who did not use it and a decrease in cholinesterase levels due to pesticide poisoning. In the opinion of the researchers, farmers rarely use PPE entirely because they do not experience any symptoms if they do not use personal protective equipment.

Farmers tend only to use masks and long-sleeved shirts when spraying pesticides, and there is a lack of awareness about the importance of using PPE because it is considered troublesome when spraying pesticides.

### Meta-analysis of Risk Analysis of Working Time with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers

Table 2. It was found that the results of the meta-analysis heterogeneity test were known that the length of work ( $p=0.001<0.05$ ), which means variation between heterogeneous studies, so it was analyzed using a random effect model that resulted in a pooled odds ratio value of 1.665 (95% CI -0.08–1.11). It is interpreted that farmers who work more than 5 hours have a 1,584 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning. The length of work refers to the time farmers spend spraying crops and using pesticides in the fields. The duration of work at the time of spraying can affect the length of exposure, which can be either acute or chronic.

According to the theory, the longer farmers spray pesticides, the more pesticides can be absorbed into the body. This pesticide then binds to cholinesterase in the blood.<sup>18</sup> Spraying for more than 5 hours without using personal protective equipment and without changing clothes after spraying can decrease cholinesterase levels by 939.049 U/L. Farmers who spray for more than 5 hours tend to experience fatigue and a weakened immune system, making it easier for pesticides to enter the body. Organophosphate and carbamate pesticides work similarly by binding to acetylcholinesterase or acting as acetylcholinesterase inhibitors.<sup>19</sup> Therefore, it is recommended that farmers do not spray farmland with pesticides for more than 5 hours. Suppose the spraying process has not been completed within 5 hours. In that case, it is recommended that the remaining unsprayed land be continued the next day or by increasing

the amount of spraying so that the process is completed within a maximum of 3 hours.<sup>20</sup>

### **Meta-analysis of Individual Hygiene Risk Analysis with Reduced Cholinesterase Levels Due to Pesticide Poisoning in Farmers**

Table 3 the results of the heterogeneity test in the meta-analysis showed that individual hygiene ( $p = 0.006 > 0.05$ ), indicating variation between studies, was homogeneous, so it was analyzed using a fixed effect model which resulted in a pooled odds ratio value of 1.954 (95% CI 0.13–1.22). It is interpreted that farmers who ignore personal hygiene have a 1,584 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning. Individual hygiene refers to self-care practices carried out to maintain physical and psychological health. This action aims to maintain a person's hygiene and health. One way to avoid exposure through the skin, separated from Individual Defensive Hardware, is to urge its use in washing hands.<sup>19</sup> Several studies examined aspects of personal hygiene in this context, including procedures for mixing pesticides, hand washing habits, changing clothes after spraying, policies prohibiting eating or drinking immediately after spraying, and methods for cleaning spraying equipment away from water and food sources.<sup>21</sup> Poor personal hygiene can increase farmers' risk of exposure to harmful pesticide substances.<sup>22</sup>

Previous research in Indonesia supports these meta-analysis findings. Personal hygiene factors and the use of personal protective equipment have been proven to affect cholinesterase levels significantly in farmers in North Sumatra.<sup>22</sup> Cholinesterase activity in workers on oil palm plantations in Central Kalimantan also highlights the importance of limiting working hours and using PPE to prevent excessive exposure.<sup>23</sup> Similar results were found in farmers in Tanah Karo, where spraying techniques, PPE use, and spraying duration were significantly related to cholinesterase levels.<sup>24</sup>

Another study on vegetable farmers in Lampung and North Sumatra found that exposure to organophosphate pesticides caused a more severe decline in cholinesterase levels in farmers with poor personal hygiene and inconsistent use of personal protective equipment.<sup>25</sup> Internationally, research in India also

confirms that the use of complete PPE can reduce the risk of pesticide toxicity in agricultural workers, especially those with long-term exposure.<sup>26</sup> This evidence strengthens the meta-analysis results that personal hygiene, the use of PPE, and working hours are important factors influencing the risk of decreased cholinesterase levels in farmers.<sup>27</sup>

**Limitations:** This study partly relied on non-academic databases such as Google Scholar and included several non-indexed articles such as theses and proceedings, which may introduce publication bias. Furthermore, variations in study design, sample size, and measurement methods across the included studies may contribute to heterogeneity. Additionally, uncontrolled confounders across studies could potentially affect the pooled estimates. Future research should prioritize peer-reviewed and indexed literature, apply standardized inclusion criteria, and adjust for potential confounding factors to improve the robustness of findings. Future research should incorporate scholarly databases, such as PubMed, Scopus, or ScienceDirect, to ensure the use of higher-quality sources.

### **CONCLUSION AND RECOMMENDATION**

The results of the heterogeneity test for Personal Protective Equipment (PPE) and length of work are known to be smaller than 0.05, namely  $p = 0.001$ , which means that variations between studies are heterogeneous, so this analysis uses a random effect model. Individual hygiene variables are known to have  $p$ s greater than 0.05, namely  $p = 0.006$ , which means that variations between studies are homogeneous, so this analysis uses a fixed effect model. Funnel Plot Risk Analysis of Personal Protective Equipment (PPE), Individual Hygiene, and Length of Work There is an indication of Publication bias because the model formed is not symmetrical, specifically a partial dark circle coming out in the triangle area. The results of Egger's test on the Use of Personal Protective Equipment (PPE) are more significant than 0.05, namely  $p = 0.356$ , on the length of work  $p = 0.395$ , which means there is no indication of Publication bias. Individual hygiene is the highest risk factor for reducing cholinesterase levels due to pesticide poisoning in farmers, with a pooled value of  $PR = e^{0.67} = 1.954$  (95% CI

0.13 – 1.22). Therefore, it can be concluded that farmers who ignore personal hygiene, specifically not bathing after spraying and not immediately changing clothes, are at 1.954 times greater risk of experiencing reduced cholinesterase levels due to pesticide poisoning.

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### AUTHOR CONTRIBUTIONS

RA was responsible for the conceptualization, methodology, and supervision of the study, and contributed to writing, reviewing, and editing the manuscript. JJ conducted validation and formal analysis, and assisted in the review and editing process. MAR contributed to data curation, software management, and formal analysis. GN was responsible for data curation and writing the original draft of the manuscript. MS carried out the investigation, visualization, and data validation. ZAS performed the literature review, data entry, and assisted in writing the original draft. ZNN contributed to data checking, figure preparation, formatting, and manuscript review. RA = R. Azizah; JJ = Juliana Jalaludin; MAR = Muhammad Addin Rizaldi; GN = Globila Nurika; MS = Mochammad Sholehudin; ZAS = Zaneta Aaqilah Salsabila; ZNN = Zafira Nuha Naura.

### CONFLICTS OF INTEREST

The writers declare that they are not associated with or involved in any group or entity that has a financial or non-financial stake in the topics or resources covered in this publication.

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