

Meta Analysis of Health Belief Model Theory on the Predictor of HPV Vaccine Uptake in Women of Reproductive Age

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Received: 10 November 2023; Accepted: 06 January 2023; Available online: 16 January 2024

ABSTRACT

Background: Lack of knowledge about the use of HPV vaccine in women of productive age can result in cervical cancer. This study aims to determine the effect of the Health Belief Model application on the predictor of HPV vaccine uptake in women of reproductive age.

Subjects and Method: Systematic review and meta-analyses were conducted using PRISMA guidelines and PICO model including: Population = women of reproductive age; Intervention= high perceived benefits, high perceived severity, high perceived susceptibility; Comparison= low perceived benefits, low perceived severity, low perceived susceptibility; Outcome= HPV vaccine uptake. Articles were collected from databases such as PubMed, Science Direct, and Google Scholar. The keywords used in the database search were "Health Belief Model" AND "Human Papilloma Virus" OR "HPV" AND "Women" AND "cross sectional study". A total of 7 articles met the inclusion criteria, namely full text primary paper, cross-sectional study design, with a measure of association was the Odds Ratio (OR), the study subjects were women of reproductive age, interventions were in the form of high perceived benefits, high perceived severity, high perceived vulnerability, and the outcome was in the form of HPV vaccine use. They were subsequently assessed for meta-analysis using RevMan 5.3.

Results: Meta-analysis from Indonesia, Ethiopia, the United Kingdom, Japan, Romania, Spain, and Italy showed that high perceived benefits of HPV vaccine use (aOR= 1.81; 95% CI= 1.00 to 3.26; p= 0.050), high perceived severity (aOR= 1.78; 95% CI= 0.94 to 3.40; p= 0.080), and high perceived susceptibility (aOR= 1.70; CI 95%= 0.75 to 3.83; p= 0.200) increased the likelihood of HPV vaccine uptake.

Conclusion: High perceived benefits, high perceived severity, and high perceived susceptibility have the likelihood of women of productive age to use HPV vaccine.

Keywords: health belief model, human papilloma virus, perceived benefits, perceived severity, perceived susceptibility.

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Cite this as:

Qomariah N, Murti B, Budihastuti UR (2024). Meta Analysis of Health Belief Model Theory on the Predictor of HPV Vaccine Uptake in Women of Reproductive Age. J Health Promot Behav. 09(01): 48-60. <https://doi.org/10.26911/thejhp.2024.09.01.05>.



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BACKGROUND

One of the reproductive health problems is the delayed early detection of cervical cancer carried out by women due to lack of knowledge about cervical cancer. In Indonesia, cervical cancer is the second most common cancer after breast cancer. Most women do not keep the feminine area (vagina) clean. Therefore, when entering the reproductive age they should be supported by a good health quality so that women have the knowledge to be able to avoid various diseases, cervical cancer in particular (Rahmadini et al., 2022).

Cervical cancer is the most common cause of death in women worldwide with 604,127 new cases and 341,831 deaths each year (Kulkarni, et al., 2023). The incidence of cervical cancer by age is 14.4 per 100,000 women from 2014 to 2018 (Uusküla et al., 2023). The cervical cancer cases in Indonesia, as many as 17.2% or 36,633 people, rank the second after breast cancer and the third as the cause of death of all cancers (Khairunnisa et al., 2023).

Cervical cancer is a malignancy that involves the growth of abnormal tissue on the cervix. One of the most common characteristics of cervical cancer is bleeding. However, the occurrence of bleeding in the cervix generally indicates the final stage of cervical cancer malignancy (Maryam dan Ariono, 2022).

Human papillomavirus (HPV) infection is a sexually transmitted virus caused by infection (Zhang et al., 2023). HPV virus is the main cause of cervical cancer, HPV infection will cause cell changes to be abnormal (malignant). A vaccine is available for HPV that aims to increase an individual's protective immunity (Morgan et al., 2022).

The Health Belief Model (HBM) theory is one of the widely used theoretical frameworks for understanding health beha-

viours, including vaccine uptake. The Health Belief Model (HBM) construction has previously been applied to studies of HPV vaccine (Fallucca et al., 2022). HBM has been used extensively to study vaccination beliefs and behaviours, and has also been used in vaccination studies to identify patient perceptions of perceived benefits, perceived severity, and perceived susceptibility to disease and vaccination (Carico et al., 2021).

The studies shows the better effect of the high perceived benefits, the high perceived severity, the high perceived susceptibility since it will affect the curiosity and increase knowledge about cervical cancer that can encourage women to use the HPV vaccine (Donadiki et al., 2014).

This condition shows a change; therefore, it requires a more thorough study toward the results of various primary studies, combined in a meta-analysis study design using the Revman 5.3 application to measure the size of effect in order to obtain a quantitative summary of the results (Murti, 2018). The study aimed to determine the effect of the application of the health belief model theory on predictors of HPV vaccine uptake in women of productive age.

SUBJECTS AND METHOD

1. Study Design

This study used systematic review and meta-analysis methods. It is a method to analyse data that derive from primary studies of databases based on a PRISMA diagram. The article search in this study was conducted through electronic databases such as PubMed, Science Direct, and Google Scholar. The keywords used in the database search were "Health Belief Model" AND "Human Papilloma Virus" OR "HPV" AND "Women" AND "Cross Sectional Study".

2. Step of Meta-Analysis

The meta-analysis was carried out in five steps as follows:

- 1) Formulate research questions in the PICO format (Population, Intervention, Comparison, Outcome). P = Women of reproductive age; C= high perceived benefits, high perceived severity, high perceived vulnerability; I = low perceived benefit, low perceived severity, low perceived vulnerability; O= HPV vaccine uptake.
- 2) Search for primary study articles from various electronic and non-electronic databases.
- 3) Conduct screening and critical assessment of primary research articles.
- 4) Perform data extraction and synthesize effect estimates into RevMan 5.3.
- 5) Interpret and conclude the results

3. Inclusion Criteria

The inclusion criteria of the study were full text paper of primary study articles using cross-sectional study design, analysis using multivariate with Odds Ratio (OR), study subjects were reproductive age women, interventions were in the form of high perceived benefits, high perceived severity, high perceived susceptibility.

4. Exclusion Criteria

Study articles published before 2013 and after 2023, outcomes from studies that do not conform to PICO criteria or formulas in the study, articles that did not include OR, and study articles published in non-English languages.

5. Operational Definition of Variables

Cervical cancer is a cancer that occurs in the cervix caused by the growth of abnormal tissue on the cervix.

Human Papilloma Virus is the main cause of cervical cancer which is easily spread through direct sexual contact, from

the skin, mucous membranes of an infected person.

Human papilloma virus vaccine is a primary prevention effort that is expected to reduce the risk of cervical cancer.

Health Belief Model is a theory that explains preventive behavior and individual response to a disease, affirms the perceived benefits, perceived severity, perceived susceptibility in health behavior decisions.

6. Data Analysis

Data analysis using RevMan 5.3. Forest plots and funnel plots are used to determine the size of the relationship and the heterogeneity of the data. The fixed effect model is used for homogeneous data, while the random effect model is used for heterogeneous data across studies.

RESULTS

The process of searching for articles in this meta-analysis was conducted by searching through journal databases, namely PubMed, Science Direct, and Google Scholar with a time span between 2013-2022. Keywords used in database search included "Health Belief Model" AND "Human Papilloma Virus" OR "HPV" AND "Women" AND "Cross Sectional Study". The searching for articles was according to the PRISMA flow diagram which can be seen as follows.

Figure 1 shows the initial search process which displays a total result of 1,250 articles, after the removing duplicated articles in more than one journals, it obtained as many as 442 articles with 80 of them were eligible for further full text review. A total of 7 articles that were eligible for full text review.

Figure 2 showed an overview of the study area used in this meta-analysis that spread across 3 continents, namely Asia, Africa, and Europe.

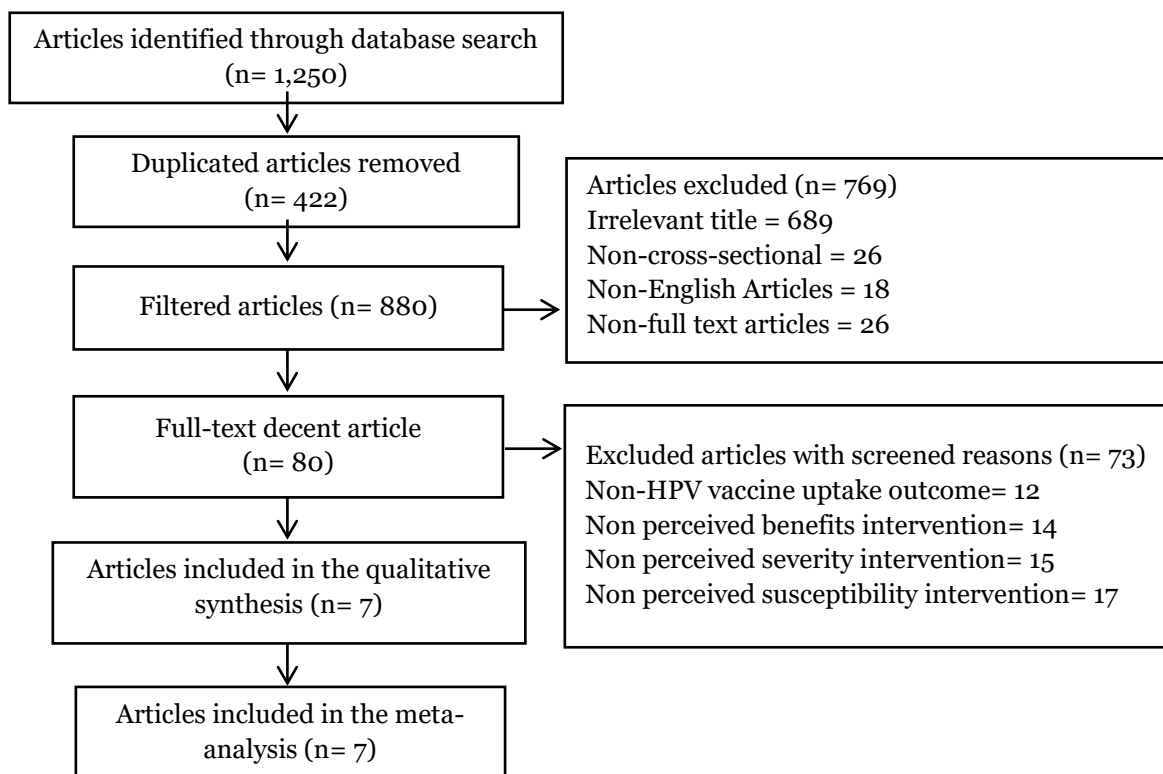


Figure 1. Results of PRISMA Flow Diagrams



Figure 2. Research Distribution Map

Table 1. The Quality Assessment Result of Articles with a Cross-Sectional Study using CEBM.

Primary Study	Criteria							Total
	1	2	3	4	5	6	7	
Cui et al. (2022)	2	2	2	2	2	2	2	14
Fitriani et al. (2018)	2	2	2	2	2	2	2	14
Feyisa et al. (2023)	2	2	2	2	2	2	2	14
Donadiki et al. (2014)	2	1	2	2	2	2	2	14
Marlow et al. (2014)	2	2	2	2	2	2	2	14
Fallucca et al. (2022)	2	2	2	2	2	2	2	14
Penta et al. (2020)	2	2	2	2	2	2	2	14

Description of the question criteria:

1. Is the population in the primary study the same as the population in the PICO meta-analysis??
2. method for selecting research subjects:
 - Descriptive cross-sectional study (prevalence): Is the sample randomly selected?
 - Analytical cross-sectional study: Are samples randomly or purposively selected?
3. Methods for measuring comparisons (intervention) and outcome variables:
 - Are both exposure/intervention and outcome variables measured with the same instruments in all primary studies?
 - If variables are measured on a categorical scale, are the cut-offs or categories used the same across primary studies?
4. Bias of the design:
 - How much is the response rate?
 - Is non-response related to outcomes?
5. Methods to control confounding:
 - Is there any confusion in the results / conclusions of the primary study?
 - Have primary study researchers used appropriate methods to control the effects of confusion?
6. Method of statistical analysis:
 - In the cross-sectional study, is multivariate analysis performed?
 - Multivariate analysis includes multiple linear regression analysis, multiple logistic regression analysis, Cox regression analysis.
7. Is there a conflict of interest with the research sponsor??

Description of scoring:

- 0= No
- 1= Hesitate
- 2= Yes

There are 7 articles with cross-sectional studies of the health belief model theory application on predictors of HPV vaccine use in women of reproductive age using perceived benefits, perceived severity, and

perceived susceptibility with a total sample of 7,767. The study was conducted in seven countries including Indonesia, Ethiopia, United Kingdom, Japan, Romania, Spain, and Italy.

Table 2. PICO of cross-sectional articles of perceived benefits toward the knowledge on HPV vaccine.

Author (years)	Country	Sample	P	I	C	O
Cui et al. (2022)	Japan	816	Women	High Perceived benefits, severity, susceptibility	Lack of perceived benefits, low severity, susceptibility	Knowledge on HPV vaccine use
Donadiki et al. (2014)	Spain	2.007	Female Students	Low knowledge, benefits, severity, susceptibility	High perceived benefits, severity, susceptibility	HPV vaccine use
Fallucca et al. (2022)	Italy	3.070	Female University Students	High perceived benefits, susceptibility, severity	Low perceived benefits, severity, susceptibility	Education of HPV vaccine use
Feyisa et al. (2023)	Ethiopia	906	Women aged 15	High benefits severity, susceptibility	Low perceived benefits, severity, susceptibility	HPV vaccine use
Fitriani et al. (2018)	Indonesia	200	Women	High benefits, severity, susceptibility	Low perceived benefits, severity, susceptibility	HPV vaccine use
Marlow et al (2014)	United Kingdom	367	Female Adolescents	Good perceived benefits, susceptibility, severity	Poor perceived benefits, severity, susceptibility	Knowledge on HPV vaccine use
Penta et al. (2020)	Romania	401	Women	The occurrence of HPV benefits, high perceived severity, susceptibility	No benefits, low perceived severity and susceptibility	HPV vaccine use

Table 3. aOR and 95% CI data of perceived benefits toward the knowledge on HPV vaccine.

(Author, year)	aOR	95% CI	
		Lower Limit	Upper Limit
Cui et al. (2022)	1.31	0.99	1.73
Fitriani et al. (2018)	2.77	1.66	4.62
Feyisa et al. (2023)	4.84	3.64	6.44
Donadiki et al. (2014)	0.69	0.52	0.92
Marlow et al. (2014)	7.63	4.04	14.41
Fallucca et al. (2022)	1.46	1.23	1.73
Penta et al. (2020)	0.57	0.42	0.77

Forest plot in Figure 3 shows that women of reproductive age with a high perceived benefit were 1.81 times more likely to use HPV vaccine compared to women of reproductive age who had low perceived benefits, this result was statistically significant (aOR= 1.81; 95% CI= 1.00 to 3.26; p=

0.050). The forest plot also shows a high heterogeneity of effect estimates across primary studies $I^2= 95\%$; $p < 0.001$. Thus, the calculation of the average effect estimates was carried out with a random effect model approach.

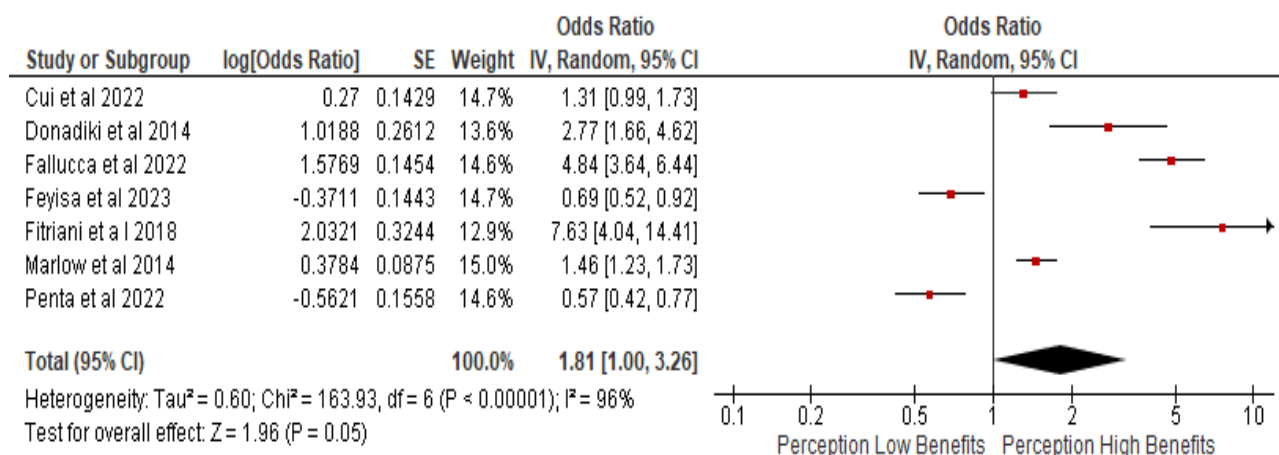


Figure 3. Forest plot of perceived benefits toward the use of HPV vaccine

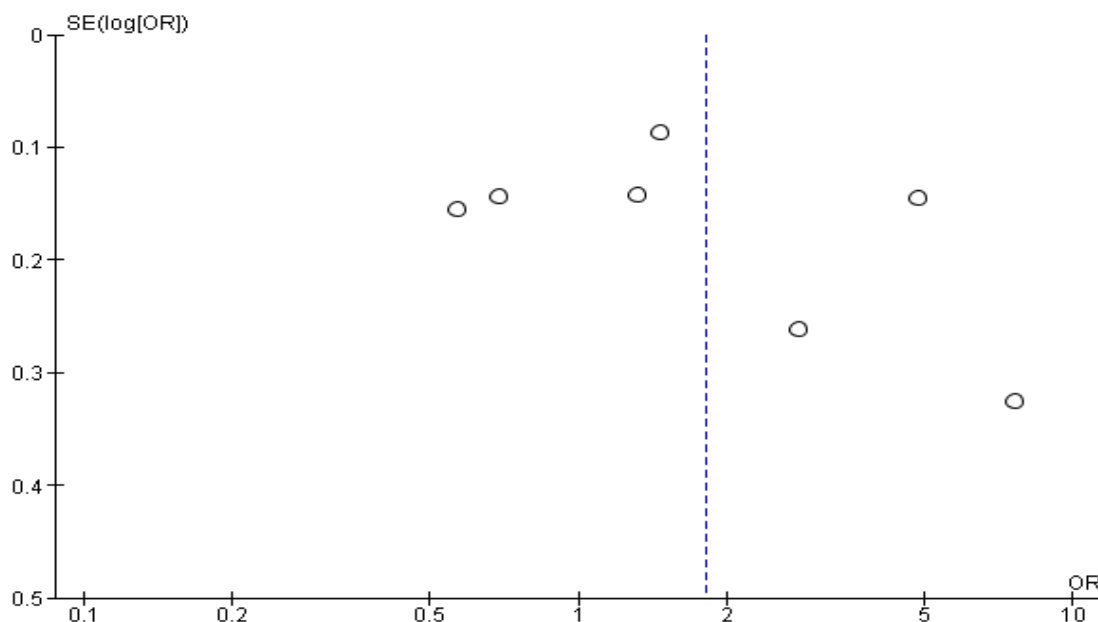


Figure 4. Funnel plot of perceived benefits toward the use of HPV vaccine

The funnel plot in Figure 4 shows that the distribution of the estimates across studies is asymmetric, that the distribution of effect estimates on the left of the vertical line of the average effect estimates was relatively larger than those on the right (overestimate). Thus, this funnel plot indicates that there was a publication bias.

The forest plot in Figure 5 shows that women of reproductive age with high per-

ceived severity were 1.78 more likely to use HPV vaccine compared to those with low perceived severity (aOR= 1.78; CI 95%= 0.94 to 3.40; p= 0.080). The forest plot in figure 4.3 shows a high heterogeneity of effect estimates across primary studies I²= 94%; P < 0.001. Thus, the calculation of the average effect estimates was carried out with a random effect model approach.

Table 4. Odds Ratio (OR) of perceived severity toward the use of HPV vaccine.

(Author, year)	aOR	95% CI	
		Lower Limit	Upper Limit
Cui et al. (2022)	0.87	0.66	1.15
Fitriani et al. (2018)	22.24	10.72	46.14
Feyisa et al. (2023)	1.71	0.89	3.29
Donadiki et al. (2014)	2.77	1.66	4.62
Marlow et al. (2014)	1.59	0.93	2.72
Fallucca et al. (2022)	0.27	0.53	0.98
Penta et al. (2020)	0.78	0.53	1.15

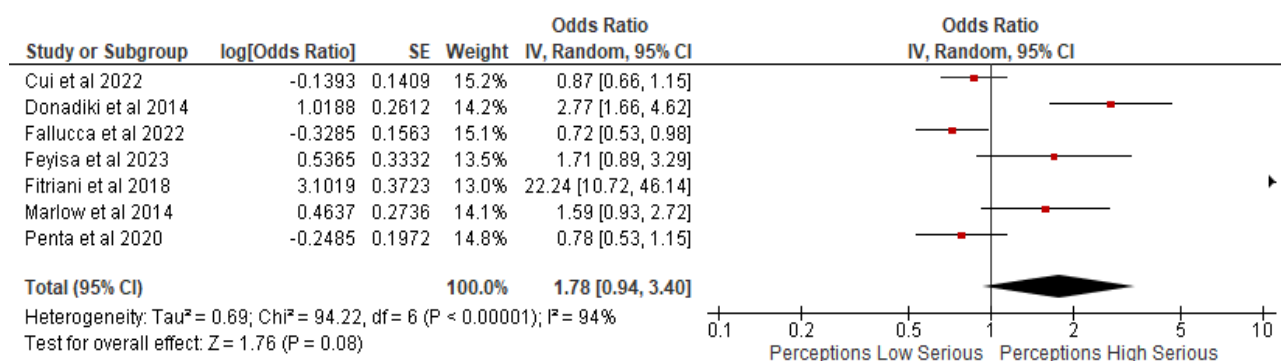


Figure 5. Forest plot of effect of perceived severity toward the use of HPV vaccine.

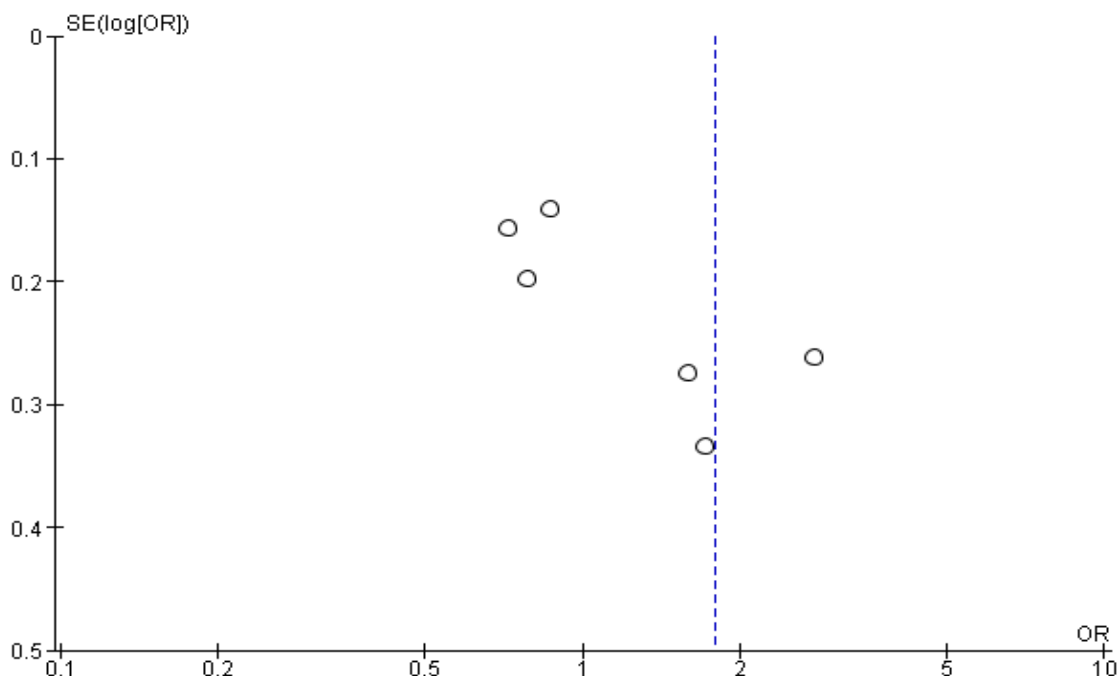


Figure 6. Forest plot of effect of perceived severity toward the use of HPV vaccine.

The funnel plot in figure 6 shows a greater distribution of effect estimates on the left

than on the right of the average vertical line. Thus, the funnel plot identifies a

publication bias in the meta-analysis. Because the distribution of effect estimates is more on the left of the funnel plot in the

opposite direction to the diamond on the right, the publication bias tended to reduce the previous effect (underestimate).

Table 5. aOR and 95% CI data of perceived susceptibility toward the knowledge on HPV vaccine.

(Author, year)	aOR	95% CI	
		Lower Limit	Upper Limit
Cui et al. (2022)	1.20	0.96	1.50
Fitriani et al. (2018)	7.75	7.25	8.28
Feyisa et al. (2023)	1.93	1.74	2.14
Donadiki et al. (2014)	1.07	0.96	1.19
Marlow et al. (2014)	1.94	1.39	2.71
Fallucca et al. (2022)	1.34	0.66	2.72
Penta et al. (2020)	0.79	0.62	1.01

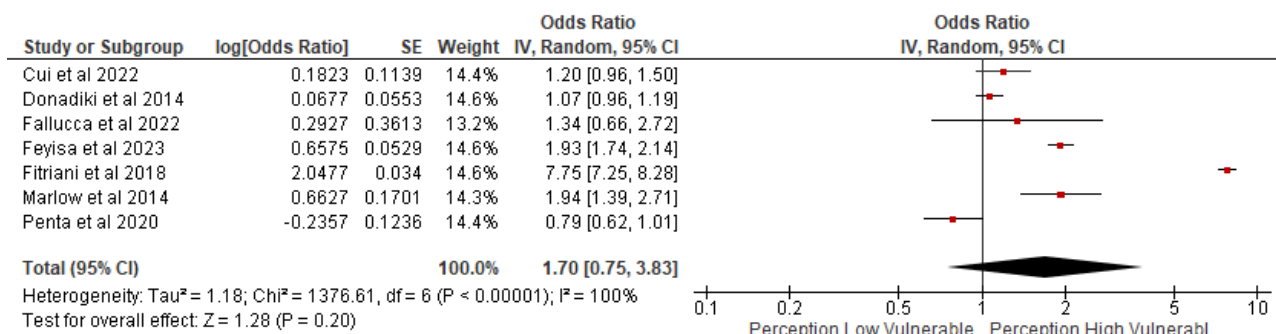


Figure 7. Forest plots of effect of perceived susceptibility toward the use of HPV vaccine.

The forest plot in Figure 6 shows that women of reproductive age with high perceived susceptibility were 1.70 more likely to use HPV vaccine compared to those with low perceived susceptibility (OR= 1.70; CI 95%= 0.75 to 3.83; p= 0.200). The forest plot in figure 7 shows heterogeneity of high effect estimates across primary studies I²= 95%; p< 0.001. Thus, the calculation of the average effect estimates was carried out with a random effect model approach.

The funnel plot in figure 7 shows a greater distribution of effect estimates on the left than on the right of the average vertical line. Thus, the funnel plot identifies there was a publication bias in the meta-analysis. Because the distribution of effect estimates is more on the left of the funnel

plot in the opposite direction to the diamond on the right, the publication bias tended to reduce the previous effect (underestimate).

DISCUSSION

The theme of the systematic review and meta-analysis in this study is the application of health belief model theory on the use of HPV vaccine in women of reproductive age. The interventions in this study were high perceived benefits, high perceived severity, high perceived susceptibility. The low perceived benefits, perceived severity, and perceived susceptibility result in women of reproductive age not knowing the use of HPV vaccine to prevent cervical cancer (Novalia, 2023).

1. Perceived benefits toward the use of HPV vaccine

Women of productive age who have a higher perceived benefits are more likely to use the HPV vaccine than women who have a lower perceived benefit. It is because if women know more about the benefits of using the HPV vaccine, women will prefer to use the HPV vaccine to prevent cervical cancer (Wardani and Harumi, 2022).

A total of 7 articles of primary studies related to the application of the health

belief model theory on the use of HPV vaccines were included in this synthetic meta-analysis and subsequently analysed using Revman 5.3. The synthesis results on 7 primary studies showed high heterogeneity across experiments ($I^2 = 95\%$; $p = 0.001$), therefore the analysis used a random effect model. High heterogeneity was based on sample size that varied across studies.

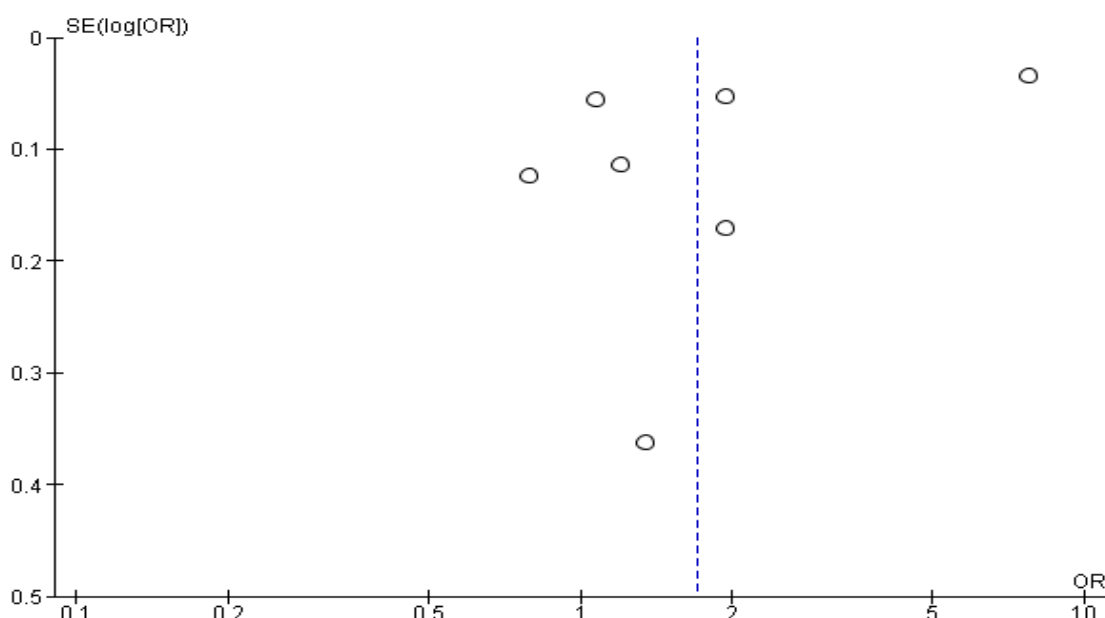


Figure 8. Funnel plots of effect of perceived susceptibility toward the use of HPV vaccine.

High perceived benefits may influence HPV vaccine use in women of reproductive age rather than low perceived benefits. This result corresponds to the hypothesis. Meta-analysis of seven cross-sectional articles related to the effect of perceived benefits on HPV vaccine use was 1.81 times compared with low perceived benefits and the effect was statistically significant (aOR= 1.81; CI 95%= 1.00 to 3.26; $p = 0.001$). This meta-analysis used studies that already controlled confounding factors, as stated in

the inclusion criteria, namely odds ratio (OR).

A study by Fitriani et al., (2018) states the use of HPV vaccine in women of reproductive age will reduce deaths from cervical cancer. Similarly, women who are in reproductive age and intend to know health problems earlier. The result of the value of perceived benefits was OR= 7.63; CI 95%= 4.04 to 14.44. This study is in line with similar study by Donadiki et al., (2014) that identifies cervical cancer prevention using HPV vaccine based on the

theory of the Health Belief Model conducted in Spain. The inclusion criteria of this study are: age 18-26 years, students, and able to speak Greek. The sample includes 2,007 students. The participation rate is 88.9% and the percentage of non-vaccination is 71.65%. Results of perceived benefits value is (OR= 2.77; CI 95%= 1.66 to 4.62).

Perceived benefits are very important to increase knowledge in the use of HPV vaccine in women of reproductive age to prevent cervical cancer (Wardani and Harumi, 2022).

2. Perceived Severity toward the Use of HPV Vaccine

One of the problems with the lack of knowledge about the HPV vaccine is the perceived severity. The perceived severity in the Health Belief Model affects the possible use of the HPV vaccine. Women of reproductive age who had a high perceived severity were 1.78 times more likely to use HPV vaccine than those with a low perceived severity, and the effect was statistically significant (aOR= 1.78; CI 95%= 0.94 to 3.40; P= 0.010).

7 primary study articles related to the perceived severity toward HPV vaccine use were included in this synthetic meta-analysis and then analysed using Revman 5.3. The result of the synthesis of 10 primary studies showed a high heterogeneity across experiments ($I^2= 91\%$; $p= 0.001$) therefore, the analysis used the Random Effect Model (REM). High heterogeneity was based on sample size that varied across studies.

Fitirani et al. (2018) women who get HPV vaccine have a higher perceived severity and are more aware of cervical cancer. This study showed that women with high perceived severity were better than women with low perceived severity (OR= 22.24; CI 95%= 10.72 to 46.14). HPV vaccination improves with better know-

ledge. The result of this study suggests that there is a statistically significant association between perceived severity and HPV vaccination. Individuals will take measures to protect themselves if they consider one's condition to be in a serious issue. An individual's perception that he has no risk is a factor that causes women of reproductive age not to get HPV vaccination. This means that if a woman is always faithful to her partner, then she is not at risk of cervical cancer.

Other study from Penta et al., (2020) conducted in Romania and Germany involves women aged 18-26 years It aims to determine the use of HPV vaccine in preventing cervical cancer. In this study the perceived severity is higher and had a significant value (OR= 0.78; CI 95%= 0.53 to 1.15).

3. Perceived susceptibility toward the use of HPV Vaccine

Health problems are also influenced by perceived susceptibility. Perceived susceptibility in the Health Belief Model influences the likelihood of HPV vaccine use. The level of susceptibility knowledge in women is low, it can increase the incidence of cervical cancer, while if the knowledge of susceptibility in women is higher, it can reduce the incidence of cervical cancer in women. Women of reproductive age who had a high perceived susceptibility were 1.70 times more likely to use HPV vaccine than those with a low perceived susceptibility, and the effect was statistically significant (OR= 1.70; CI 95%= 0.75 to 3.83; $p=0.01$).

Fitirani et al. (2018) women who take the HPV vaccine and know are more aware of the higher susceptibility so as to prevent cervical cancer. Based on the significant study result (OR= 7.75; CI 95%= 7.25 to 8.28) in this study, women with a high perceived vulnerability were motivated and

sought higher knowledge about cervical cancer. This study is also reinforced by a study by Feyisa et al., (2019) a cross-sectional study using the Health Belief Model theory with 906 female respondents aged 15 years states that women who had a higher perceived vulnerability are more aware of cervical cancer (OR= 1.93; CI 95%= 1.74 to 2.14). The level of knowledge about susceptibility is important in women to prevent the occurrence of cervical cancer so that it can reduce the mortality rate caused by cervical cancer. Women of reproductive age who have a high perceived benefit, a high perceived severity and a high perceived susceptibility have the possibility of using the HPV vaccine.

AUTHOR CONTRIBUTION

Nurul Qomariah was the main researcher who chose the topic, conducted a search for data collection in this study.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGMENT

The researcher would like to thank all those who have helped in the formulation of this article and also send the gratitude to the database providers Google Scholar, PubMed, and Science Direct.

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