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Meta-analysis

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Meta-Analysis: The Influence of Knowledge, Hormonal Contraceptive Use, and Sexually Transmitted Disease on Cancer Screening Uptake

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ABSTRACT

Background: Cervical cancer is still the most common problem among women. Prevention of cervical cancer can be done prospectively through human papillomavirus (HPV) vaccination and screening or early diagnosis. Screening is essential to reduce the incidence and death of cervical cancer. This study aims to analyze and estimate the influence of knowledge, the use of hormonal contraceptives, and the history of sexually transmitted diseases on cervical cancer screening.
Subject and Method: This study is a meta analysis using the PRISMA flowchart and the PICO model. Population: women of childbearing age. Intervention: using hormonal contraceptives, having good cervical cancer knowledge, and having a history of sexually transmitted infections. Comparation: not using hormonal contraceptives, poor cervical cancer knowledge and no history of sexually transmitted infections. Outcome: cervical cancer screening. The process of searching for articles by searching through databases in Google scholar, Scopus, ProQuest, PubMed, Elsevier, and Science direct. The keywords used are "hormonal contraception" OR "pill" OR "injection" OR "implant" AND "Cervical cancer screening" OR "sexually transmitted infection" OR "HIV" OR "STD" OR "syphilis" OR "gonorrhea" AND "cancer knowledge" AND "cross sectional" AND "aOR". Articles are selected based on inclusion criteria, namely multivariate articles with a cross sectional design published in 2014-2024. Data analyzed using Revman 5.3.
Results: A meta analysis was conducted on 15 primary studies from Ethiopia, Cambodia, and Uganda. The results showed that the use of cervical cancer screening increased with good knowledge (aOR= 2.03; CI 95%= 1.70 to 2.43; p<0.001), use of hormonal contraceptives (aOR= 1.83 CI 95%= 1.70 to 1.96; p<0.001), and history of sexually transmitted diseases (aOR= 2.32; CI 95%= 1.81 to 2.97; p<0.001).
Conclusion: Good knowledge, use of hormonal contraceptives, and history of infectious diseases increase the use of cervical cancer screening performance.

Keywords: sexually transmitted diseases, cervical cancer, hormonal contraceptives

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BACKGROUND

Globally, cervical cancer is still a major health problem for women (Christensen et al., 2022). Cervical cancer has the second highest incidence rate of cancer in women after breast cancer. As many as 7.7% of all cervical cancer cases have died (Abebaw, 2023). The main cause of cervical precancer and cancer is persistent infection with one or more high-risk oncogenic types of human papillomavirus (HPV) that interfere with the normal function of the cell, resulting in marked changes in epithelial cells of the cervical transformation zone (Dangal et al., 2024).

Cervical cancer is estimated to cause 530,000 new cases each year. More than 2.7 million women, 85% of whom live in low- and middle income countries, are at risk of contracting cervical cancer (Yimer et al., 2021). Based on data from the International Agency for Research on Cancer (IARC), every year more than 300,000 women die from cervical cancer (Misgun and Demissie, 2023). In developing countries, every minute a woman is diagnosed with cervical cancer, 9 out of 10 women who die are found in advanced stages (Vigneshwaran et al., 2023). In Indonesia, the prevalence of cervical cancer has increased in the last five years. Data from the Ministry of Health of the Republic of Indonesia in 2019 shows that the prevalence of cervical cancer cases reached 23.4 per 100,000 population with a mortality rate of 13.9 per 100,000 population (Bante et al., 2019).

Prevention of cervical cancer can be done prospectively through human papillomavirus (HPV) vaccination and screening or early diagnosis. Most cervical cancer patients (80%) come to health care in advanced conditions, with 94% of these cases dying within two years (Saimin et al. 2018). Cervical cancer screening detects cervical cell abnormalities, pre-cancerous lesions and early stages of cervical cancer, reducing incidence and mortality (Chali et al., 2021). Early diagnosis and treatment are essential to reduce the incidence and death of cervical cancer (Lemma et al., 2022).

Many factors affect cervical cancer screening. Knowledge about cervical cancer and its screening is important in filtering the information provided (Jemal et al., 2023). Women with a low level of knowledge about cervical cancer and its prevention are less likely to access screening services (Abebaw, 2023). The use of hormonal contraceptives has benefits, namely as a delay in pregnancy, but can have a high risk of developing cervical cancer if used for a period of more than five years (Al-Oseely et al., 2023). In addition, women who have a history of sexually transmitted diseases are also more likely to be screened for cervical cancer (Endalew et al., 2020).

Therefore, the researcher is interested in conducting a systematic review and meta-analysis of the knowledge, use of hormonal contraceptives, and history of sexually transmitted infections on cervical cancer screening. This study aims to analyze and estimate the influence of knowledge, the use of hormonal contraceptives and the history of sexually transmitted infections on cervical cancer screening.

SUBJECTS AND METHOD

1. Study design

The research design used is systematic review and meta-analysis using the PICO model. Population: women of childbearing age. Intervention: using hormonal contraceptives, having good cervical cancer knowledge, and having a history of sexually transmitted infections. Comparation: not using hormonal contraceptives, poor cervical cancer knowledge, and no history of sexually transmitted infections. Outcome: cervical cancer screening. The process of searching for articles is carried out through

databases in Google scholar, Scopus, ProQuest, PubMed, Elsevier, and Science direct. The keywords used are "hormonal contraception" OR "pill" OR "injection" OR "implant" AND "Cervical cancer screening" OR "sexually transmitted infection" OR "HIV" OR "STD" OR "syphilis" OR "gonorrhea" AND "cancer knowledge" AND "cross sectional" AND "aOR". This study was analyzed using RevMan 5.3 software.

2. Meta-Analysis Steps

The stages carried out are:

a. Formulate research questions in PICO (Population, Intervention, Comparation, and Outcome) format.
b. Search for major study articles from online databased, namely Google scholar, Scopus, ProQuest, PubMed, Elsevier, and Science direct.
c. Conducting screening by determining inclusion and exclusion criteria and conducting cross-sectional critical assessments.
d. Performing data extraction and analysis using RevMan 5.3 Software.
e. Carefully interpret the results obtained from the data analysis by examining patterns, relationships, or differences that emerge, and then draw logical, evidence-based conclusions.

3. Inclusion Criteria

The inclusion criteria in this study are full-text articles using English with a cross-sectional research design, published from 2014 to 2024, the measure of relationship used is the aOR value.

4. Exclusion criteria

The exclusion criteria were studies that had incomplete data, studies that had biased results, articles with RCT designs, and studies that had low methodological quality.

5. Variable Operational Definition

The search for articles is carried out taking into account the eligibility criteria determined by using the PICO model.

Knowledge: An information that a person has related to cervical cancer and cervical cancer screening.

Use of hormonal contraceptives: An action taken to prevent pregnancy by using injectable contraceptives, implants, or pills.

History of sexually transmitted diseases: A person who has been/is suffering from sexually transmitted diseases such as HIV/AIDS, gonorrhoea, syphilis, and hepatitis.

6. Instrument

The research stage follows the PRISMA flow chart and the assessment of the quality of the article research using the Check list Critical Appraisal for cross-sectional studies from the Master of Public Health Sciences Study Program, Graduate School, Sebelas Maret University.

7. Data analysis

The data in this study was analyzed using the Review Manager application (RevMan 5.3). Forest plots and funnel plots are used to determine the size of the effect and heterogeneity of the data. Data processing is carried out based on variations between studies with a fixed effect model.

RESULTS

The process of searching for articles is by searching through online journal databases, namely Google scholar, Scopus, ProQuest, PubMed, Elsevier, and Science direct in 2014-2024. The process of filtering articles based on research criteria can be seen on the PRISMA flowchart. The keywords used were "hormonal contraception" OR "pill" OR "injection" or "implat" and "Cervical cancer screening" OR "Sexually transmitted infection" or "HIV" OR "STD" OR "syphilis" or "gonorrhea" and "Cancer knowledge" and "Cross sectional" and "aOR". The initial search process obtained 8,094 articles, then after going through the screening process, 25 articles were considered as primary

articles of this study and 15 articles were included in the meta-analysis.

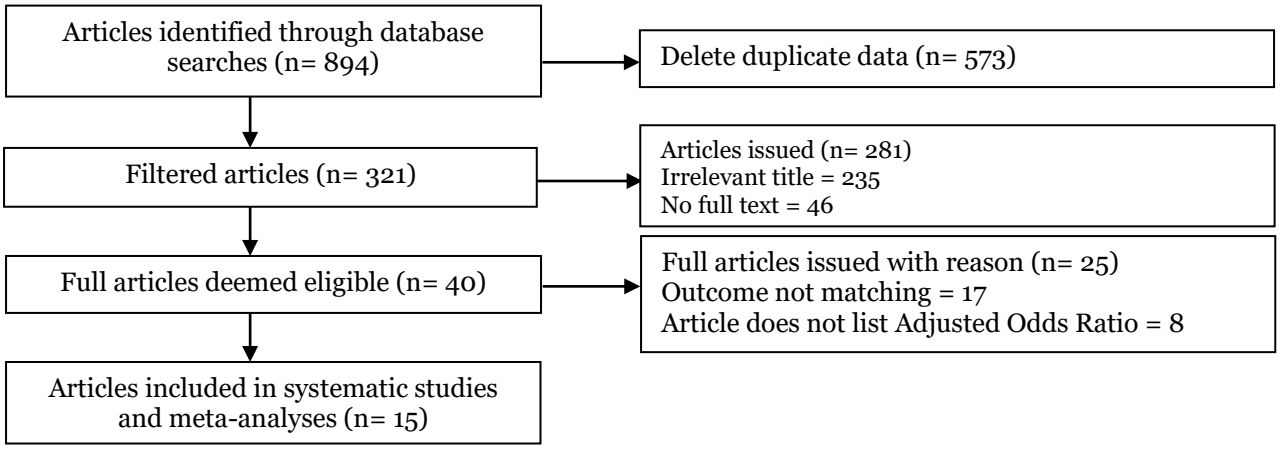

Figure 1. PRISMA flow chart

Figure 2. Map of the study area

Table 1. Cross-sectional critical appraisal on the influence of knowledge, use of hormonal contraceptives, and history of sexually transmitted diseases on cervical cancer screening

Author (Year)	Critical Appraisal													Total
	1a	1b	1c	1d	2a	2b	3a	3b	4	5	6a	6b	7	
Abebaw et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Abera et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Amado et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Assefa et al. (2024)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Aynalem et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Bante et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Damtie et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Desta et al. (2022)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Jemal et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Mekuria et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Mesfin et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26

Author (Year)	Critical Appraisal													Total
	1a	1b	1c	1d	2a	2b	3a	3b	4	5	6a	6b	7	
Misgun et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Mukama et al. (2017)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Um et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26
Tadesse et al. (2023)	2	2	2	2	2	2	2	2	2	2	2	2	2	26

Description of the question criteria:

1. Formulation of research questions in the acronym PICO

a. Is the population in the primary study the same as the population in the PICO meta-analysis?
b. Is the operational definition of intervention, i.e. the state of exposure in the primary study, the same as the definition intended in the meta-analysis?
c. Is the comparison, i.e. the unexposed status used by the primary study the same as the definition intended in the meta-analysis?
d. Are the outcome variables studied in the primary study the same as the definition intended in the meta-analysis?

2. Methods for selecting research subjects

a. In cross-sectional analytical studies, do researchers select samples from the population randomly (random sampling)?
b. Alternatively, if in a cross sectional analysis study the sample is not randomly selected, whether the researcher selects the sample based on outcome status or based on intervention status?

3. Methods for measuring exposure and outcome variables

a. Are exposures and outcome variables measured with the same instruments in all primary studies?
b. If the variables are measured on a categorical scale, are the cutoffs or categories used the same between primary studies?

4. Design-related bias

If the sample is not randomly selected, has the researcher made efforts to prevent bias in selecting the research subjects? For example, in selecting subjects based on outcome status is not affected by the exposure status (intervention), or in selecting subjects based on exposure status (intervention) is not affected by outcome status.

5. Methods to control confounding

Whether the primary study researcher has made an effort to control the influence of confounding (e.g., conducting multivariate analyses to control the influence of a number of confounding factors).

6. Statistical analysis methods

a. Did the researcher analyze the data on this primary study with a multivariate analysis model (e.g., multiple linear regression analysis, multiple logistic regression analysis).
b. Whether the primary study reported the effect size or relationship of the multivariate analysis results (e.g., adjusted OR, adjusted regression coefficient).

7. Conflict of interest

Is there no possibility of conflict of interest with the research sponsor, which causes bias in concluding the research results?

Rating instructions:

Number of questions = 13 questions
Score 0 = no
Score 1 = hesitant
Score 2 = Yes
Score ≥ 22 = included in the meta-analysis
Score < 22 = not used in meta analysis.

Based on Table 2 of the PICO main study "the influence of knowledge on cervical cancer screening" conducted on 7 articles with research locations in Ethiopia, Cambodia, and Urganda. The similarity with this study is that the research design uses cross sectional and the magnitude of the AoR (Adjusted Odds Ratio) relationship, the research population is women of childbearing age, the intervention provided is less knowledge with the comparison, namely good knowledge.

Table 2. PICO summary table of cross-sectional articles on the influence of knowledge on cervical cancer screening

Author (Year)	Country	Sample	P	I	C	O
Abebaw et al. (2022)	Ethiopia	404	Women of childbearing age aged 20-35 years	Good knowledge, using hormonal contraception	Poor knowledge, no use of hormonal contraception	Cervical cancer screening
Abera et al. (2020)	Ethiopia	1.010	Women of childbearing age aged 20-35 years	Using hormonal contraception, having a history of sexually transmitted diseases	No use of hormonal contraception, no history of sexually transmitted diseases	Cervical cancer screening
Amado et al. (2022)	Ethiopia	460	Women of childbearing age aged 20-35 years	Good knowledge, using hormonal contraception, having a history of sexually transmitted diseases	Poor knowledge, no use of hormonal contraception, no history of sexually transmitted diseases	Cervical cancer screening
Assefa et al. (2024)	Ethiopia	299	Women aged 30-49 years	Using hormonal contraception	No use of hormonal contraception	Cervical cancer screening
Aynalem et al. (2020)	Ethiopia	822	Women of childbearing age aged 20-35 years	Good knowledge, having a history of sexually transmitted diseases	Poor knowledge, no history of sexually transmitted diseases	Cervical cancer screening
Bante et al. (2019)	Ethiopia	517	Women of childbearing age	Having a history of sexually transmitted diseases	No history of sexually transmitted diseases	Cervical cancer screening
Damtie et al. (2023)	Ethiopia	816	Women of childbearing age aged 20-35 years	Good knowledge	Poor knowledge	Cervical cancer screening
Desta et al. (2022)	Ethiopia	855	Women aged 30-65 years	Using hormonal contraception, having a history of sexually transmitted diseases	No use of hormonal contraception, no history of sexually transmitted diseases	Cervical cancer screening
Jemal et al. (2023)	Ethiopia	241	Female health workers	Good knowledge	Poor knowledge	Cervical cancer screening
Mekuria et al. (2021)	Ethiopia	855	Women aged 30-65 years	Having a history of sexually transmitted diseases	No use of hormonal contraception, no history of sexually transmitted	Cervical cancer screening

Author (Year)	Country	Sample	P	I	C	O
					diseases	
Mesfin et al. (2023)	Ethiopia	429	Women with HIV	Using hormonal contraception	Poor knowledge	Cervical cancer screening
Misgun et al. (2023)	Ethiopia	361	Women of reproductive age	Good knowledge	No history of sexually transmitted diseases	Cervical cancer screening
Mukama et al. (2017)	Uganda	900	Women aged 25-49 years	Having a history of sexually transmitted diseases	Not using hormonal contraception	Cervical cancer screening
Tadesse et al. (2023)	Ethiopia	458	Women aged 25-59 years	Good knowledge	Poor knowledge	Cervical cancer screening
Um et al. (2023)	Cambodia	19.496	Women of childbearing age	Using hormonal contraception	No history of sexually transmitted diseases	Cervical cancer screening

Table 3 showing a summary of the aOR and 95% CI values in the article related to the influence of knowledge with cervical cancer screening. AOR data on the influence of knowledge on cervical cancer screening were taken from 7 articles. The forest plot in Figure 3 illustrates that there is an influence of knowledge on cervical cancer screening. Individuals with good knowledge may improve cervical cancer screening practices by 2.03 compared to individuals with poor knowledge and this result is statistically significant (aOR= 2.03; 95% CI= 1.70 to 2.43; p= 0.003). The forest also showed high effect estimate heterogeneity between primary studies I^2= 70%; p<0.001. The calculation of the average effect estimate was carried out using the random effect model approach.

Table 3. AOR data and confidence interval from the article on the influence of knowledge on cervical cancer screening

Author	aOR	95% CI	
		Lower Limit	Upper Limit
Abebaw et al. (2022)	3.20	1.08	8.45
Amado et al. (2022)	5.40	1.50	19.5
Aynalem et al. (2020)	4.02	2.07	7.77
Damtie et al. (2023)	1.52	1.21	5.82
Jemal et al. (2023)	4.02	2.07	7.77
Misgun et al. (2023)	2.34	1.21	4.52
Tadessee et al. (2023)	4.64	2.10	10.26

The results of the funnel plot in Figure 4 show that the distribution of the estimated effect is uneven. The effect estimation distribution shows that the effect estimation distribution tends to be more located to the right of the average vertical line of effect estimation than to the left. Thus, this plot funnel image shows the existence of publication bias. Because the distribution of the effect estimate is located to the right of the average vertical line in the direction of the diamond in the forest plot, the public-

ation bias tends to overestimate the actual effect (over estimate).

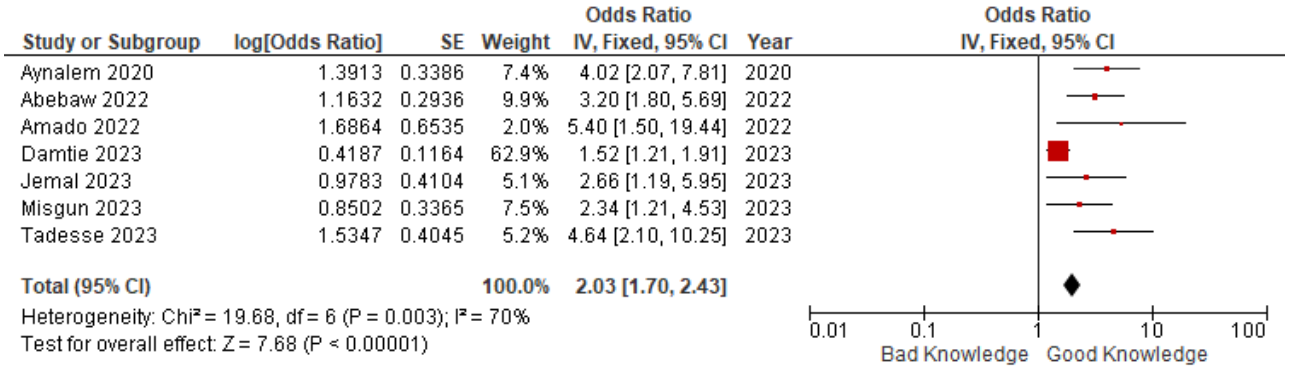

Figure 3. Forest plot : The influence of knowledge on cervical cancer screening

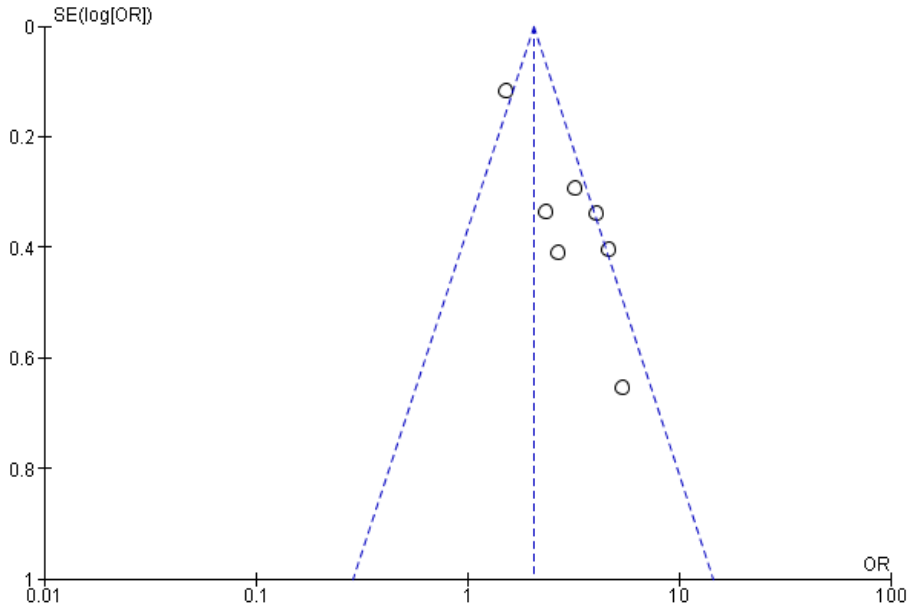

Figure 4. Funnel plot on the influence of knowledge on cervical cancer screening

Table 4. AOR and confidence interval data from the article Effect of Hormonal Contraceptive Use on Cervical Cancer Screening

Author	aOR	95% CI	
		Lower Limit	Upper Limit
Abebaw et al. (2022)	2.70	1.56	7.45
Abera et al. (2020)	1.27	0.85	1.89
Amado et al. (2024)	1.80	0.60	5.30
Assefa et al. (2024)	2.49	1.04	5.96
Desta et al. (2022)	1.78	1.31	2.42
Mesfin et al. (2023)	2.43	1.05	5.64
Um et al. (2023)	1.83	1.70	1.98

aOR data was taken from 7 articles. *The forest plot* in Figure 5 shows that there is an effect of hormonal contraceptive use on cervical cancer screening. Individuals using hormonal contraceptives may increase cervical cancer screening by 1.83 times compared to individuals who do not use hormonal contraceptives, and this

result is statistically significant (aOR=1.83 CI 95%= 1.70 to 1.96; p<0.001). The forest plot showed high heterogeneity to the estimated effect between primary studies I^2= 1%. Thus, the calculation of the average effect estimate is carried out using the random effect model approach.

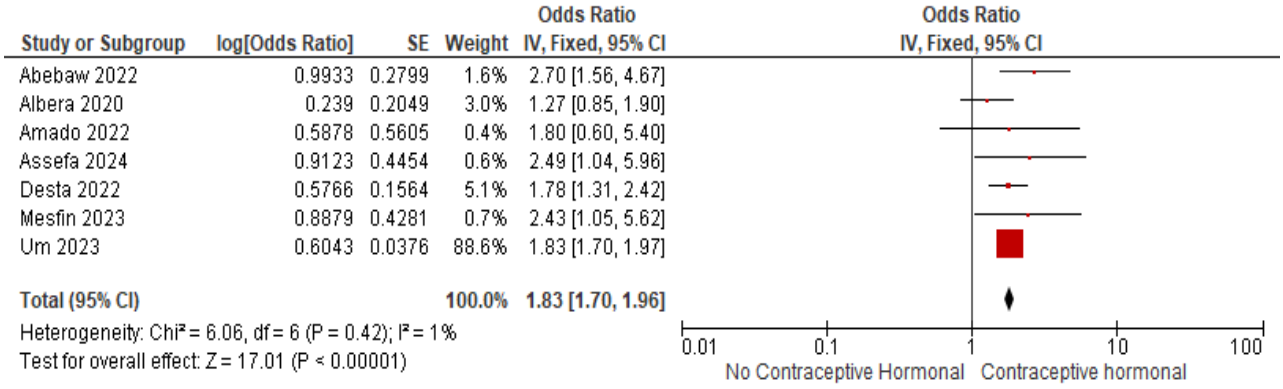

Figure 5. Forest plot of the effect of hormonal contraceptive use on cervical cancer screening

The results of the plot funnel in Figure 6 show that the distribution of the effect estimates is uneven. The effect estimation distribution shows that the effect estimation distribution tends to be more to the right of the average vertical line of the effect estimate than to the left. Thus, this plot funnel image shows the existence of publiccation bias. Because the distribution of the effect estimate is located to the right of the average vertical line in the forest plot, the publication bias tends to overestimate the actual effect.

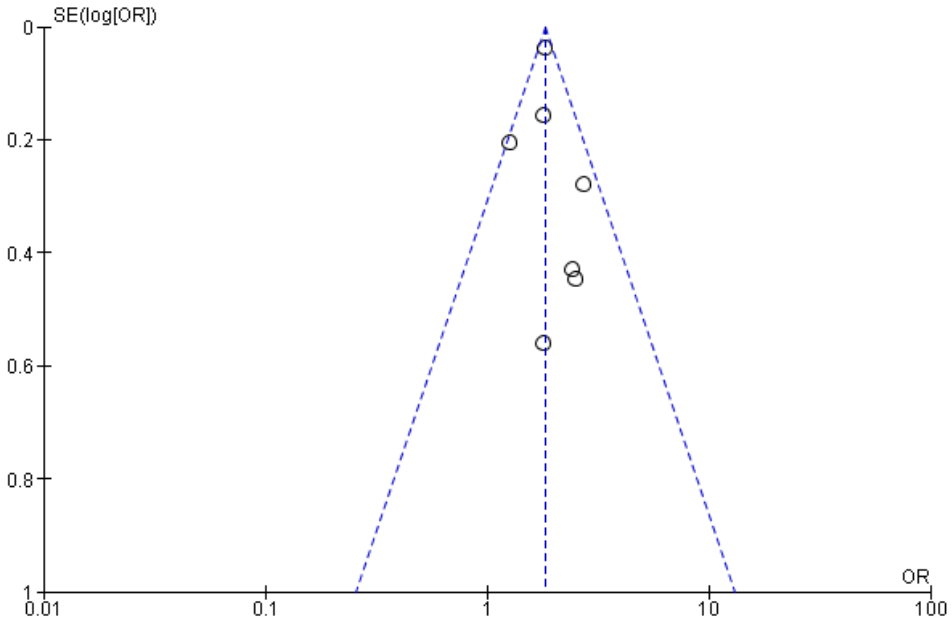

Figure 6. Funnel plot of the effect of hormonal contraceptive use on cervical cancer screening

Table 5. AOR and confidence interval data from the article on the effect of sexually transmitted disease history on cervical cancer screening

Author	aOR	95% CI	
		Lower Limit	Upper Limit
Abera et al. (2020)	1.71	1.05	2.79
Amado et al. (2022)	4.2	1.40	12.8
Aynalem et al. (2020)	4.03	1.68	9.72
Bante et al. (2019)	2.37	1.11	5.07
Desta et al. (2022)	3.7	1.60	8.64
Mekuria et al. (2021)	6.76	1.14	3.90
Mukama et al. (2017)	1.99	1.34	2.96

The forest plot in Figure 9 shows that individuals with a history of sexually transmitted diseases increase cervical cancer screening by 2.32 times compared to individuals without a history of sexually transmitted diseases and this result is statistically significant (aOR=2.32; CI 95% = 1.81 to 2.97; p<0.001). The forest plot showed high heterogeneity to the estimated effect between primary studies I^2= 18%; p<0.001. Thus, the calculation of the average effect estimate is carried out using the random effect model approach.

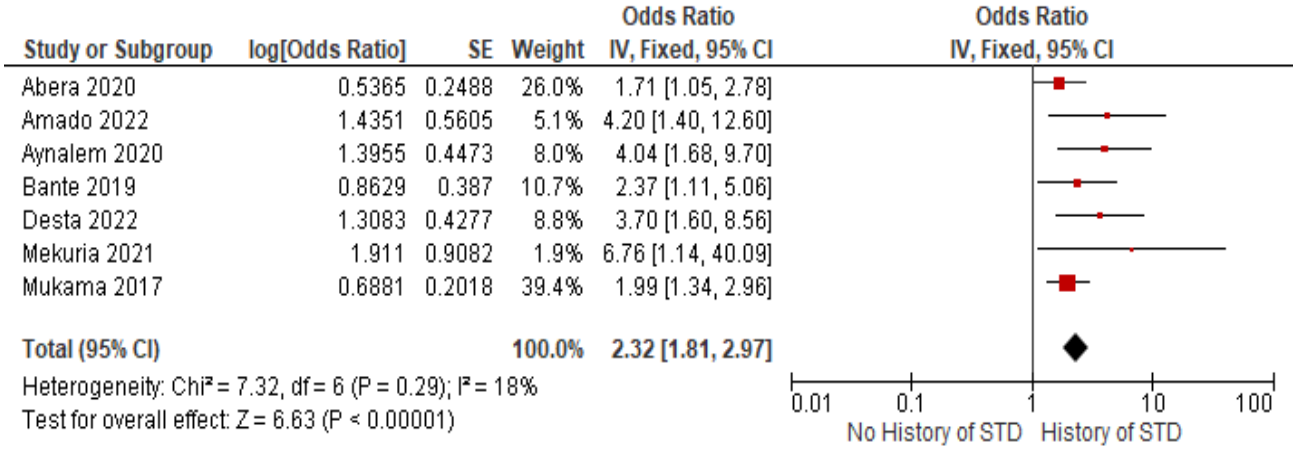

Figure 7. Forest plot of the effect of a history of sexually transmitted diseases on cervical cancer screening

The results of the plot funnel in Figure 10 show that the distribution of the estimated effect is uneven. The effect estimation distribution shows that the effect estimation distribution tends to be more to the right of the average vertical line of the effect estimate than to the left. Thus, this plot funnel image shows the existence of publication bias. Because the distribution of the effect estimate is located to the right of the average vertical line in the direction of the diamond in the forest plot, the publication bias tends to overestimate the actual effect (over estimate).

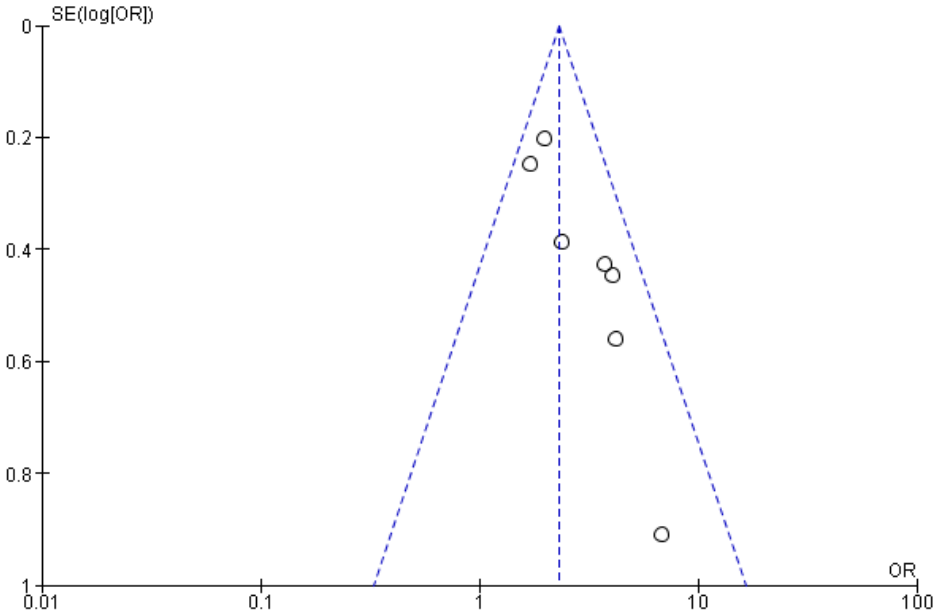

Figure 8. Funnel plot of the effect of a history of sexually transmitted diseases on cervical cancer screening

DISCUSSION

This meta-analysis study analyzed the factors that affect cervical cancer screening. This study uses aOR results of multivariate analysis which aims to obtain the same final result for the study to be analyzed.

1. The influence of knowledge on cervical cancer screening

This study showed that person with good knowledge has better cervical cancer screening practices compared to those with poor knowledge. Women's knowledge of cervical cancer screening is an important factor in the utilization of cervical cancer screening services (Phaiphichit et al., 2022). Knowledge in general is not necessarily interpreted into practice in many cases as it is perceived on certain occasions. For example, despite the improved awareness of cervical cancer prevention in a study conducted in Legos, Nigeria, prevention practices are still low where out of all knowledge about cervical cancer, only 18.5% have undergone a Pap smear test (Toru et al., 2022).

This is comparable to the results of the study by Vigneshwaran et al. (2023) where among cervical cancer participants who had good knowledge about cervical cancer and screening, only 16.9% underwent cervical cancer screening. This is in line with the findings of research in the cities of Arba Minch, Mekelle, and Jimma who have good knowledge about cervical cancer screening independently related to cervical cancer screening. This may be explained by the increasing level of women's knowledge about the benefits of screening directly leading them to cervical cancer screening uptake (Yimer *et al.*, 2021).

2. Effect of hormonal contraceptive use on cervical cancer screening

This study showed that hormonal contraceptives use increase cervical cancer screening uptake compared to those without hormonal contraceptives use. The funnel plot showed that the estimated distribution of influence between studies was more to the right than to the left of the vertical line, especially in primary studies with small

samples. Thus these variables indicate publication bias. The estimated distribution of the effect is more to the right of the average vertical line. Therefore, this publication bias tends to overestimate the actual impact.

The use of hormonal contraceptives was found to be a significant factor in the utilization of cervical cancer screening (Endalew et al., 2020). Women who use hormonal contraceptives are more likely to be screened for cervical cancer than women who do not use hormonal contraceptives. This evidence is in line with previous research that found that women who use hormonal contraceptives can obtain additional information about cervical cancer and their screening when participating in family planning services. Frequent contact with health care providers rather than non-modern contraceptive users may be another reason (Toru *et al.*, 2022).

3. Effect of a history of sexually transmitted diseases on cervical cancer screening

The results showed that individuals with a history of sexually transmitted diseases increased cervical cancer screening by 2.32 times compared to individuals without a history of sexually transmitted diseases and this result was statistically. A history of sexually transmitted infections is a significant factor in cervical cancer screening. This study is in line with a study in Kenya, Kasarani and Mekelle, when women are treated for STIs in institutions, they can be informed about the relationship between cervical cancer and STIs by a healthcare provider so that they can be screened (Musonda *et al.*, 2022). Patients may also be near reproductive health services so they can further check out other reproductive services such as cervical cancer screening (Chali *et al.*, 2021).

AUTHOR CONTRIBUTION

Diani Fadmi Putri as the main researcher who designed the research, searched for articles and analyzed data. Andri Setyawan collects articles and data analysis. Nathanael Aditya Santoso reviews the article document.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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