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A meta-analysis of the association between HPV vaccination and cervical cancer incidence

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ADMINISTRATIVE INFORMATION

Support - There was no funding for this work.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2025 and was last updated on 17 June 2025.

INTRODUCTION

Review question / Objective Objective: This meta-analysis aims to evaluate the efficacy of HPV vaccination in reducing the incidence of cervical cancer, cervical carcinoma in situ, and high-grade cervical lesions. We will synthesize evidence from relevant studies to provide a comprehensive assessment of the impact of HPV vaccination on cervical cancer prevention.
Population: Females who have received HPV vaccination and those who have not (control group), including cervical cancer patients, AIS, CIN3, and CIN2.
Interventions: HPV vaccination, including bivalent, quadrivalent, and nine-valent vaccines.
Comparison: No HPV vaccination or placebo.
Outcome: The incidence of cervical cancer, cervical carcinoma in situ, and high-grade cervical lesions (CIN2 and CIN3).
Study type: Cohort studies and randomized controlled trials.A meta-analysis of the association between HPV vaccination and cervical cancer the aim of this study is to systematically review the relationship between HPV vaccination and cervical cancer incidence,and to provide evidence-based support for the prevention of cervical cancer incidence.

Condition being studied Cervical cancer, a significant gynecological malignancy globally, is primarily caused by human papillomavirus (HPV) infection. It is the fourth most common cancer among women worldwide and a leading cause of cancer-related deaths. HPV, particularly high-risk types like HPV 16 and 18, is responsible for the vast majority of cervical cancer cases. This condition not only affects the health and quality of life of women but also poses a substantial burden on healthcare systems. The development of cervical cancer is a gradual process, often preceded by precancerous lesions such as cervical intraepithelial neoplasia (CIN) and adenocarcinoma in situ (AIS). The goal of this meta-analysis is to evaluate the impact of HPV vaccination on preventing cervical cancer and its precancerous

lesions, providing evidence-based support for cervical cancer prevention strategies.

METHODS

Participant or population This review will address females who have received HPV vaccination and those who have not, including cervical cancer patients, AIS, CIN3, and CIN2 patients, with varying age ranges across studies.

Intervention The intervention evaluated in this review is HPV vaccination, including bivalent, quadrivalent, and nine-valent vaccines, with varying vaccination doses (1-3 doses).

Comparator No HPV vaccination or placebo.

Study designs to be included Cohort studies and randomized controlled trials.

Eligibility criteria Inclusion criteria: ① Study type: cohort study, randomized controlled study; ② Study subjects: cervical cancer patients, AIS, CIN3, CIN2; ③ Outcome indicator: relative risk (RR).
Exclusion criteria: ① Literature is not in Chinese or English; ② Statistical data are inconsistent; ③ Duplicate publication; ④ Unnecessary literature types (conference abstracts, reviews, etc.).

Information sources Electronic databases including Web of Science, Embase, PubMed, Cochrane, CNKI, Wan fang, VIP from their inception to February 26, 2025.

Main outcome(s) The main outcomes of this review are the incidence of cervical cancer, cervical carcinoma in situ, and high-grade cervical lesions (CIN2 and CIN3). The effect measure is relative risk (RR) with its 95% confidence interval (95% CI).

Additional outcome(s) The quality of randomized controlled trials will be assessed using the Cochrane Handbook 5.1.0, evaluating factors like sequence generation, allocation concealment, blinding, and incomplete outcome data. For cohort studies, the Newcastle-Ottawa Scale (NOS) will be used, assessing selection, comparability, and outcome.

Strategy of data synthesis Data synthesis will involve using Stata 15.1 software to calculate relative risks (RR) and 95% confidence intervals (95% CI). Heterogeneity will be assessed with I^2 and Q tests. If $I^2 > 50\%$ and $P < 0.1$, a random-effects model will be used; otherwise, a fixed-effects model will be applied. Sensitivity analysis and funnel plots will assess publication bias.

Subgroup analysis Subgroup analyses will be conducted based on age groups, vaccine types (bivalent, quadrivalent, nine-valent), and vaccination doses (1-3 doses) to explore potential differences in the effectiveness of HPV vaccination across these subgroups.

Sensitivity analysis Sensitivity analysis will be performed using sequential exclusion of individual studies.

Country(ies) involved China.

Keywords HPV vaccination; cervical cancer; cervical carcinoma in situ; high-grade cervical lesions; meta-analysis.

Contributions of each author
Author 1 - Xin Gong.
Author 2 - Yan Zhou.
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