

Prevalence of human papillomavirus DNA and p16INK4a positivity in vaginal cancer and vaginal intraepithelial neoplasia: a systematic review and meta-analysis

INPLASY2023110022

doi: 10.37766/inplasy2023.11.0022

Received: 06 November 2023

Published: 06 November 2023

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Li, YH¹.**ADMINISTRATIVE INFORMATION****Support -** No.**Review Stage at time of this submission -** Data extraction.**Conflicts of interest -** None declared.**INPLASY registration number:** INPLASY2023110022**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 November 2023 and was last updated on 06 November 2023.**INTRODUCTION**

Review question / Objective Prevalence of human papillomavirus DNA and p16INK4a positivity in vaginal cancer and vaginal intraepithelial neoplasia: a systematic review and meta-analysis.

Condition being studied The primary cause of vaginal cancer and vaginal intraepithelial neoplasia (VaIN) is the presence of human papillomavirus (HPV) DNA and positive expression of p16INK4a. This study focused on determining the worldwide prevalence of positivity HPV DNA and p16INK4a in vaginal cancer and VaIN.

METHODS

Participant or population The histological subtypes of vaginal cancer and VaIN were reclassified according to the WHO Classification of Female Genital Tumors and the International Society for the Study of Vaginal Diseases term "vaginal squamous intraepithelial lesion."

Intervention We examined the prevalence of single or combined positive HPV DNA and p16INK4a in vaginal cancer and VaIN across 70 studies, revealed that approximately half of the cases of vaginal cancer analyzed (952 cases) were associated with HPV DNA infection.

Comparator The histological subtypes of vaginal cancer and VaIN were reclassified according to the WHO Classification of Female Genital Tumors and the International Society for the Study of Vaginal Diseases term "vaginal squamous intraepithelial lesion".

Study designs to be included For our systematic review and meta-analysis, we conducted searches in Embase, PubMed, and Cochrane Library databases for relevant studies which published in English between January 1, 1986, and May 1, 2023.

Eligibility criteria Duplicate records were removed, and the reference lists of included in the study were examined for additional relevant

publications. The complete retrieval strategy applied in each database.

Information sources A systematic review and meta-analysis were conducted with studies published between January 1, 1986, and May 1, 2023, retrieved from PubMed, Embase, and Cochrane Library databases. Included studies reported histologically confirmed positivity HPV DNA or p16INK4a in vaginal cancer or VaIN.

Main outcome(s) A total of 70 studies were included. The prevalence of HPV DNA in vaginal cancer was determined to be 71.2% [95% confidence intervals (CI): 64.8%-78.2%], while in VaIN, it was 87.2% (95% CI: 83.9%-90.5%). The most frequently detected HPV genotypes in vaginal cancer were HPV16 (70.0% [95%CI 60.8%-80.7%]) and HPV31 (14.8% [95%CI 0%-38.0%]). Similarly, HPV16 (45.8% [95%CI 35.5%-58.9%]) and HPV58 (8.5% [95%CI 7.3%-10.0%]) were the predominant genotypes in VaIN.

Quality assessment / Risk of bias analysis

Duplicate records were removed, and the reference lists of included in the study were examined for additional relevant publications. The complete retrieval strategy applied in each database.

Strategy of data synthesis Among the overlapping study populations, the studies with the most relevant data or the largest populations were included. All titles, abstracts, and full texts are evaluated independently by the two authors (JH and ZY), and any inconsistencies are discussed until consensus is reached (YL). In addition, there are no restrictions on the definition of detection methods or positive thresholds. This study followed the Preferred Reporting Project for Systematic Review and Meta-Analysis (PRISMA) guidelines.

Subgroup analysis immunohistochemical assays utilizing p16INK4a were included in the study, and additional analysis was conducted to categorize the combined p16 INK4a based on the percentage of positive cases defined by p16 INK4a.

Sensitivity analysis Meta-regression was applied to investigate sources of heterogeneity.

Language restriction No language restrictions were imposed.

Country(ies) involved China.

Keywords human papillomavirus, p16INK4a, vaginal cancer, vaginal intraepithelial neoplasia, prevalence, meta-analysis.

Contributions of each author

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