INPLASY PROTOCOL

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None declared.

Association between human papillomavirus vaccination and serious adverse events in females aged 9 to 26 years: a systematic review and meta analysis

Aidibai, S[1]; Hui, J[2].

Review question / Objective: **Is human papillomavirus (HPV) vaccination associated with any serious adverse events? Population: females aged 9 to 26 years; Intervention: human papillomavirus (HPV) vaccine; Comparison: females aged 9 to 26 years who received HPV vaccine versus who did not receive HPV vaccine. Outcome: All the serious adverse events related to HPV vaccination.**
Condition being studied: **Human papillomavirus (HPV) is the most common sexually transmitted infection among worldwide, and is linked to cervical, vulvar, vaginal, anal, and oropharyngeal cancers in females. However, adverse events(AEs) following injection of HPV in females and adolescents have been reported nationwide, and they are still a major public health problem globally. Despite the large-scale use of the HPV vaccine worldwide, safety concerns about HPV vaccination have not decreased, and concerns about vaccine related serious adverse events (SAEs) have undermined public confidence about immunization. We aimed to to systematically review SAEs and non-serious AEs following injection of HPV among young females aged 9 to 26 years to inform future efforts to improve the safety of HPV vaccination and integrate valuable evidence to observe the whole picture across HPV vaccinations.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 February 2022 and was last updated on 13 February 2022 (registration number INPLASY202220040).

INTRODUCTION

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METHODS

Search strategy: We searched PubMed, Medline, Web of Science, Scopus, Embase, Ovid and the Cochrane Library from inception to Jan 10th 2022, without date, publication status or language restrictions. The search contained a combination of following Medical Subject Heading (MeSH) terms: ("papillomavirus vaccine", "papillomavirus vaccination", "HPV vaccine", or "HPV vaccination") and ("females", "women", or "girls") and ("adverse events", "adverse effects", or "side effects"), using the function "AND" and "OR".

Participant or population: Females aged 9 to 26years.

Intervention: HPV vaccine.

Comparator: Females aged 9 to 26 years who received HPV vaccine versus who did not receive HPV vaccine.

Study designs to be included: There are no restrictions on the types of study.

Eligibility criteria: Inclusion criteria: (i) Participants had received HPV vaccination; (ii) participants were females aged 9 to 26 years; and (iii) the control group was unvaccinated or received placebo or other vaccines which are not against HPV. (iiii) at least one AEs or SAEs following HPV vaccination was reported on each HPV vaccinated group and the control group.

Information sources: We searched PubMed, Medline, Web of Science, Scopus, Embase, Ovid and the Cochrane Library from inception to Jan 10th 2022, without date, publication status or language restrictions.

Main outcome(s): All the serious adverse events related to HPV vaccination. Serious adverse events were defined as any AE that resulted in death, were deemed by the investigator to be life-threatening, resulted in a persistent or significant disability or incapacity, resulted in or prolonged an existing in-patient hospitalization, or was a cancer, a congenital anomaly, or an other important medical event.

Additional outcome(s): We will estimate the association between concrete AEs and HPV vaccination in females aged 9 to 26 years.

Data management: Measures of effect: Risk ratio(RR), or Odds ratios(OR). We will extract the following data: first author, publication year, study country, study design, vaccine types of the experimental group and the control group, sample size, age range of participants, number of all SAEs and non-serious AEs, number of injection-site adverse events and systematic adverse events.

Quality assessment / Risk of bias analysis: The methodological quality of each randomized controlled trial will be evaluated for risk of bias using standard criteria as recommended by the Cochrane Collaboration. We will assess the risk of bias across six domains, each domain was

categorized as low, high, or unclear. Studies that were assigned a high risk for allocation concealment, blinding of outcome assessment, or completeness of outcome data will be considered to have a high risk of bias. The Newcastle-Ottawa scale will be used to assess the methodological quality of included cohort and case-control studies.

Strategy of data synthesis: RR and its 95% confidence intervals (95% CI) will be calculated for the outcome of incidence of adverse events. Due to expected heterogeneity among the trials, meta-analysis using the random-effects model will be conducted to pool RR.

Subgroup analysis: We will conduct subgroup analysis according to study design (RCT versus non-RCT), age of participants (adolescents versus adults), sample size (larger than1000 versus smaller than1000), intervention type of control group (placebo versus unvaccinated/HAV), and study period (longer than 12months versus shorter than 12months).

Sensitivity analysis: A sensitivity analysis using influence analysis will be performed to assess the impact of a single study on the overall pooled estimates by removing one study at a time.

Country(ies) involved: China.

Keywords: Human papillomavirus, vaccine, females, serious adverse events.

Contributions of each author:

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