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A quinquennial review of the WHO's global call for action to eliminate cervical cancer – an Indian perspective

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INTRODUCTION & OBJECTIVE

- Bivalent (2vHPV) and quadrivalent (4vHPV) vaccines were introduced in India in 2008 (around ₹3500/dose), with a nonavalent (9vHPV) vaccine introduced in 2018 (around ₹8500/dose).
- 2vHPV provides direct protection against high-risk types HPV-16 and HPV-18. 4vHPV additionally provides protection against low-risk types HPV-6 and HPV-11. 9vHPV targets 9 oncogenic HPV types: HPV-16, HPV-18, HPV-6, HPV-11, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58.
- Cervical cancer (CC) is the fourth most common cancer in women globally. In 2018, the World Health Organization (WHO) made a global call for cervical cancer elimination (CCE).
- As of 2020, about 90% of all CC cases were recorded in lower middle-income countries, with 21% of all cases and 23% of all deaths occurring in India.
- As per GLOBOCAN 2020, the age-standardized incidence rate per 100 000 women in India was 18, which is markedly above the WHO threshold (4 cases per 100 000 women).
- We aimed to assess, through a targeted review, the disease burden of CC in India and the role of HPV vaccination in CCE.

METHODS

- Searches were conducted in Embase and MEDLINE to identify economic, clinical, epidemiological, and observational studies from 2021–2023 as per the PICOS criteria below (Table 1).

Table 1. PICOS selection criteria

PICOS	Inclusion criteria	Exclusion criteria
Population(s)	Male or female population aged 9 years and above	• Population below age 9 years • Population ineligible for the HPV vaccine
Interventions	• Bivalent HPV vaccine • Quadrivalent HPV vaccine • Nonavalent HPV vaccine	Any interventions not specified under inclusion criteria
Comparisons	• Cytology-based Pap test • HPV DNA testing • Cervical cancer screening program • No vaccination	Any comparisons not listed under the inclusion criteria
Outcomes	• Epidemiological data • Clinical data • Cost-effectiveness of HPV vaccination • Burden of disease • Cervical cancer elimination	Any other outcome not specified under inclusion criteria
Study design	• Randomized controlled trials (RCTs) • Non-RCTs • Cost-effectiveness studies – Cost-effectiveness analyses – Cost-minimization analyses – Cost-utility analyses • Cervical cancer elimination studies – Mathematical models – Markov models • Observational studies	Systematic literature review, review, letter, editorial
Others	• Publications from (including) 2021 onwards • Country: India • Language: English	• Publications prior to 2021 • Not applicable • All other languages

RESULTS

- In total, 64 articles (37 survey, 7 economic, 13 genotype, 3 epidemiological, 3 clinical, and 1 screening) were included.

Cervical cancer profile in India

- CC is the second most common cancer in Indian women, accounting for 29.9% of all cancer cases in women in India.
- The National Cancer Registry Program reported that the Papum Pare district in the state of Arunachal Pradesh accounts for the highest age-adjusted incidence rate of CC (27.7 per 100 000) in India.

Genotype prevalence

- As per the evidence from the studies, high-risk HPV-16 was noted to be the most prevalent genotype in the Indian population.

RESULTS

- The second most common genotype was high-risk HPV-18.
- Genital warts–causing genotypes HPV-6 and HPV-11 were not frequently observed.

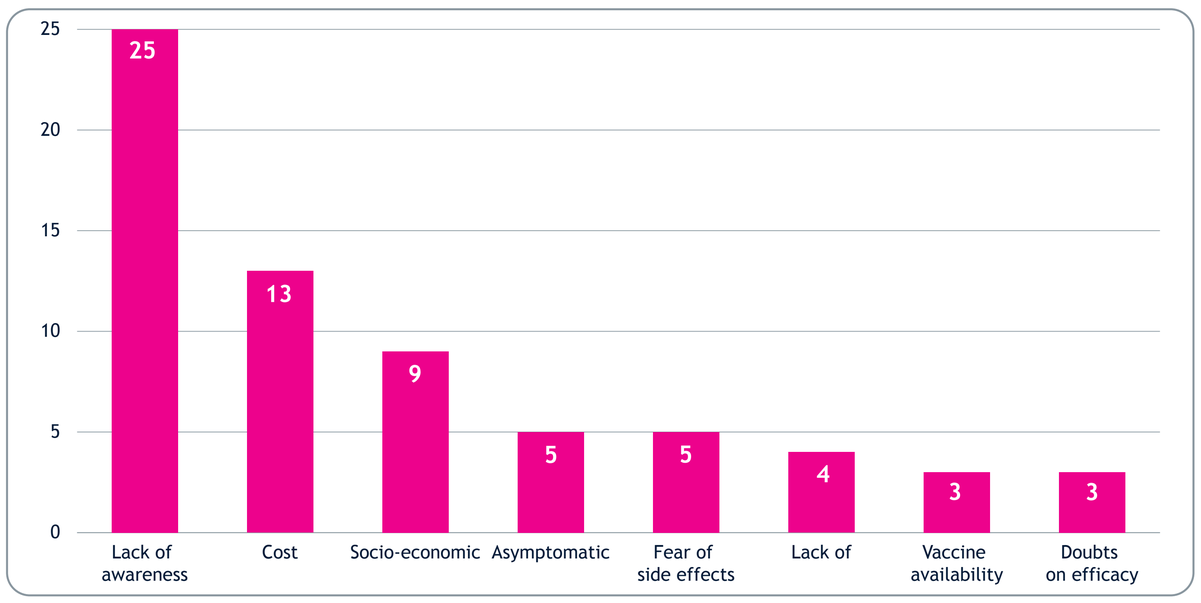
Effectiveness of vaccines

- The clinical trials conducted in India included participants of both genders ranging in age from 9 to 45 years.
- These trials demonstrated that 3-dose regimens of both the 4vHPV and 9vHPV vaccines elicited strong antibody responses, with an immune rate exceeding 95%.
- The vaccines were generally well tolerated, with no vaccine-related serious adverse events or discontinuations reported.

Cost-effectiveness of vaccines

- In total, 7 publications have evaluated the cost-effectiveness of HPV vaccines within the Indian population.
- The findings indicate that implementing a vaccination program targeting girls aged 9 to 12 years is a cost-effective approach.
- The assumptions included high vaccination coverage rates, ranging from 60% to 90%, and lifelong vaccine protection.
- Cross-protection against the non-vaccine types was considered in 4 studies, and no study included herd effects.
- Gender-neutral vaccination is considered a costly strategy, although it is recommended for CCE.

Figure 1: Number of studies reporting implementation challenges for HPV vaccination



Data source: 37 cross-sectional surveys. The studies do not add up to 37 as a study could be counted more than once.

Implementation challenges of HPV vaccination program

- Thirty-seven cross-sectional surveys investigated awareness, perception, and uptake of the HPV vaccine amongst the general population in India (Figure 1).
- The results indicated that very few (<20%) or no patients in rural India were aware of CC or HPV vaccination.
- In urban areas, awareness of the HPV vaccine varied widely, from 5% to 82%, depending on factors such as education, age, and socio-economic status.
- Healthcare professionals in urban areas had higher awareness levels.
- Vaccination rates in the population were very low, ranging from 4% to 24%.
- Currently, HPV vaccination is not included in the national immunization program.
- Additionally, inadequate screening programs, high vaccine costs, socio-economic issues including feelings of shame and shyness, cultural concerns, parental hesitancy, and shortages of vaccine supply contribute to the challenges to CCE.
- Other challenges included lack of interest due to asymptomatic cases, fear of side effects, and lack of endorsement or recommendation by physicians and government.

Steps to accelerating CCE

- In 2022, an indigenous 4vHPV (₹2000/dose) was approved by the Indian government which showed non-inferiority to the already marketed 4vHPV vaccine.
- The vaccine targets both women and men aged 9-26 years and is significantly cheaper, with local production impacting access and affordability.
- Further, in 2023, WHO evaluated the results from the International Agency for Research in Cancer study conducted in India, where a single-dose schedule of 4vHPV provided comparable efficacy as that of the 2-dose or 3-dose schedule.
- Based on this, WHO made an updated recommendation to adopt a single-dose policy.

CONCLUSIONS

- Despite the WHO global call for CCE, the disease burden of CC in India remains high.
- This may improve in the coming years given the recent approval of the indigenous 4vHPV.
- Educational programs, single-dose vaccination, and introduction of the new vaccine might accelerate CCE in India, paving the way for CCE in other lower middle-income countries.

REFERENCES: Full reference list available upon request.

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