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Letter to the Editor

One dose, one billion girls: the scientific and public health imperative of India's single dose human Papillomavirus vaccination strategy

Sir,

Cervical cancer remains one of the leading causes of cancer mortality in women across low- and middle-income countries (LMICs). In India, an estimated 1,27,526 new cases and 79,906 deaths were recorded in 2022, accounting for approximately 19% of the global burden.[1] Every day, nearly 200 Indian women lose their lives to a disease that a vaccine can prevent. Against this backdrop, the phased introduction of the human Papillomavirus (HPV) vaccine under India's Universal Immunisation Programme (UIP), following the Union Budget announcement in February 2024 and sustained advocacy by the National Technical Advisory Group on Immunisation (NTAGI), represents a watershed moment in preventive oncology.[2]

The deliberate adoption of a single-dose schedule, initially viewed by some as an off-label compromise born of resource constraints, is, in fact, a triumph of evidence-based pragmatism. As community medicine specialists, we argue that India's single-dose strategy is not a concession; it is the correct answer.

IMMUNOLOGICAL CASE: WHY ONE DOSE WORKS

Unlike traditional inactivated or attenuated vaccines, the HPV vaccine is built on virus-like particles (VLPs) — hollow shells of the L1 major capsid protein that are structurally indistinguishable from the native virion but contain no viral DNA. The dense, repetitive epitope spacing on these VLPs enables cross-linking of B-cell receptors, triggering a qualitatively different humoral response from the outset.[3]

A single dose of VLP-based vaccine is sufficient to drive differentiation into long-lived plasma cells in the bone marrow. These cells provide a persistent, low-level but avid production of neutralising antibodies at the cervical mucosa — the critical site of HPV entry. Although a booster dose reliably elevates peak antibody titres, the sustained plateau achieved after a single dose remains several orders of magnitude above the protective threshold, and above the titres associated with natural immunity following cleared infection.[3] The avidity of this polyclonal antibody response does not increase significantly after boosting, which supports the adequacy of a single immunogenic event.

A landmark nationwide register-based study from the Karolinska Institute, Sweden, published in The BMJ in February 2026, followed over 926,000 girls and women for up to 18 years after quadrivalent HPV vaccination and found no evidence of waning protection throughout the entire follow-up period. Women vaccinated before the age of 17 demonstrated approximately 80% lower risk of invasive cervical cancer — with the risk reduction remaining at 77% even 13–15 years' post-vaccination.[4] Duration of protection is, therefore, not a legitimate concern with HPV VLP vaccines.

CLINICAL EVIDENCE

The policy basis for single-dose scheduling rests on peer-reviewed data from multiple countries and study designs. Two landmark studies are particularly consequential.

The India IARC multicentre prospective cohort study by Basu et al published in The Lancet Oncology, provided early and compelling evidence. Due to the premature suspension of a larger trial, a cohort of Indian girls received only a single dose of the quadrivalent HPV vaccine. After a decade of follow-up, this single dose demonstrated 95.4% efficacy against persistent infections of HPV types 16 and 18 with no evidence of waning immunity.[5] The fact that this evidence was generated in an Indian population makes it directly applicable to program planning.

The KEN SHE trial by Barnabas et al, a randomised, double-blind, placebo-controlled trial published in the New England Journal of Medicine, provided the first prospective, controlled evidence. Among young women in Kenya, a single dose of bivalent or nonavalent HPV vaccine demonstrated 97.5% efficacy against persistent HPV infection at three years of follow-up.[6] Taken together with real-world program data from Sweden, England, Scotland, Denmark, and the Netherlands — all showing sharp declines in cervical precancerous lesions and invasive cancer following population-level HPV vaccination.[4,7]

These findings culminated in the World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) formally recommending a single-dose schedule in April 2022, subsequently incorporated into the WHO HPV Position Paper in December 2022.[8] NTAGI India echoed this conclusion, endorsing a single-dose catch-up approach for adolescent girls aged 9–14 years.[2]

POPULATION LEVEL HEALTH ECONOMICS

In Public health, the efficacy of an intervention must always be weighed against its reach. An intervention that achieves 97% efficacy but covers only 60% of the target population is functionally inferior to one achieving 95% efficacy but reaching 90%. This is the decisive public health argument for single-dose scheduling in India.

Adolescent immunisation programmes in LMICs are vulnerable to dropout. Unlike infant immunisation, which occurs within an established clinical framework, adolescent vaccination requires school-based or outreach mechanisms. In many Indian states, achieving second-dose coverage among adolescent girls has historically resulted in 20–30% dropout, leaving a substantial proportion clinically unprotected.[9] A single-dose schedule eliminates this attrition by definition: every girl reached is a girl fully protected.

The economic evidence reinforces this argument. Modelling by Abbas et al published in The Lancet Oncology, estimated the incremental cost-effectiveness ratio (ICER) of a single-dose strategy in India at approximately US $405 per disability-adjusted life year (DALY) averted — well below India's per-capita GDP threshold for cost-effectiveness.[10] Transitioning to a two-dose schedule would more than quadruple the ICER (exceeding $2,000 per DALY) for negligible additional clinical benefit. Savings from procurement and delivery approximately 50% can be reinvested in expanding catch-up age brackets, strengthening cold-chain infrastructure, and scaling screening services: a comprehensive cervical cancer elimination ecosystem, not merely a vaccination exercise.

BUILDING THE INFRASTRUCTURE FOR ELIMINATION

The primary delivery mechanism employs school-based immunisation camps, which maximise coverage of the target 14-year-old cohort in a structured, time-bounded manner. For out-of-school girls — India's unparalleled frontline health network of accredited social health activists (ASHAs) and auxiliary nurse midwives (ANMs) is mobilised for outreach, leveraging village health sanitation and nutrition days (VHSNDs) as delivery platforms. This dual-channel approach addresses the historically excluded marginalised girls from preventive services.

Digital infrastructure underpins programme accountability. The U-WIN platform developed from the lessons of India's COVID-19 Co-WIN experience enables individual beneficiary registration, longitudinal tracking, and robust adverse events following immunization (AEFI) surveillance. This surveillance capability is not merely administrative; it is essential for detecting rare adverse events in a programme of this scale and for generating the real-world safety data that will inform future policy.

Communication strategy deserves particular attention. Vaccine hesitancy in India has historically been fuelled by the conflation of HPV vaccination with sexual permissiveness. The deliberate decision to frame the HPV vaccine as a "cancer prevention vaccine" — decoupled from its mode of transmission — represents a sophisticated application of health communication science. Evidence from multiple LMIC settings demonstrates that cancer-centred messaging significantly reduces parental hesitancy and improves acceptance among target communities.[9]

ATMANIRBHAR BHARAT: CERVAVAC

The long-term sustainability of India's cervical cancer elimination strategy rests on Cervavac, the indigenously developed quadrivalent HPV vaccine by the Serum Institute of India (SII). While the initial phase of the national program utilises Gardasil (procured through Gavi, the Vaccine Alliance), Cervavac represents both an economic and geopolitical imperative. Once single-dose immunobridging studies in adolescents aged 9–15 years are completed and regulatory approval is obtained, the integration of Cervavac is projected to reduce per-dose costs by an order of magnitude relative to internationally licensed alternatives.[11]

The implications extend beyond India. With a manufacturing capacity projected to scale to 70 million doses of Cervavac annually by the end of 2025,[11] India is positioned to become the primary supplier of affordable single-dose HPV vaccines to the global south, addressing the supply bottleneck that has historically been the binding constraint on cervical cancer elimination in sub-Saharan Africa and South-East Asia. India's programme, in this sense, is not merely a national health intervention it is a global public health contribution.

CHALLENGES AND THE ROAD AHEAD

Vaccine hesitancy driven by misinformation campaigns on social media and operational gaps in cold-chain coverage across remote sub-districts are the main challenges. The pending WHO prequalification of Cervavac currently limits its inclusion in international procurement agency portfolios, restricting its immediate deployment.[11]

Vaccination is only the first pillar of cervical cancer elimination. The WHO 90-70-90 targets — 90% of girls vaccinated by age 15, 70% of women screened with high-performance tests by age 35 and 45, and 90% of women identified with disease receiving treatment[8] — require that India simultaneously scale its screening and treatment infrastructure.

HPV vaccination without concurrent investment in cervical screening is a half-built shield. Integration of visual inspection with acetic acid (VIA), HPV DNA testing, and the "screen-and-treat" approach into primary health care platforms must proceed in parallel.

CONCLUSION

The integration of the HPV vaccine into India's UIP with a single-dose schedule is a policy decision that is simultaneously bold and scientifically sound. It encapsulates a core principle of community medicine: that the optimal strategy is not the one that achieves perfect individual protection for the few, but the one that achieves sufficient, durable protection for the many. Reaching 90% of girls with highly immunogenic single doses is epidemiologically superior to reaching 65% with multi-dose regimens that carry the inherent operational penalties of adolescent dropout. The message is unambiguous: one dose, delivered equitably, can save a generation.

Meenakshi Khapre[1], Anjali Mukkunnoth[2]*

[1]Department of Community Medicine, AIIMS, Rishikesh, Uttarakhand, India
[2]Department of Community Medicine, Kasturba Medical College, Mangalore, Karnataka, India

***Correspondence to**
Dr. Anjali Mukkunnoth,
E-mail: m.anjali@manipal.edu

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