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Human papillomavirus vaccination strategies for accelerating action towards cervical cancer elimination



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Cervical cancer, the fourth leading cause of cancer death among women, was diagnosed in over 600 000 women worldwide in 2020. More than 90% of new cases and deaths occur in low-income and middle-income countries.¹ Together with the pillars of screening and treatment, human papillomavirus (HPV) vaccination presents a transformational opportunity to save lives, making cervical cancer a realistic target for elimination through vaccinating 90% of adolescent girls by 2030.² Although HPV vaccine is in use in 120 countries, first-dose global vaccine coverage by age 15 years among girls stagnated at 20% in 2019, with further backsliding to 15% in 2021.³ Given the urgency of achieving high coverage, the WHO Strategic Advisory Group of Experts on Immunization in April, 2022, highlighted the evidence of comparable efficacy between single-dose and two-dose or three-dose HPV vaccine regimens,⁴ leaving the choice open to countries.

Further strengthening the basis for pragmatic policy decisions, Élodie Bénard and colleagues,⁵ in *The Lancet Global Health*, use elegant transmission-dynamic modelling to assess population-level vaccine effect in cervical cancer case reduction offered by the HPV vaccination extended schedule, by incorporating scenarios derived from four countries in Africa and Asia (Uganda, Nigeria, India, and Viet Nam), using varying parameters of vaccine efficacy, coverage, and duration of protection. To address concerns of breakthrough HPV infections after the first dose and diminished second-dose coverage, the authors expertly provide a framework of equivalence between the two-dose and the extended-dose schedule. In the scenario mitigating the risk of second dose drop-off, the model indicates an unexpected benefit of an all-adolescents catch-up campaign approach irrespective of first-dose receipt. The resultant increased single-dose coverage can potentially translate to greater numbers of cases of cervical cancer averted.

The study⁵ highlights strengths and new considerations. First, it provides actionable results. Building on early predictive explorations of Ronald Ross on malaria prevention through iterations of imperfect mosquito control,⁶ mathematical models of infectious diseases are recognised for producing expeditious

assessment of intervention effect using real-world assumptions without the ethical and cost encumbrances of field work. Caution is to be exercised when formulating policy; the proliferation of mathematical models addressing COVID-19 was instructive in revealing their use and fallacies.⁷ Model-based results have an important role in planning when triangulated against empirical epidemiological evidence from multiple contexts.⁸

Second, few diseases reflect global inequities as deeply as cervical cancer, with the uneven geographical distribution of HPV vaccination further exacerbating outcome disparities. By providing alternative HPV schedules, this model is useful for countries balancing prioritisation of other life-saving vaccine introductions, such as rotavirus vaccine and pneumococcal conjugate vaccine. Harnessing innovation to improve coverage with alternative schedules and new HPV vaccine products manufactured by the Global South can alleviate cost and supply challenges, thus forging a pathway towards addressing vaccine equity.

Third, although there are clear benefits for switching to single-dose schedules or extending the second dose by 3–5 years, programmatic implications merit consideration. Changes in vaccine schedules require resource allocation and revision of vaccination guidelines, vaccine records, and training; actions which require advanced planning that can use model results.

Finally, although the model makes a case for the HPV vaccine extended-dose schedule, the time gained between the ages of 9–14 years and beyond can be used not just for acquiring supplies and awaiting new evidence for single-dose HPV, but can be spent in developing risk reduction activities, addressing vaccine hesitancy, and implementing programmatic improvements in cervical cancer screening and treatment access.

Model robustness could be enhanced by realistic—even pessimistic—assumptions regarding levels of HPV vaccination coverage and expanding coverage to boys. Notwithstanding these caveats, the model as presented lends credence to achieving global targets for vaccine coverage and makes elimination of cervical cancer possible.

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