Commentary

HPV vaccination bridges to HPV screening

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Human papillomavirus (HPV) has more than 140 types that infect human epithelium; of these, 40 infect the genital/oral tract, and 14 are considered oncogenic for mucosal epithelium such as occurs on the cervix, vagina, vulva, anus, penis, and oropharynx. The seven most common cervical HPV infections are types 16, 58, 31, 18, 56, 35, 33 [1]. This order is different for those with cervical cancer: 16, 18, 45, 31, 33, 58, 52, where types 16 and 18 cause about 70% of the cancers [2]. The quadrivalent HPV vaccine protects against HPV 16/18 oncogenic infections.

This final follow up report of the quadrivalent HPV vaccine shows it works long enough to bridge women to the age of screening [3]. This study also shows that the serologic endpoints have much less meaning than the clinical biological endpoints. While this report shows that the quadrivalent HPV vaccine provides complete prevention of HPV 16/18 CIN 2/3 lesions among the women followed for a median of 11.9 years with maximum of 14.0 years from the third vaccine dose, there were still 64 CIN 2/3 lesions and one cervical cancer among 2355 women with one or more HPV types not included in the vaccine, indicating ongoing HPV transmission and carcinogenesis. Accounting for the other five HPV types that could have been covered by the nonavalent vaccine, 27 CIN 2/3 and one cervical cancer still could have occurred [3]. Given these findings, HPV vaccination alone cannot reach the WHO goal of cervical cancer elimination defined as a cancer incidence of 4/100,000 or less.

The risk of HPV infections is lifelong. Lack of vaccine coverage against all oncogenic HPV types over a woman’s lifetime means that cervical cancer control must be a collaborative process between vaccination and screening. Finland was able to move the incidence of cervical cancer by screening alone to 3/100,000 in 1993 [4] but was unable to sustain control because of decreased population participation. Women 30–39 years old actively opted not to screen which led to a fivefold increase in cervical cancer rates than would have been predicted had they screened.

Both HPV vaccination and cervical cancer screening have, to date, been programs that require others “to do” onto the targeted population; and have been programs with economic costs largely borne by society. Consent to receive vaccines has long been a barrier for even the deadliest childhood infections, such as polio; and, while not terribly expensive, without public financial resources, individuals, alone, could likely not pay the full cost of vaccinations. HPV vaccination hesitancy is a world-wide concern, compounded by the constraint that it cannot prevent all cervical cancers. The cost of HPV vaccination to governments and foundations continues to climb, making it the most expensive prophylactic vaccine ever [5]. In fact, its current cost in the US is significantly higher than its cost effective pricing [6] that led to its FDA approval, bringing into question its current cost effectiveness.

This diminished return on vaccine investment is partially balanced, on the other hand, by the simplification in screening procedures that offer women the power to screen themselves. Current cervical cancer screening, in its traditional cytology format and speculum based retrieval, has not been able to penetrate all communities over the past 75 years despite multiple programmatic efforts [7]. Cytology screening was initially a loss leader for pathology labs to gain more lucrative screening and diagnostic referrals within a highly organized environment. Now, screening is a molecular test more than a morphologic impression and can be done either in the office or by the woman.

Cervical cancer screening is most cost effective as primary HPV testing for women 30–65 years every 5 years providing greater health benefits than cytology alone every 3 years [8]. In addition, there have been many studies showing that primary HPV screening can be done by the woman herself adding a dimension of empowerment for cancer control [9], that could also decrease the overall cost. Encouraging both HPV vaccination and screening will continue to take institutional and government resources, but also an active re-alignment to encourage women to control their own cancer screening.

Again, the risk of HPV infection is lifelong. Therefore, both vaccination and screening must be applied across the lifespan. Together primary and secondary preventions are powerful; alone they offer partial solutions. HPV vaccination is an effective prophylactic for blocking future HPV infections. Girls and boys as young as 9 years old can be inoculated, with the opportunity for vaccinations until 45 years of age in some countries. This allows those who did not choose vaccination early to have the option to choose it later in life. Likewise, screening starts as early as 21 years in some countries, extending to 65 or 70 years. While perfect adherence to screening recommendations, although not guaranteeing complete cancer prevention, is a

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public health goal, women drop in and drop out of screening throughout their lives. We know that even a once in a life-time screen between 35 and 45 years provides significant cancer incidence reduction [10].

While organized vaccination and screening programs together can accomplish significant cervical cancer reductions, women must see cervical cancer prevention as within their own power, rather than someone else’s. This may lead to both increased vaccination and screening uptake and downstream cancer prevention.

Declaration of Competing Interest

None

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2020.100435.

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