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Cervical cancer screening and vaccination in India

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Cervical cancer is the most common cancer among women in the less developed countries which account for 80% of the global burden of the disease and over 80% of the global mortality due to cervical cancer. Latin America and the Asia-Pacific region account for about 60% of cervical cancer cases worldwide. An estimated 2,05,496 new cases and 1,19,097 deaths due to cervical cancer will occur in India by 2020, contributing to 29% and 30% respectively of the global burden of cervical cancer cases and mortality (1).

The human papilloma virus (HPV) as a causative agent for cervical cancer was first proposed in the 1970s and was soon shown to be the primary etiology of the disease (2-4). Several studies later established that all cervical cancers were the outcome of a process that was initiated by infections due to a specific group of high-risk human papilloma viruses (5-10).

Randomised controlled studies suggest that VIA (Visual Inspection with Acetic Acid) is an attractive alternative to Pap smear screening (11-13). A recently published report from India indicates that screening women once in their lifetime at the age of 35 with HPV DNA testing reduced the lifetime risk

of cervical cancer by up to 36%, at a cost of less than $500 per life saved (14). Low cost HPV tests that would provide quality results within one working day and would allow for screen-and-treat protocols have been recently tried in China (15). When available, these tests would help reduce the costs of the cervical screening programmes significantly worldwide, making them sustainable even in the less developed countries.

HPV vaccines are certainly a major breakthrough in the primary prevention strategies for cervical cancer and vaccine trials till date have shown very good immunogenicity in HPV-naive girls and have been reported to be generally safe. The currently licensed HPV vaccines – quadrivalent HPV 16, 18, 6, 11(Gardasil(r), Merck & Co., Inc., Whitehouse Station, NJ USA) and bivalent HPV 16, 18 (Cervarix(tm), GlaxoSmithKline Biologicals, Rixensart, Belgium) – contain virus-like particles and are expected to prevent an estimated 70% of cervical cancers. Immunisation of young women with virus-like particles of oncogenic HPV types 16 and 18 has been shown to confer almost 100% protection against infection and disease related to these virus types (16-23).

Vaccine pricing, cost of vaccine delivery to the eligible population, eligible population coverage, long term sustainability and cultural acceptability should be the driving variables in the adoption of any population-based vaccination programme. The HPV vaccines currently available have not been proven to be therapeutic, necessitating the identification of very young pre-pubertal girls who are likely to be HPV naive for vaccination. This is likely to raise cultural and ethical issues. Besides the final proof of vaccine efficacy – reduction in cervical cancer mortality – is yet to be proven and might take another 10-15 years to be conclusively demonstrated.

Reviewing countrywide HPV vaccination strategies in the above context, I would advise a limited number of pilot programmes that study, in depth, vaccine efficacy, safety, acceptability and sustainability in girls of different age groups in a variety of population groups across the country. Such data and the evidence therein, when available in the next four to five years, should form the basis of future national policies on the subject.

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The HPV vaccine demonstration projects: we should wait, watch and learn

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The introduction of newer vaccines into the immunisation programmes in India has been the subject of heated debates in recent years. While a number of concerns have been identified, the often obvious commercial interest of the vaccine manufacturing lobby has been the major point of objection based on which civil society groups have taken their position. Recently there have been many concerns raised about the demonstration projects on HPV vaccines in India (1), ranging from those regarding the vulnerability of researched populations to the cost-effectiveness of the vaccines used in national programmes. While acknowledging the threat of potential commercial interests in shaping vaccine policy decisions, we call for a balanced approach to various research projects on this subject. We shall look at the various concerns raised by others and give our point of view.

A genuine debate is about our health priorities; India has several other health priorities; inclusion of the HPV vaccine in the government programme may not be among the top in the list. Similarly, considering the present low health expenditure by the government of India, some have raised doubts as to how it proposes to meet the cost of this vaccine, even at the negotiated prices, unless this is done by putting other programmes in jeopardy.

We do agree that, given the present health expenditure by central and state governments in India, the cost of introducing the vaccine may not be justified. But we cannot anticipate what will happen a few years down the road when and if the contour of government expenditure expands. One should consider that the present level of health spending by the government of India is abysmally low and this needs urgent correction. More than 25% of the total number of women dying globally due to cervical cancer are from India. This fact should not be far from our minds (2,3). No doubt the cost effectiveness and opportunity costs need to be considered while deciding a health intervention. But we call for much wider considerations while prioritising. In India, marriage and associated initiation into sexual activity are universal. HPV infection occurs in the early phases of initiation of sexual activity but can remain dormant for decades. From the rights perspective on health, as HPV threatens every young girl in the phase of her initial exposure to sexual activity, we need to take this into the calculus of our decisions; we need to find ways of offering universal protection to all young women in the country.

India as a country has regions in different stages of health transition. Even if we consider states to be co-terminous with different stages, each state may want to prioritise differently. Legislatively, health choices for a state are within the purview of the state under the Indian Constitution. We therefore cannot speak for the country as a whole when we talk of prioritisation.

Another debate is about vaccine effectiveness; is it enough to show that the prevention of precancerous lesions by the vaccine is going to prevent cervical cancer? According to the WHO position paper on HPV vaccines, persistent HPV infection may lead to the development of precancerous lesions or severe adenocarcinoma *in situ* which have a high chance of progressing to squamous cell cancer or adenocarcinoma respectively within an average of about 20 years (4). The interventions based on screening and testing for early identification of precancerous lesions and its treatment have already proved their efficacy for prevention of cervical cancer.

Ambiguity also arises as there is no evidence on how many shots of vaccine are required for lifetime protection. Most studies, including those which have estimated cost effectiveness, having assumed three doses of the vaccine along with screening as sufficient to prevent lifetime occurrence of cancer of the cervix, showed an effective reduction of 63% of the lifetime risk (2). The quadrivalent vaccine was found to offer significant protection against HPV-16 or HPV-18 after follow-up for three years following the initial dose (5). There is definitely a need for long-term follow-up in order to determine the duration of actual protection, if possible.