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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.

It may not be wrong to argue that any new vaccine introduced without creating a demand among the population may have poor coverage. This is true of the other vaccine that target women, that is tetanus toxide given to women in the antenatal period which has a coverage of about 75%(6). Thus poor coverage with the HPV vaccine may defeat its purpose which is protection of a significant number of needy women. This is also a strong possibility. We do hope that vaccine preparedness studies and many other studies examining the logistics of service delivery and the health system's requirements are undertaken in addition to the clinical trials to test efficacy and safety of the vaccines before we even consider the option of making the HPV vaccine available through the immunisation programme in the country.

Another major area of contention concerns the present research on Indian (less educated rural) populations which is projected as unethical. It is true that populations in India in general and women in particular are vulnerable to unethical research. But this is also the population that is most vulnerable to HPV and cervical cancers. As has already been mentioned, more than 25% of all women dying globally due to cervical cancer are from India (3). The most dominant types of HPV – namely HPV 16 and 18 - are responsible for 70% of the cervical cancers found globally (5). Within Asia, HPV types 16 and 18 account for about 67% of all HPV infections (7). This seems sufficient reason to initiate studies in India. The results of such studies should be used to benefit these populations and others like them. As civil society players, should not researchers and activists within this country work with research groups to ensure that the trial is not unethical and does not exploit vulnerable women?

Experts have pointed to the difficulty in creating acceptability for the vaccine as it is going to generate several debates situated in moral and cultural contexts. This is very true given the manner in which many health debates tend to get politicised and polarise populations (8) It has also been found that compulsory vaccination recommendations for prophylactic vaccines tend to be opposed for a range of reasons based on philosophical, political, scientific and ideological grounds (9). Therefore, undertaking well crafted and scientific studies on the way to deliver such vaccines and the implications for the health system that gears to deliver it is extremely important. This, according to PATH's summary sheet on the cervical cancer vaccine project, is the objective of the demonstration project being undertaken in India and three other countries, Peru, Uganda and Vietnam (10) Should we not then wait for the results of these studies and evaluation of the demonstration projects both within India and elsewhere in order to strengthen the debate?

Finally, we need to address the issue of the vaccine option itself, when screening alone may, in theory, reduce incidence significantly (11). Many screening programmes have failed to deliver significant reductions in cervical cancer incidence or associated mortality. It is now acknowledged that the best prevention strategy includes both vaccination of adolescents before initiation of sexual activity and screening for surrogate markers of cervical cancer – such as precancerous lesions – and treating them.

The WHO position paper states: "WHO recognizes the importance of cervical cancer and other HPV-related diseases as global public health problems and recommends that routine HPV vaccination should be included in national immunization programmes, provided that: prevention of cervical cancer or other HPV-related diseases, or both, constitutes a public health priority; vaccine introduction is programmatically feasible; sustainable financing can be secured; and the cost effectiveness of vaccination strategies in the country or region is considered." (4)

The first of the recommendations is open to debate. Should a condition that disables 5,00,000 and kills 260,000 women globally every year (4) not be prevented by all means possible? But in order to decide on the second and third criteria recommended by the WHO, we need sound scientific studies that examine the required health system preparedness and costs involved in delivering the vaccine and the screening programmes to women in poor rural settings. If this has to happen we need to de-link our concerns emerging out of potential commercial exploitation of vaccine lobbies with that of our analysis of potential benefit of health interventions. After all, in India we do have options such as compulsory licensing to be used in the face of a public health emergency, (12), and indeed countries such as Thailand, Indonesia, Malaysia, Mozambique, Zambia and Brazil have should the various options available to enhance access(13).

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