

Row erupts over study of HPV vaccine in 23 000 girls in India

Ganapati Mudur

New Delhi

A study in India in which girls were being vaccinated against the human papillomavirus (HPV), which had previously attracted criticism on ethical grounds, had no justification on the grounds of public health either, a team of health researchers in the United Kingdom has said.

The researchers, from the University of London and the University of Edinburgh, said in a review of the study that India's surveillance system for cancer and its information on the incidence of cervical cancer in the country were too patchy to justify any further roll out of the vaccine.¹

But the organisers of the study countered their criticisms by saying that the researchers had "seriously misunderstood or misrepresented" the data from the Indian cancer registry, and had belittled the threat from cervical cancer in India, despite the fact that deaths from the disease outnumbered maternal deaths. They also said that the study was completely ethical.

Two years ago, women's groups and health activists in India had questioned the ethics and the rationale of the study, in which more than 23 000 girls aged 10-14 years in Andhra Pradesh and Gujarat were vaccinated against the human papillomavirus.²

The study, by the international non-profit making Programme for Appropriate Technologies in Health (PATH), based in Seattle, Washington state, was approved by the Indian Council of Medical Research and implemented by state health authorities using vaccines donated by two manufacturers.

India's health ministry stopped the study amid allegations of irregularities and asked a panel of doctors to investigate the claims. Last year the panel confirmed that certain problems, including violations of rules governing informed consent, had emerged during the implementation of the study. This report is not yet in the public domain.

"India seems to have jumped into this study without examining whether there is a real need for it and whether the country has a surveillance system to measure the protective efficacy of the vaccine across the population," said Allyson Pollock, professor of public health research at Queen Mary, University of London, and one of the review's authors.

Pollock and her colleagues have used data from India's National Cancer Registry to point out that the incidence of cervical cancer in India has decreased from 42.3 per 100 000 women in 1983 to 22.3 per 100 000 women in 2005. The highest age adjusted mortality rate from cervical cancer in India, at 7.7 per 100 000, is lower than the death rate of 283 per 100 000 women from

diabetes and cardiovascular disease and 26 per 100 000 from tuberculosis.

"From a public health perspective, a roll out of the vaccine against the human papillomavirus seems totally irrational," Pollock told the *BMJ*. "The Indian government must first determine whether it works, whether it is needed, and whether it is a health priority."

A spokesperson for the Programme for Appropriate Technologies said that Pollock and her colleagues, who are not cancer specialists, have "seriously misunderstood or misrepresented" the cancer registry data from India. "They simultaneously make a bold claim that cervical cancer rates in India are declining based on the very same registry data that they describe as incomplete and unrepresentative," the programme official said.

"They also ignore the warning [in a study from India] that low rates in registries are most often due to significant under reporting, especially of deaths," the official said, adding that the authors have not acknowledged that the decline in the rates of cervical cancer they cite applied primarily to urban areas, and was not reflected in a rural registry in the pooled estimate. Experts from the World Health Organization's International Agency for Research on Cancer estimate that more than 130 000 Indian women develop cervical cancer each year—far more cases than any other country in the world even though there may be countries with higher rates, he continued.

The national cancer registry programme has projected that the number will climb by about 20% by 2020 due to population growth and ageing. The nearly 73 000 annual cervical cancer deaths that WHO estimates for India already surpass Indian maternal deaths estimated at 56 000, the spokesperson said.

"We believe that by following the guidance provided by India's highest medical research authority, two state governments, and three ethical review committees, we designed a project that reflected the country's existing regulatory standards and would provide the greatest benefit to Indian women," the spokesperson continued. The organisation had never called for the "general roll out of HPV vaccination either in India or in the two states where the research was done."

"While we certainly agree that it would be good to have better cancer registry data in India and in many other countries, it seems counterproductive to say that we should not save lives using new, proven medical advances until we have universal healthcare and integrated healthcare systems," as called for by

the authors. That would be an example of the ideal being an enemy of the real, or possible,” the spokesperson concluded.

Opponents of the vaccination programme include health activists and women’s groups, who had questioned the choice of a vulnerable population—rural or tribal girls, many living in hostels away from their parents—for the vaccine study. They had also complained to the health ministry that pamphlets handed to girls or parents contained misleading claims and that appropriate informed consent procedures had been violated. The health ministry’s investigative panel had also found that the study lacked procedures to monitor vaccine recipients for adverse events.

Anjali Sheno, a project coordinator with Sama, a women’s health group that has been tracking the ethics of clinical trials in India, said, “There has been no visible follow-up action since the panel submitted its report to the government confirming the ethical irregularities we had pointed out. There has been no attempt to pinpoint responsibilities for the ethical irregularities.”

Indian health officials say the study has provided “a learning experience” that will help improve future research protocols. Vishwa Mohan Katoch, currently the director general of the Indian Council of Medical Research but who was not in this

position when the study was approved, said, “We believe there was no intentional wrongdoing.”

Katoch told the *BMJ* that the study was not aimed at evaluating the protective efficacy of the vaccine against cervical cancer. “Its primary objective was to assess public acceptability of the vaccine and to assess the logistics of delivering this vaccine through the public health machinery,” he said.

The vaccine has been available in India through private medical practitioners since October 2008.

Elizabeth Vallikad, a professor and head of gynaecological oncology at the St John’s Medical College Hospital, Bangalore, said, “Cervical cancer prevention in India will have to depend on health education and visual inspection. It is labour intensive but inexpensive, and it’s the only public health intervention we can afford at the moment.”

- 1 Mattheij I, Pollock AM, Brhlikova P. Do cervical cancer data justify HPV vaccination in India? Epidemiological data sources and comprehensiveness. *J R Soc Med* 2012; 105:250-62, doi:10.1258/jrsm.2012.110343.
- 2 Mudur G. Human papillomavirus vaccine project stirs controversy in India. *BMJ* 2010;340:c1775.

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