Cervical cancer prevention should focus on vaccinating adolescent girls

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The cost-effectiveness of vaccination in the United States against human papillomavirus (HPV), a sexually-transmitted virus that causes cervical cancer, will be optimized by achieving universal vaccine coverage in young adolescent girls, by targeting initial "catch-up" efforts to vaccinate women younger than 21 years of age, and by revising current screening policies, according to an analysis by Harvard School of Public Health (HSPH) researchers in the August 21, 2008 issue of *The New England Journal of Medicine.*

In the U.S. in 2007, cervical cancer developed in more than 11,000 women and killed 3,600 women. Cervical cancer is caused by infection with high-risk "oncogenic" types of HPV, also associated with other cancers. Worldwide, HPV types 16 (HPV-16) and 18 (HPV-18) cause approximately 70% of cervical cancer cases. Vaccines against HPV-16 and HPV-18 appear to be highly efficacious in preventing HPV-16 and HPV-18 infections and cervical disease in females who have not previously been infected with these types. The quadrivalent vaccine currently licensed in the U.S. also prevents low-risk HPV types 6 and 11 (HPV-6 and HPV-11) infections, which are responsible for most genital warts and juvenile-onset recurrent respiratory papillomatosis (JORRP), a rare but severe respiratory condition usually diagnosed in infancy that may be related to a mother's infection with genital warts.

Cervical cancer prevention in the U.S. has traditionally relied on a screening program involving frequent cytology (Pap smear) and/or HPV DNA testing, recommended annually or biennially for sexually-active

women. HPV vaccination raises questions regarding the age at which to vaccinate females, target groups for temporary catch-up programs, and appropriate changes to screening practices.

Jane Kim, assistant professor of health decision science in the Department of Health Policy and Management at HSPH, led the study which involved synthesizing epidemiologic, clinical, and demographic information using sophisticated computer-models that simulate the U.S. population. The models were used to predict the health and economic outcomes of HPV vaccination of preadolescent girls (i.e., 12 years of age) and catch-up vaccination over a 5-year period for girls and women over 12 years of age, in the context of routine cervical cancer screening; strategies differed in the upper age of catch-up programs, to ages 18, 21, or 26 years. While the study focused on the prevention of cervical disease, the investigators also examined the benefits of the quadrivalent vaccine on genital warts and possible benefits of averting other HPV-related cancers and JORRP.

A novel part of this study involved examining how uncertain scenarios might impact the appropriate policies for the U.S., such as the duration of vaccine protection and whether or not a booster dose will be needed, whether or not the vaccine will also prevent infections with other HPV types, and what might occur to rates of cancer if women change their screening practices after being vaccinated.

Kim and co-author Sue Goldie, professor of health decision science at HSPH, found that vaccination against HPV-16 and HPV-18 would lead to lower cervical cancer rates and be economically attractive if high coverage can be achieved in the most important target group of 12-year-old girls, and if vaccine protection against infection lasted for at least 20 years. The study predicted that if most 12-year-old girls were vaccinated, their future cervical cancer screening could begin somewhat later than currently recommended and be conducted less frequently (i.e., every 3 to

5 years).

At an additional expense, a catch-up program for girls between 13 and 18 years of age appears to offer benefits and be reasonably cost-effective compared to other vaccine programs in the U.S. The cost-effectiveness of extending the catch-up program to 21 years of age is less certain, and depends on whether the vaccine will eventually be proven to prevent other cancers caused by HPV-16 and -18. Including women to age 26 was consistently not cost-effective because the vaccine is quite expensive, but is less effective in women who are already sexually active. Current CDC recommendations and a recent CDC summary suggest routine vaccination of girls aged 11-12 and catch-up vaccination of girls and women aged 13 to 26.

There is no absolute criterion that dictates whether a vaccine or public health intervention is cost-effective in the U.S.; however, most policy-makers agree that interventions that have a cost-effectiveness ratio less than $50,000 per quality-adjusted life year (QALY) gained, a metric used to describe cost-effectiveness, are very good value for money. While vaccination of 12-year-old girls was less than this threshold, vaccinating girls into their mid- to late-20s as part of a catch-up program was not.

Kim and Goldie caution that these results could change if future information shows that vaccine protection does not last, or if there is an unexpected increase in other cancer-causing HPV types not included in the vaccine.

Kim emphasizes, "Our results are the best prediction we can make with the information available now, but it will be critical to update the analysis as we learn more about the long-term vaccine effects."

An editorial, Human Papillomavirus Vaccination – Reasons for Caution,

by Charlotte J. Haug, MD., PhD. Editor in Chief of the Journal of the Norwegian Medical Association, also appears in this issue of NEJM. A long-term followup study of HPV vaccination is underway in Norway.

Kim and Goldie also emphasize that it will be important to achieve high coverage among all 12-year-old girls, and not just a small subset, and to ensure girls are screened for cervical cancer beginning in their early- to mid-20s, since HPV types not included in the vaccine can still cause cancer. From a public health perspective, if women who are at continued risk for HPV infection and cervical cancer are not regularly screened, and if only some adolescents have access to the vaccine, cervical cancer rates in the U.S. may not change. Ensuring U.S. women equal access to both preadolescent vaccination and adult cervical cancer screening, is imperative.

Source: Harvard School of Public Health