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Editorials

Should HPV vaccine be given to men?

The best investment is to vaccinate preadolescent females, not males

On 9 September 2009, a US Food and Drug Administration (FDA) advisory panel recommended that the FDA approve Gardasil (Merck)—the quadrivalent human papillomavirus (HPV) vaccine against HPV types 6, 11, 16, and 18—for use in males aged 9-26 years to prevent genital warts (condyloma acuminata). The vaccine was 90% effective in preventing genital warts and reducing the incidence of persistent HPV 6 and HPV 11 anogenital infections¹—which cause about 90% of genital warts in HPV naive males—and 79% effective at reducing of the incidence of persistent anogenital HPV 16 infections and 96% of HPV 18 infections. Therefore, carriage in the male population of the two HPV genotypes that cause 70% of cervical cancer worldwide in women could be greatly reduced by widespread HPV vaccination. The question is should men be vaccinated?

In the linked study (doi:10.1136/bmj.b3884), Kim and Goldie report an independent analysis of the cost effectiveness of male HPV vaccination in the United States.² They found that only under the most favorable assumptions for the benefits of adding male HPV vaccination to female vaccination did the cost per quality adjusted life year (QALY) fall below \$100 000 (£62 700; €68 400) per QALY, the threshold below which an intervention is considered a good economic investment. Under no scenario (such as reduced coverage of HPV vaccination in 12 year old girls) did including males in HPV vaccination programmes fall below \$50 000 per QALY, perhaps a more fiscally responsible threshold given the need to lower healthcare costs and increase efficiency. By comparison, HPV vaccination of 12 year old girls was always a good health investment.

Kim and Goldie's findings concur with those reported in Austria,³ although they differ substantially from an analysis conducted by Merck.⁴ This may be because Kim and Goldie's analysis included "recent data on efficacy against vaccine type infection and diseases in males," and because of the higher than anticipated sensitivity of cytology for detecting cervical intraepithelial neoplasia types 1-3.

As acknowledged by the authors,² the models used to generate cost effectiveness projections have limitations imposed by uncertainties about the course of HPV related diseases. They also did not explicitly simulate (or include) men who have sex with men, who face a higher risk of anal cancer and may benefit more from the vaccine than other men. Conversely, some of the assumptions regarding the benefits of HPV

vaccine may have been too generous. Nevertheless, the relative benefits of HPV vaccination of females compared with vaccination of both sexes is unlikely to differ greatly with fine tuning of the models, and the health economic implications are clear—good coverage of females obviates the need to vaccinate boys.

However, in the exceptional situation in which the uptake of HPV vaccination is poor in females, male HPV vaccination may become better value by improving herd immunity. Since the FDA approval of Gardasil in June 2006, HPV vaccination coverage of at least one vaccine dose in 13-17 year old girls has steadily increased from 25% in 2007 to 37% in 2008.^{5 6} However, only 18% of 13-17 year olds had received all three doses in 2008; the protection and durability of receiving fewer than three doses is not yet known.

Kim and Goldie did not explore the effect of age at vaccination but focused on age 12, an age at which most adolescents in the US are not yet sexually active, so that vaccination at that age would provide the greatest protection against incident HPV infection.⁷ However, uptake of all three doses is lower in younger girls—15% in 13 year olds and 21% in 17 year olds.⁶ If coverage in females does not increase substantially, it may be reasonable to consider male HPV vaccination, provided that it is cost effective at similarly low coverage in males, which remains to be determined.

Advocacy for male HPV vaccination is also made on ethical grounds—to promote equality and social responsibility in both sexes.⁸ However, consistent use of condoms can partially protect against HPV⁹ and provide cheap protection against all sexually transmitted infections, including HIV, as well as unwanted pregnancy. Vaginally applied microbicides are another promising way of preventing HPV infections and other sexually transmitted diseases.^{10 11}

A far greater social inequity exists, however—more than 80% of the 500 000 annual cases of cervical cancer occur in low resource settings and developing countries, which cannot afford or access HPV vaccines. Targeting young women in these populations for HPV vaccination and screening older women would have a bigger effect on reducing the burden of cervical cancer than widespread HPV vaccination of young men from resource rich areas.¹²

In the face of skyrocketing healthcare costs in the US, any preventive intervention must be safe and cost effective. Widespread inclusion of males in any HPV vaccination programme should be weighed against other unmet health needs. Kim and Goldie found that adding male HPV vaccination to female vaccination is only borderline cost effective under the best of circumstances.⁴ Increasing coverage in males is unlikely to be more cost effective than increasing coverage in females whatever the circumstances. And, as shown, the better the coverage in females the less cost effective it becomes to add males to the vaccination programme. The best policy is to ensure that preadolescent females are vaccinated worldwide.

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