Michels and zur Hausen misquote Elbasha and colleagues[4] as saying that inclusion of men in HPV vaccination programmes is "the most cost-effective approach". Even the models in that paper indicate that vaccinating men, at significant additional cost, would produce only a modest gain in quality-adjusted life-years. This was the *least* cost-effective strategy. Furthermore, a systematic review[5] of economic models concluded that: "Studies had a consistent message... a male and female [HPV] vaccination programme is generally not cost effective compared with female-only vaccination."

Given the challenges that developing countries face, available resources should focus on the most effective, efficient, and affordable immunisation intervention: vaccinating girls before sexual debut.

We declare that we have no conflicts of interest.

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Karin Michels and Harald zur Hausen[1] discuss the results of the adjuvanted human papillomavirus (HPV) vaccine trial by J Paavonen and colleagues[2] and conclude that men and boys, as well as women and girls, should be vaccinated. Although the study findings bode well for both eventual effectiveness in select populations and broader-spectrum protection, the report suggests that vaccination of women with previous HPV 16 or 18 infection might actually increase their risk of high-grade cervical disease—an observation strikingly consistent with reports on the quadrivalent HPV vaccine.[3]

Although each trial's finding was attributed to imbalances in the baseline characteristics of the vaccine and placebo groups, the biological phenomenon of antibody-dependent enhancement of disease should be considered.[4,5] These clinical trials include thousands of vaccinees previously exposed to HPV 16 or 18; those women could be studied further with appropriate comparison groups. Cross-protection data in Paavonen and colleagues' study[2] suggest that such investigations should include women with baseline HPV 31, 33, or 45.

What if HPV vaccination were contraindicated for women and girls previously infected? It might be argued that, in ideal settings, increased disease risk in a minority of vaccinees would be managed by the safety net of continued cervical cancer screening. Or perhaps HPV testing could precede vaccination. For developing nations, where a vaccine is most needed, such logic disintegrates. Furthermore, restricting vaccinations to prepubescent girls might be particularly prudent in the developing world. Young or old, a woman's previous infection risk can be difficult to ascertain, particularly in cases of unacknowledged rape or other sexual molestation.

Although the global eradication of HPV infection is a noble goal, we currently have neither sufficient evidence nor the requisite understanding of the immunology of HPV infection to suggest HPV vaccination for all.[1]

I have received funding for unrelated (viral hepatitis) contractual research from GlaxoSmithKline and from Merck.

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Authors' reply

Unlike Vivien Tsu and Scott Wittet, we are indeed convinced that life-long immunity after human papillomavirus (HPV) vaccination is unlikely and question the relevance of mathematical models based on hepatitis B vaccination. Results from long-term follow-up are not yet available, and it remains to be seen whether a quadrivalent or bivalent HPV vaccine will elicit a response similar to that produced by a monovalent hepatitis B vaccine. Additionally, it is very likely that the observed weak cross-reactivity with types 31, 33, and 45 will require a booster injection after 10–15 years, given the current vaccination protocol.

We disagree with Tsu and Wittet's contention that cervical cancer is a public health problem but that HPV infections are not. It would be short-sighted to disregard the large number of cervical lesions that develop after infections with high-risk HPV types requiring surgical interventions. Since cervical cancer is caused by HPV infections, the most effective strategy to prevent this cancer, its precursor lesions, and the associated pain and suffering is the prevention of infection.

Elbasha and colleagues[1] found that inclusion of men and boys in the vaccination programme was more effective than inclusion of only girls