

*Point/Counterpoint***Human Papillomavirus Vaccination Should Be Offered to Young Males: Counterpoint**

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The science of the newly approved prophylactic human papillomavirus (HPV) vaccines is clear: vaccination of young women prevents genital type-specific infection with HPV 16 and 18, thereby preventing the development of CIN2/3, the lesion that precedes cervical cancer. Although there exist several methods for screening for cervical cancer and effective treatments for early-stage disease, this cancer remains the second leading cause of cancer death in women worldwide. One might be tempted to conclude that all young people should have access to prophylactic HPV vaccine, a valuable good. However, in this imperfect world, even in a high resource setting such as the United States, the metrics governing this allocation are not scientific. They are not epidemiologic; rather, the ethical variables are defined by economics. What is just is dictated by what is possible.

In women, protection from HPV infection correlates with levels of neutralizing antibodies to virus-like particles, which in turn correlates with vaccination. Studies are ongoing now to determine whether young men, when vaccinated, generate similar levels of neutralizing antibodies. However, because a quantifiable clinical endpoint is more difficult to define in males than in females, that is, genital HPV infection, for the near future, it will be difficult to define efficacy of vaccination in males. Using models that incorporate continuous variables taking into effect a broad range of assumptions about percentage of cohort vaccinated, duration of protective effect, sexual behaviors, and gender, female-only vaccination strategies all, in the end, have less effect on herd immunity than population-based strategies. Female vaccination strategies have more effect on incidence of cervical cancer and its precursors than vaccinating males. In any model, although vaccinating both genders is more effective in preventing disease than vaccinating females alone, the increase in benefit is incremental.

The definition of value added is not ethical but is economic. In the United States, the burden of cervical disease is relatively low compared with low resource

settings, because we enjoy an expensive and cumbersome, but established, funded infrastructure for screening. Annual costs for treating cervical dysplasia exceed \$1.5 billion. Cytologic screening costs an additional \$2 billion. To sustain health, defined by low rates of disease, it will be necessary to maintain screening for disease for decades into the era of vaccination. For many reasons, the prophylactic HPV vaccines are the most expensive vaccines in the world. The three-vaccination administration schedule is not easy to achieve even in motivated cohorts with logistic and financial resources. The greatest concern is that the barriers to getting vaccinated, in the end, are very similar to the barriers to getting screened and treated for disease and that, therefore, even in a wealthy country, "availability" of vaccine may not translate into a significant reduction in cervical disease.

Our society values choice; we are a nation founded on the premise that the pursuit of the determination of the individual is a right. It is our greatest privilege and our greatest liability. Historically, mandates, even those having to do with consequences that affect public health, have been achieved as the result of enormous, coordinated effort on the part of committed scientists and policy makers and the endorsement of the people. Happily, several of our best medical successes have been in the field of prophylactic vaccination, including polio, smallpox, and rubella.

Whether or not to make prophylactic HPV vaccines available to young males is not the real issue. Sure, make it available. Whoever can pay for it will obtain it. The Vaccines for Children resource will obtain vaccines for a limited cohort of children at the bottom of the economic spectrum, children of families with resources will obtain vaccine if their families choose, and the children in between will fall into a doughnut hole for children.

The issue is not whether to offer vaccine. If we make it "mandatory," on the other hand, even with "opt-out," that implies responsibility for making safe vaccines available. How will we pay?