

HPV Vaccine Mandates: Just Say 'No' to the "Great Big Public Health Experiment"

by Robert F. Onder, MD, JD

For numerous reasons mandating HPV vaccination as a condition of school enrollment would be poor policy and bad science.



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Abstract

While many states are seriously considering requiring vaccination of pre-teen girls as a condition of middle school admission, the case for mandatory human papillomavirus (HPV) vaccine is very weak. Such a requirement lacks the traditional justification for vaccine mandates and therefore represents an unjustified usurpation of parental authority. Moreover, serious questions remain as to whether the vaccine is effective in preventing cervical cancer. The vaccine is the most expensive pediatric vaccine in history. Given the uncertainties surrounding the vaccine, Missouri lawmakers and taxpayers should reject this expensive and intrusive "public health experiment."

Introduction

The subject of human papillomavirus (HPV) and HPV vaccination mandates is both timely and important. See "HPV Infection in Adolescent and Young Women" by Melissa Lawson, MD, on page 38. Given the causal relationship between HPV infection and cervical cancer, it is understandable that the introduction of a vaccine against a few strains of HPV would be greeted with

enthusiasm. It is another question, however, whether such a vaccine should be mandated by state law as a condition of school admission.

In 2007 legislators in over 20 states considered making mandatory Merck & Co.'s Gardasil[®] vaccination. The Governor of Texas ignited a firestorm of protest when he sought to impose an HPV mandate by executive order.¹ In Missouri, a bill was filed that would have required HPV vaccination as a condition of girls entering the 6th grade.² All of this legislative activity was engendered at least in part by an unprecedented marketing campaign by the manufacturer of the vaccine, targeting not physicians and patients but—inappropriately—state legislators and policy makers.³

This article will argue that an HPV mandate would be poor public policy. In doing so it will first look at the data supporting the use of the vaccine in general and contends that significant doubt remains as to whether the vaccine will really prevent cervical cancer. Second, this article will look at the issue of the cost of the vaccine, particularly in light of the relative rarity of cervical cancer and the availability of effective screening tests for precancerous lesions. Third, this article will look at the policy of mandating such a vaccine and show how traditional



The American Cancer Society does not recommend universal vaccination,¹⁸ and the American Academy of Family Practice stated that it is “premature to consider school entry mandates for human papillomavirus vaccine (HPV) vaccine until such time as the long term safety with widespread use, stability of supply, and economic issues have been clarified.”¹⁹

Read more on HPV infection by Melissa Lawson, MD, on page 42.

defenses of vaccine mandates do not apply in the context of HPV vaccination. For numerous reasons mandating HPV vaccination as a condition of school enrollment would be poor policy and bad science.

How Good is the HPV Vaccine?

Merck’s website, www.gardasil.com, dramatically proclaims its product to be “the only cervical cancer vaccine,” and promises, “Your daughter could become one less life affected by cervical cancer.”⁴ The promotional materials further assert that HPV types 16 and 18, which are covered by Gardasil, cause 70% of cases of cervical cancer. The implication is that Gardasil will lower a woman’s risk of cervical cancer by 70%. What is the actual level of risk reduction? Clearly, the lower the efficacy of the vaccine, the weaker the case for mandatory vaccination.

The widely quoted statement that HPV 16 and 18 cause 70% of cases of cervical cancer is based on a handful of epidemiological studies published between 1995 and 2000.^{5, 6} In these studies conducted in women with cervical

cancer, a high percentage of patients were infected with HPV 16 or 18. This statistic, however, cannot be directly translated into a 70% reduction in the risk of cervical cancer for girls or women who receive the vaccine.

The 70% figure is misleading because it is based on viral types present in women with cervical cancer. The average age of diagnosis of women with cervical cancer is between 50 and 55 years. As with many other cancers, such as colon cancer, there is a long period of latency between early precancerous lesions and development of invasive cancer. In the case of cervical cancer, this period is estimated at up to 15 years. In addition, there is a period of latency between HPV infection and the development of precancerous lesions. The problem with quoting the 70% figure is that it represents the viruses that were prevalent internationally a decade or two ago. While some viruses such as smallpox and polio remain stable over time, we know that many viruses mutate readily, and different viral types are prevalent from year to year. An example would be influenza; formulating a vaccine each year requires choosing the viral types that are predicted to be most prevalent that

influenza season. Is HPV more like polio virus or more like influenza? The answer is probably somewhere in between, accounting for the relatively poor protection of HPV vaccine.

To get a better idea of the possible efficacy of HPV vaccination in preventing cervical cancer, one must take a closer look at the data. The pivotal data regarding the efficacy of Merck’s Gardasil vaccine comes from two vaccine trials, called Females United to Unilaterally Reduce Endo/Ectocervical Disease (FUTURE) I and II. In these trials, what is the efficacy of vaccination? In the FUTURE I trial,⁷ without regard to HPV strain, rates of precancerous lesions or adenocarcinoma in situ per 100 person-years were 4.7 in vaccinated women and 5.9 in unvaccinated women. Analyses by lesion type indicate that this reduction was largely attributable to a lower rate of grade 1 cervical intraepithelial neoplasia (CIN); no efficacy was demonstrable for higher grade disease.^{7, 8} Given that CIN 1 is not considered precancerous and treatment is not recommended,⁹ this might be considered a negative trial.

In the larger FUTURE II trial,¹⁰ rates of grade 2 or 3 CIN or

adenocarcinoma in situ were 1.3 in vaccinated women and 1.5 in unvaccinated women, an efficacy of 17%. In analyses by lesion subtype, the efficacy was significant only for grade 2 CIN; no efficacy was demonstrable for grade 3 CIN or adenocarcinoma in situ.^{8, 10} Reviewers in the same issue of the *New England Journal of Medicine* made note of the “modest efficacy of the vaccine.”⁸ One of these reviewers subsequently told the *San Francisco Chronicle* that she considered an HPV vaccine mandate “extremely premature.”¹¹

The reason for the poor efficacy of HPV vaccination lies in the fact that there are more than 30 oncogenic types of HPV.¹² An assessment of the potential efficacy of a vaccine directed at HPV type 16 and 18 requires knowing what types of HPV are prevalent in the population of at-risk women today. The National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC) used a representative sample of U.S. females aged 14 to 59 years and measured HPV prevalence by polymerase chain reaction.¹³ NHANES found overall HPV prevalence to be high, 26.8%, with the highest prevalence among women 20 to 24 years old. The prevalence of vaccine types of HPV, types 16 and 18, was very low, 1.5% for HPV-16 and 0.8% for HPV-18. Extrapolating these data to the potential efficacy of an HPV vaccine mandate, such a mandate would have the potential to reduce cervical cancer a decade or two from now, not by 70% but by 2.3%. In another recent U.S. epidemiologic study, 6% of women were infected with HPV-16 and 2% with HPV-18.¹⁴

Dr. Eileen Dunne, the lead author of the NHANES study, made note of the “complex natural history” of HPV and recommended, not a vaccine mandate for schoolchildren, but that women continue “routine screening with Pap tests, and appropriate groups of women

receive the preventive vaccine that’s now available.”¹⁵

Another concern with vaccine mandates is that the duration of immunity conferred by HPV vaccination has not been documented, so it is impossible to infer that vaccinating 11 or 12 year-old girls will prevent an infection that is generally acquired in women’s late teens or twenties. In fact, trials of Gardasil did not look at vaccine efficacy in this age group at all; girls age 9 to 15 were merely vaccinated and evaluated for antibody responses.¹⁶ Clearly more data are needed about the long term safety and efficacy of this vaccine before considering a mandate for this age group.

It is true that the Centers for Disease Control and Prevention have recommended that girls and women between ages of 11 and 26 years receive the HPV vaccine.¹⁷ On the other hand, the American Cancer Society does not recommend universal vaccination,¹⁸ and the American Academy of Family Practice stated that it is “premature to consider school entry mandates for human papillomavirus vaccine (HPV) vaccine until such time as the long term safety with widespread use, stability of supply, and economic issues have been clarified.”¹⁹

In summary, although enthusiasm for a new vaccine is understandable, the efficacy of HPV vaccine in reducing cervical cancer may be far lower than hoped. The less effective the product, the weaker the case for mandatory immunization.

Costs and Risks in Perspective

What would a universal school entry HPV vaccination mandate cost? Gardasil is the most expensive pediatric vaccine ever approved by the FDA. The American Academy of Family Practice estimates that it would cost approximately \$900 million per year to provide coverage for the female birth

cohort (2 million girls; \$120 per dose plus \$25 administration fee; three doses).¹⁹ The Academy’s concern that this would “place a significant burden on state public health budgets” played a part in its recommendation that the vaccine not be mandated.¹⁹

The possible benefits of widespread HPV vaccination should also be considered in light of the fact that in the United States cervical cancer is a relatively rare disease. Invasive cervical cancer was diagnosed in 9,710 women in 2006 and approximately 3,700 died of the disease.²⁰ Many of these cases could be prevented with regular screening. In contrast, 350,000 women died of heart disease, 70,000 died of lung cancer, and 40,000 died of breast cancer.^{20, 21} And while the efficacy of HPV vaccination in preventing cervical cancer remains speculative, 36,000 women die each year of influenza, which is up to 50 to 70% preventable by vaccination.²¹ Might not scarce health care resources be better spent on other diseases or on cervical cancer screening, which has proven effective, rather than on compelled vaccination with an unproven product?

Mandates and Public Policy

Apart from the practical questions of the costs and possible benefits of HPV vaccination, the question remains whether the state should compel parents to vaccinate their eleven or twelve year-old daughters as a condition of school attendance. What is the rationale for the state compelling vaccinations? The usual rationale is that diseases such as measles, smallpox, polio, rubella, and pertussis are highly contagious, usually through the air or by casual contact, and are life-threatening to those who contract them. So if one child is not vaccinated and has measles, he is a public health threat to other children. This of

course is not the case with HPV, which is transmitted only by sexual contact.

The historical justification for compulsory vaccination was enunciated by the United States Supreme Court in *Jacobson v. Commonwealth of Massachusetts* in 1905.²² This case involved a requirement that children be vaccinated against smallpox prior to school admission. The Court upheld the law because “upon the principle of self-defense, of paramount necessity, a community has a right to protect itself against an epidemic” of “dangerous and contagious disease.” As Dr. Robert Zavoski told the *Hartford Courant*, “Vaccines previously mandated for universal use are those which protect the public’s health against agents easily communicated, responsible for epidemics, or causing significant morbidity or mortality among those passively exposed to the illness. HPV is not an agent of this sort.”²³

Given that HPV is not an agent that is highly transmissible in the school setting, there is no justification for usurping parental authority and requiring all preteen girls to be vaccinated as a condition of school admission. Parents, in consultation with their pediatricians or family physicians, are the ones who should decide whether HPV vaccination is appropriate for their daughters.

Conclusion

While many states are seriously considering requiring vaccination of preteen girls as a condition of middle school admission, in many ways the case for HPV vaccine mandates is the weakest for any such mandate ever proposed. Such a requirement, while potentially very lucrative for the vaccine manufacturer, lacks the traditional justification for vaccine mandates and therefore represents an unjustified usurpation of parental authority. Moreover, serious questions remain as

to whether the vaccine is effective in preventing cervical cancer. The vaccine is the most expensive pediatric vaccine in history. Given the uncertainties surrounding the vaccine, and absent traditional public health justifications, a mandate can appropriately be characterized as what HPV researcher Diane Harper called “a great big public health experiment.”²⁴ Missouri lawmakers, taxpayers, and physicians should reject this expensive and intrusive experiment.

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Disclosures

None reported.

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