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Commentary

Bolstering trust in the human papillomavirus vaccine through improved communication in the vaccine information statement

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Marking a major victory in public health, the FDA approved the first safe and effective vaccine for human papillomavirus (HPV) in 2006. HPV infects nearly all sexually active men and women, and causes approximately 5% of all cancers worldwide. Gardasil, the original vaccine developed by Merck, protects against the two HPV subtypes associated with the highest proportion of cancers in all regions of the world, HPV 16 and 18, as well as two types that cause most genital warts. Almost all cases of cervical cancer, over 90% of anal cancers, 70% of oropharyngeal cancers, 75% of vaginal cancers, 70% of vulvar cancers and over 60% of penile cancers are caused by high-risk HPVs [1]. The FDA granted marketing authorization to Cervarix and Gardasil 9, two additional HPV vaccines, in 2009 and 2014, respectively. Cervarix provides immunity against the HPV 16/18 types, but not against those associated with genital warts. Gardasil 9 expands on Gardasil with protection for five additional high-risk HPVs, and has replaced Gardasil in the U.S. HPV vaccination has already contributed to declines in genital warts [2] and cervical precancerous lesions [3].

However, hesitancy among parents has contributed to slow uptake. Current U.S. vaccination rates hover at around 53% for girls and 44% for boys [4], far below the targets of 80% for boys and girls ages 13–15 put forth by the U.S. government's HealthyPeople initiative, which provides national objectives and establishes and monitors benchmarks to promote public health [5]. Although the safety profiles of HPV vaccines have stood up to scrutiny in post-marketing epidemiological studies [3], many factors have contributed to an erosion of trust in the HPV vaccines over and above historical hesitancy about childhood vaccines. These have included public resistance to state mandate proposals, given that HPV infection is transmitted sexually (a concern particularly prevalent among religious conservatives), and controversy surrounding the role of Merck in promoting mandates. To date, however, the two most commonly cited reasons for parental refusal are safety concerns and perceived lack of necessity [6].

Many researchers, including one of the authors of this Viewpoint, have been focused on improving provider communication strategies, which are known to be a major determinant of parental consent for the HPV vaccine [7]. At the same time, however, there is opportunity to improve the clarity of the CDC's HPV Vaccine Information Statement (VIS), which must be presented to parents prior to administration of the vaccine. Augmenting the information in the VIS would support clinicians in their communication efforts and better equip the person making the vaccination decision. Given that distrust of the safety and efficacy of the vaccine are major barriers to parental consent for adolescent vaccination, public health efforts to bolster public confidence in this vaccine should at minimum optimize the transparency and clarity of standardized communication of the vaccine's benefits and risks.

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In its current version, the HPV VIS does not present benefits and risks in forms that are easily compared. The VIS states that HPV infects 14 million Americans each year, and accurately lists the types of cancers caused by HPV. It also includes the annual incidence of cervical cancer diagnoses and deaths from cervical cancer, one of the most common cancers associated with HPV: *"In the U.S., about 12,000 women get cervical cancer every year, and about 4,000 women die from it. HPV vaccine can prevent most of these cases of cervical cancer."* In contrast, the risks of the vaccine are presented as ratios: soreness (about 9 people in 10), redness or swelling (about 1 person in 3), mild fever (about 1 person in 10), moderate fever (about 1 person in 65) and headache (about 1 person in 3). Other problems are presented as well:

> *People sometimes faint after a medical procedure, including vaccination. . .*
> *Some people get severe pain in the shoulder and have difficulty moving the arm where a shot was given. This happens very rarely. Any medication can cause a severe allergic reaction. Such reactions are very rare, estimated at about 1 in a million doses. . .As with any medicine, there is a very remote chance of a vaccine causing a serious injury or death.*

From this sheet, a parent would be unable to determine whether the benefits of the vaccine justify its risks, since the probabilities of contracting an HPV-related disease and the probabilities of experiencing an adverse event from the vaccine are not presented in comparable formats. Given that the risks of the vaccine are listed as ratios, the risk of developing cervical cancer should also be expressed as a ratio (currently estimated at 1 in 161). For greater context, risk reduction data should be presented as well. While more time post-licensure is needed to establish cancer outcomes, what is currently known is that in young women and girls who are negative for high-risk HPV types prior to vaccination, risk of precancer from HPV 16/18 is reduced from 164/10,000 to 2/10,000. These ratios can be presented in the same format outlined above, i.e. "from 1 in 61 to 1 in 5000" [3]. Further, the risk of developing other cancers and the risk of contracting genital warts should be added and presented in the same fashion. While these disease risks are patently lower than the risks of mild or moderate adverse events specific to the HPV vaccine, a parent may reasonably judge them to be the more determining factors in their decision. Armed only with an incomplete presentation of benefits and risks, a parent's decision to vaccinate—a prophylactic intervention on a healthy child—hinges on his or her trust of the healthcare provider and the medical community at large.

There is considerable variability in the way information is presented in VISs in general. For some vaccines (e.g. pneumococcus), information is presented the same way as for the HPV vaccine, with the risk of disease stated in absolute numbers and adverse reactions represented as ratios. Other VISs neglect to quantify the risk of adverse reactions (measles-mumps-rubella, hepatitis B, varicella). Indisputably, the VIS needs to be tailored to reflect the public health context for each vaccine. For diseases that are less prevalent in the U.S. (e.g. measles), the risk to the individual of contracting the disease may be negligible, but may increase sharply with the rise of unvaccinated pockets—a more than theoretical concern, as demonstrated by recent measles outbreaks in New York and several other states [8]. Where maintaining herd immunity is the priority, appeals to individual risk may be less to the point, given the low risk to the average American of contracting measles outside of outbreak zones. On the other hand, current prevalence of HPV-related disease should be a strong motivator for parents considering the vaccine. This information should be coupled with rates of adverse reactions, in a comparable format.

To be sure, HPV vaccine uptake is impacted by a number of complex factors and interactions between stakeholders. These include government action such as state mandates, healthcare provider communication and support for the vaccine, as well as reactions from the parent community. Further research is needed to determine whether communicating the risks and benefits of vaccination in the format suggested will increase uptake. Notably, in a recent study, parents that accepted vaccination were more likely to report being offered the chance to ask questions about VISs, suggesting value in improved clarity [9]. Some parents will have concerns about possible harms that are not founded in existing biological and epidemiological evidence, which would not be appropriate to include in the VIS. However, it is the duty of government health agencies and healthcare providers to educate parents and supply factual information that supports the recommendation to vaccinate, especially in light of the abundance of misinformation and considerable distrust. To meet this goal, the HPV VIS must provide parents with clear and transparent risk/benefit information that demonstrates why it is in the interest of the public health—as well as of the individual—to get vaccinated.

Expressing the benefits and risks of the HPV vaccine in clear language and ratios that are directly comparable will better satisfy the requirements of informed and shared decision-making. There is an ethical duty to optimize clarity in health communication, apart from the public heath objective of promoting recommended vaccines. Presenting evidence-based quantitative information in the HPV VIS more clearly and completely would be a positive step towards both dispelling misinformation and building up trust in the value of HPV vaccination.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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