



## Correspondence

## Response to Harper and De Mars, HPV vaccines: A review of the first decade



In “HPV vaccines – A review of the first decade,” Drs. Harper and DeMars set out to detail a comparison of the successes and failures of human papillomavirus (HPV) vaccine efficacy and usage (Harper and DeMars, 2017). In my opinion, the article raises more questions than it answers and could add to barriers limiting immunization rates by fueling hesitancy to vaccinate.

## 1. Coverage and herd immunity

In the United States, an estimated 31,500 new cancers in men and women each year are attributable to HPV; 90% are caused by viral subtypes infections prevented by the Gardasil 9 vaccine (<https://www.cdc.gov/cancer/hpv/statistics/cases.htm>, n.d.). In August of 2017, the National (US) Teen Immunization Survey reported that 43.4% of all teens were up to date with the HPV vaccination series (49.5% for females; 37.5% for males);  $\geq 1$ -dose HPV vaccination coverage among teens was 60.4% (Walker et al., 2017). Although more improvement is needed, this is encouraging! In fact, when only 51% of 14–19-year-old girls received  $\geq 1$  doses, there was a 56–71% decrease HPV 16/18 prevalence owing to herd immunity (Markowitz et al., 2013). Furthermore, data suggests that vaccination coverage in females leads to a dramatic reduction in HPV prevalence in unvaccinated males (Chow et al., 2017).

## 2. Cervarix vs Gardasil

The authors emphasize a long-debated, but to date, clinically irrelevant argument regarding the increased immunogenicity of Cervarix over Gardasil. To a less-informed reader, this information could leave the impression that Gardasil is not as effective as Cervarix. However, there is no clinical justification for the inference. In fact, both the Cervarix and Gardasil vaccines have been proven effective and safe.

The observed “sero-negativity” of Gardasil against HPV 18 reflects the stringency of the competitive Luminex immunoassays (cLIA) assay. It is important to recognize differences in serologic assays used in clinical trials (Brown et al., 2011). The authors refer to studies using cLIA and imply that the decrease in titers might affect the long-term duration of protection against HPV 18, yet, there is no evidence of waning protection clinically regardless of detection methods. We don't know the “lowest” serum antibody level that is effective for protection; there is not yet a defined immune correlate of protection because, to date, there have been no vaccine failures over time! (Schiller et al., 2008)

We now have 8–9 years of data on both earlier vaccines, and there have been no reported failures in protection to HPV 18 in Gardasil. Gardasil 9, with 6 years documented effectiveness, has 97.4% vaccine efficacy against the 5 “new” HPV types, and its protection against HPV 6, 11, 16, and 18 is similar to Gardasil (Joura et al., 2015; Huh et al., 2017).

## 3. Value of vaccination vs screening programs

It is far more difficult to develop a high-quality cervical cancer-screening program in a low-resource setting than to develop a vaccination program. In the US, over 12,000 women are still diagnosed yearly with cervical cancer. Even in the “developed” city of Houston, Texas, with 54 medical institutions, 21 hospitals, skilled pathologists, endless supplies, expert colposcopists, and > 40 Federally Qualified Health Centers, I continue to see women with newly diagnosed cervical cancer on an almost weekly basis. Never are all of these screening facilities and specialists present in adequate levels in lesser-developed countries. In fact, some working in countries most impacted by cervical cancer have reluctantly suggested that it might be necessary to strategically, but tragically “lose” a generation and forgo establishing screening programs in order to concentrate resources on vaccinating to prevent cancer in future generations.

The authors do not discuss the insurmountable difficulties of screening in developing countries, and furthermore, don't mention vaccination program successes. Rwanda, for example, became the first African country to initiate a national HPV vaccination program achieving 96.6% 3-dose coverage in 2012. The Global Alliance for Vaccines and Immunization will be the main organization supporting the program in Rwanda, as well as in 9 other low income African Countries. Although many hurdles of mass coordination and buy-in from national health agendas are necessary, these kinds of efforts cannot be ignored.

## 4. Conclusion

The most prominent reason for low HPV vaccination rates in the United States is the lack of a strong, clear, and on-time recommendation by the provider. Providers may be hesitant to recommend HPV vaccination for a variety of reasons. Misperceptions are even more common among patients and parents. In fact, it is hard to show a YouTube link about the benefits of HPV vaccination during a conference without having to quickly end the video before the next feed starts and shows an unfortunate “consequence” of the “harmful vaccine.” Although most providers are familiar with the

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concepts of causation vs. correlation and can easily recognize that science has disproven any link to these tragic situations, the public may not have the scientific understanding to do so. Even Dr. Harper's comments from years ago, based on a strong personal preference for screening over vaccination, are repeatedly taken out of context and used by many “antivax” organizations for their own purposes (Harper, 2009).

Cervical cancer is one of the greatest tragedies of our lifetime, and all 3 FDA-approved vaccines dramatically reduce the risk of cervical cancer and other HPV-associated cancers. We, the medical community, need to be careful not to cause more confusion that may contribute to lower vaccination rates and potentially cause more children and their parents to forgo vaccination that will protect from cancers we should no longer see on this planet.

**What we don't know:**

We don't know the lowest serum immunogenicity level that will provide protection against HPV.

We don't know how to get ALL women screened, even in the US.

We don't know if a booster will be needed.

**What we know:**

We know that HPV cancer incidences are rising annually.

We know that vaccination for HPV 9 protects against more subtypes than HPV 2 or HPV 4.

We know both Cervarix and Gardasil are extremely effective in an HPV-naïve population.

We know that HPV prevalence, warts and dysplasia are decreasing in the vaccinated population.

We know we don't have time to wait. Vaccinate!

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