



## Correspondence

## Hypothesis generating data – HPV vaccines – A decade in review



We thank Dr. Ramondetta for her enthusiastic embrace of all clinical cervical cancer prevention, early detection and treatment opportunities including vaccination and screening strategies in her response to our scientific review (Ramondetta, 2017; Harper and DeMars, 2017). It is important for gynecologic oncologists to support the primary care efforts of prevention as well as the treatment of invasive disease. With the advent of highly effective HPV vaccines, cervical cancer can be controlled through the combination of screening and vaccination.

The implementation of vaccination and screening programs, though, is a very real aspect of cervical cancer prevention that has met with variable success in different populations. Our review does not focus on implementation, but rather on the three vaccines currently in use throughout the world, as the primary reading audience of Gyn Oncology is a global audience. The data presented in our 10 year review reflect the knowledge base of HPV vaccines deduced from randomized controlled trials in multi-national population cohorts of females from 9 years to 72 years of age. Immunogenicity and efficacy have been measured in different assays for all three vaccines in proprietary and independent laboratories, with differing defined single and combination endpoints and with differing statistics. These differences lead to immunogenicity data that are not comparable across vaccines, with the stability of titers and minimal levels to prevent infection still to be determined. Our review presents in a comprehensive fashion the data as it has unfolded over time; the purpose of our review is not to speculate on long term promises for health benefits. We would be delighted as primary care and oncology specialists to know that cervical cancer might be eradicated in 100 years, but the current data are only valid for the past 10 year population experience.

Population data evaluating the effect of HPV vaccination in the US are much less rigorous than the registries maintained in other countries, and hence its trending reports must be reviewed with objective, not optimistic, interpretation. The National Health and Nutrition Examination Survey (NHANES) collects self-reported sexual history and vaccine uptake information among participants aged 14 to 59 years by using a computer-based self-interview; women provide cervico-vaginal swabs by self-sampling of the vagina at the time of the survey. This is not a longitudinal survey; a different representative population is chosen for each NHANES cycle (Markowitz et al., 2016). The National Immunization Survey (NIS) is a telephone survey of parents or guardians which reports remembered childhood and adolescent vaccine uptake that may or may not have data corroboration by the site of vaccination (Walker et al., 2017). The Youth Risk Behavior Surveillance System (YRBSS) is a self-reported survey, usually school based, that monitors sexual behaviors related to unintended pregnancy and sexually transmitted diseases (Bhatta and Phillips, 2015). The Behavioral Risk Factor Surveillance System (BRFSS) monitors self-reported HPV vaccine uptake and screening (Hirth et al., 2014; Tiro et al., 2008). Each of these CDC based surveys contributes to our knowledge and may provide glimpses to changes in cervical cancer prevention. It was this set of surveys that helped change the professional societies' recommendations for frequency of cytology screening from annually to every three years after decades of data analysis. But their data are early and need verification.

Registries in the US whose data are significantly more rigorously collected and cataloged for longitudinal trends specific to HPV and cervical cancer include NM-HOPES-PROSPR Research Center, publishing data from the New Mexico HPV Pap registry. We look forward to the data from this registry for evidence of population effectiveness and true cervical cancer reductions as HPV vaccination programs continue to be widely disseminated.

Ramondetta cites data that suggest that vaccination programs are easier to implement than screening programs in low resource countries. Allocation of health resources solely to vaccination will increase harm to women without access to the vaccine, whose harm is compounded by no access to screening.

At this time, in developed countries with robust cervical cancer screening systems in place using primary HPV testing with cytology, simultaneously or in triage, a simulation model has been presented to reduce the insurance covered screening for women to three times in her lifetime (Landy et al., 2017). This model assumes 100% vaccination rate of all girls at 12 years of age, no waning of protection over time, and 100% HPV 16/18 cervical cancer prevention. These modeling exercises are interesting to probe 'what -if' scenarios, but are not inclusive for human health behaviors. It will be many years until a significant reduction in cervical cancer is actually documented from vaccination. Current cervical cancer screening and vaccination strategies need to remain in place. Primary care is messy; and redundancies in screening and vaccination help provide a safety net for best possible outcomes.

## Conflict of interest

The authors have no conflicts of interest to disclose.

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