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Letter to the Editor

A mixed two-dose vaccination schedule: Not enough evidence to support a policy change in Quebec

In the November 2018 issue of *Vaccine*, Gilca et al. conclude that a mixed two-dose HPV vaccination schedule (9vHPV and 2vHPV) was as immunogenic and had a similar safety profile when compared to two doses of 9vHPV [1]. 9vHPV covers 7 high-risk types and 2 low-risk types related to anogenital warts. 2vHPV covers only 2 oncogenic types (16 & 18). Based on this rather small study (n = 47 boys; 47 girls aged 9–10 years for the new proposed schedule arm of the study) and short-term follow-up, we express concerns regarding the conclusions drawn by the authors that resulted in a major policy decision in the province of Quebec (population ~ 8 million) to implement a mixed schedule in 80,000 9-year-old children in the school-based program without solid supporting data about clinical efficacy.

Gilca et al. found that a mixed schedule demonstrates substantially lower immune response to HPV types 6 & 11 (causing anogenital warts), and while the seroprotective antibody threshold remains unknown, they did not present data to suggest adequate protection [1]. Treatment for genital warts does not prevent local (or possibly distal) recurrence in the long-term. There is strong evidence on the effectiveness of the 4-valent and 9-valent HPV vaccines in providing long-term protection, as well as significantly reducing the incidence of recurrence in individuals already experiencing anogenital warts who are vaccinated subsequently. Furthermore, there have been significant reductions in anogenital warts incidence in males in Australia (prior to implementation of the male HPV vaccine program) [2]. Hindering the potential reduction of the incidence of genital warts in Quebec (currently 45% in females aged 15-19 in the first 3 years of the school-based program) would be unacceptable [3].

Recent data [4] suggests that results with even one dose of the 4vHPV, persistent infection with HPV 16, 18, 6, and 11 were comparable to two or three doses, but clearly concluded that further assessment was needed [4]. More than 12 years after the initiation of HPV vaccination programs, the outcome literature supports the 2-dose 4-valent (previously) or the more recent 9-valent HPV vaccines, as the safest and most effective combination in the prevention of anogenital warts.

There are no studies demonstrating clinical efficacy against anogenital warts and anal cancer, specifically in boys for the 2vHPV vaccine and no protection for HPV types 6 or 11 even in studies of girls [5]. The effectiveness of a single 9-valent dose for the additional high-risk HPV types covered is yet unknown; 8–10 years are needed to evaluate this endpoint. Gilca et al. indeed report that a central limitation to their work is that this study only reports on short-term antibody response, though they plan a follow-up assessment of antibodies at three or more years. Given that long-term data for a mixed two-dose vaccination schedule is limited and unlikely to be protective, how can we accept this as a public health policy in Quebec? We have much to learn from our current, effective programs. It is not too late to reverse course.

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