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Author Response to Letter: Will Increasing Dosing Intervals Decrease the Loss of Anti-HPV Seropositivity Over Time?

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We appreciate the interest of Drs. DeMars and Harper in our report of antibody responses among young women to standard and delayed dosing of the quadrivalent HPV vaccine. Their letter noted the loss of HPV 18 seropositivity in other clinical trials, emphasizing that although this loss occurs among women it may occur even more quickly and in higher proportions among men. In our study, we evaluated antibody titers at one and six months after vaccination in women; including the latter time point so we could compare, to some extent, the durability of the antibody response following different vaccination schedules. We were reassured to find that antibody responses among women in the study groups with delayed dosing remained superior to the control group with standard (0, 2, 6 month) dosing at the six month time point.

The letter expresses concern that the more rapid loss of antibody in men might impact protection although it acknowledges that protective levels of antibody for HPV are not known. We also note that seropositivity has not been correlated to protection of HPV associated cancers. Furthermore, seropositivity is dependent, in part, on assay characteristics. The competitive luminex assay used in many HPV vaccine clinical trials has a lower sensitivity for type-specific HPV 18 antibody response compared to a direct ELISA (1, 2). A higher specificity to HPV 18 antibody response at the cost of sensitivity might explain the continued protection observed in clinical trials, despite the loss of seropositivity in some participants. Long term vaccine follow up studies have demonstrated protection, including protection against HPV 18, up to ten years after vaccination despite the loss of detectable antibody that occurred in some vaccinees (2,3) and trials examining immune memory after a 4th vaccine dose have demonstrated robust induced immune memory, including against HPV 18 (4, 5). We agree that further studies in men as well as women could inform the cost effectiveness and efficacy of HPV vaccination and add to our understanding about the duration of protection and relation of protection to antibody levels.

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