Why the American Academy of Pediatrics recommends initiating HPV vaccine at age 9

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ABSTRACT

The American Academy of Pediatrics (AAP) recommends starting the human papillomavirus (HPV) vaccine series between 9 and 12 years, at an age that the provider deems optimal for acceptance and completion of the vaccination series. This recommendation differs from the Advisory Committee on Immunization Practices (ACIP), which recommends HPV vaccination be initiated at age 11 or 12 years, stating the series can be started at age 9 years. This commentary discusses the reasoning behind AAP’s decision to differ from ACIP, as the AAP and ACIP schedules are essentially harmonized for all other vaccines. Reasons include recognition that (1) vaccination uptake is suboptimal; (2) offering vaccination earlier offers provider flexibility in introducing the vaccine; (3) initiating the vaccine at age 9 or 10 may be preferable for parents or adolescents who do not want to receive ≥3 concomitant vaccines at age 11 or 12; (4) earlier initiation may disentangle HPV vaccination recommendations from discussions of sexuality; (5) earlier recommendation might alleviate HPV vaccine hesitancy “fatigue”; (6) the immune response is robust at younger ages with no evidence of waning protection; and (7) there is a dearth of evidence supporting starting the recommendation at age 11 or 12 within the “adolescent immunization platform.”

Historically, there have been two distinct groups that make recommendations for the immunization of children and adolescents in the United States: the Advisory Committee on Immunization Practices (ACIP), which advises CDC, and the Committee on Infectious Diseases (COID) on behalf of the American Academy of Pediatrics (AAP), which advises pediatricians. These two entities work closely to ensure harmony of the immunization schedules they create; differences, if any, are almost always minor. In rare cases, though, recommendations may differ in a meaningful way. The most notable example in recent memory is the difference in the wording of the AAP and ACIP recommendations regarding human papillomavirus (HPV) vaccination.

ACIP’s recommendation is as follows: “ACIP recommends that routine HPV vaccination be initiated at age 11 or 12 years. The vaccination series can be started beginning at age 9 years.”

The AAP recommendation, introduced in the 2018–2021 Red Book, acknowledges the ACIP recommendation but is more forceful in recommending the vaccine at an earlier age:

“The American Academy of Pediatrics and the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention recommend routine HPV vaccination for females and males. The AAP recommends starting the series between 9 and 12 years, at an age that the provider deems optimal for acceptance and completion of the vaccination series. The ACIP recommends starting the series at age 11 or 12 years and states that vaccination can be administered starting at 9 years. So what prompted the difference in recommendations? Both ACIP and AAP recognized that the vaccine is safe and effective and that it prevents HPV infection, with the consequent prevention of anogenital warts, respiratory papillomatosis, cervical neoplasia, and cancer, with data on the impact on cancer becoming more robust with each passing year.

However, despite its remarkable safety record and high effectiveness, HPV vaccination is well below national goals and lags behind other vaccines in the so-called “adolescent immunization platform,” which also includes tetanus diphtheria acellular pertussis (Tdap) and quadrivalent meningococcal (MenACWY) vaccines. The most recent National Immunization Survey-Teen showed that the uptake of Tdap vaccine was 89.6% and the first dose of MenACWY was 89.0%. HPV rates remain significantly behind these vaccines, with initiation at 76.9% and completion at 61.7%.

In contrast to vaccination coverage, the burden of HPV-related mortality in the U.S. far surpasses the mortality from tetanus, diphtheria, pertussis, and meningococcal disease combined. In the U.S., there are roughly 4,000 deaths per year from cervical cancer, not to mention the mortality burden from the other types of HPV-related cancer (mortality data for non-cervical HPV-related cancers are not systematically tracked). The vast majority of these deaths are preventable with the nine-valent HPV vaccine. Thus, there was and continues to be an urgent need to increase HPV vaccination uptake. With this in mind, the COID, on behalf of AAP, considered policy options that could increase HPV uptake and ultimately decided to recommend starting the series between 9 and 12 years.

There were several considerations that led to this decision. First, offering the vaccination earlier would allow providers more flexibility in introducing the vaccine. Second, initiating

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the vaccine at age 9 or 10 may be preferable for parents or adolescents who do not want to receive three or four (in influenza season) concomitant vaccines at age 11 or 12. (Now, with COVID-19 vaccination, this could mean as many as five vaccines recommended at a single visit, even for an individual who is otherwise “up-to-date” on vaccines.) We were also aware that some providers reported that initiating the vaccine earlier made it easier to disentangle the HPV recommendation from discussions of sexuality they often have with patients at age 11 or 12, which was a known barrier for providers.7 Changing the timing of the recommendation might also address HPV vaccine hesitancy “fatigue,” as many physicians defer recommending HPV vaccine at age 11–12 because they assume parents will refuse.8

Finally, we could not identify any evidence supporting the practice of starting the recommendation at age 11 or 12 within the so-called “adolescent immunization platform.” In fact, we felt we had evidence against that strategy given the low uptake. Initiation at age 11 or 12 is rooted in the concept of the aforementioned “adolescent platform” of vaccines. This “adolescent platform” concept stressing the importance of the 11–12-year-old visit was introduced in 19969,10 and has been at the heart of messaging campaigns promoting adolescent vaccination from CDC, AAP, and others. In 1996, well-child visits beyond kindergarten were relatively uncommon, so CDC, AAP, and the American Academy of Family Physicians (AAFP) wanted to establish an 11–12-year-old visit for catch-up on routine vaccinations, particularly hepatitis B vaccine. Twenty years on from that recommendation, though, AAP and AAFP were routinely recommending that children have a well-child visit every year, and the vast majority of children (79% of 6–11-year olds) were doing so.11 Thus, the 11–12-year-old visit no longer carried the importance it once did.

For the HPV vaccine specifically, ACIP’s initial recommendation in 2007 for vaccination at 11–12 rather than at 9 years was also based on concerns regarding potential waning immunity.9 Although HPV vaccine had been licensed down to age 9, with excellent immunogenicity and safety, duration of protection was relative unknown at the time, so ACIP also considered age 11 or 12 as a good “middle ground” for vaccination: prior to sexual debut for most adolescents, but close enough to provide protection through the highest risk years. It has become clear to us within AAP, however, that the bundling approach was failing for HPV vaccine. When a vaccine is delayed at the 11–12-year-old visit, it is almost always HPV vaccine,12–14 despite the fact that deaths from HPV-related diseases in the US exceed deaths from the other diseases prevented by adolescent vaccines by orders of magnitude.4,5 Now, we also have strong evidence that HPV vaccination offers durable protection,15 further eroding any justification for waiting until age 11 or 12. The immune response is robust at younger ages, and there is no evidence of significant waning protection after antibody levels plateau approximately 18–24 months after series completion.

What about data suggesting that a strategy of earlier initiation would lead to higher HPV vaccination uptake? At the time of our discussions, there were no randomized trials that compared introduction at 9 or 10 years to introduction at 11 or 12 years (there is one large trial ongoing now with results expected in the next few years).16 There were, however, some observational data supporting earlier initiation. A retrospective study showed that adolescents who started the HPV vaccine series at age 9 or 10 were 22 times more likely to complete the two-dose series by age 15 than those who initiated the series at age 11 or 12.17 Other observational studies also showed promise for earlier initiation.18,19 A report on a quality improvement initiative performed in the Nationwide Children’s Hospital system utilizing electronic medical record alerts showed rapid uptake of HPV vaccine prior to age 11, suggesting a willingness by parents and providers to initiate the vaccine earlier than previously recommended.20 Subsequent to our deliberations and the change in the AAP recommendation, there have been other studies demonstrating both the promise of earlier initiation and provider willingness to try it.21,22

Ultimately, the goals of ACIP and AAP with regard to HPV vaccination are the same: to prevent HPV-related diseases and cancers. The AAP policy aims to encourage pediatricians to introduce the HPV vaccine at an earlier age to achieve higher initiation and completion rates. This, however, is but one of many strategies AAP encourages to increase uptake of HPV vaccine (e.g., reminder/recall, standing orders, and prescriptive recommendations).23 There is no one single intervention that will bring us to 100% uptake, but we believe that by combining multiple evidence-based strategies with earlier introduction, we can make significant progress toward eliminating HPV-related cancers in the U.S. and beyond.

Disclosure statement
Dr O’Leary is the Chair of the Committee on Infectious Diseases for the American Academy of Pediatrics. He has no financial conflicts of interest. He is a co-investigator on the NIH-funded clinical trial comparing introduction of HPV vaccine at age 9 or 10 with introduction at 11 or 12 mentioned in the commentary (Kempe, Szilagyi, multi-Pls, 5R01 CA240649-03). He is also the PI of several NIH- and CDC-funded HPV-related clinical trials (1R01 CA254931-01A1, 5R21 CA230878-02, U01 IP001091).

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