American Cancer Society and American Cancer Society Cancer Action Network Comments to the Advisory Committee on Immunization Practices: Docket No. CDC-2025-0024

June 20, 2025

The American Cancer Society (ACS) and the American Cancer Society Cancer Action Network (ACS CAN) are pleased to provide comments to the Advisory Committee on Immunization Practices (ACIP) in advance of the June 25-27th, 2025 meeting. The ACS is a nationwide, community-based, voluntary health organization dedicated to eliminating cancer as a major health problem by preventing cancer, saving lives, and diminishing suffering from cancer through research, education, advocacy, and service. The ACS, operating through its national office and throughout the United States, is the largest voluntary health organization in the United States. ACS CAN is the nonprofit, nonpartisan advocacy affiliate of ACS, supporting evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. ACS CAN is making cancer a top priority for public officials and candidates at the federal, state, and local levels, and empowering advocates across the country to make their voices heard and influence evidence-based public policy. **Our comments focus on Human Papillomavirus (HPV) Vaccine Workgroup.**

ACS and ACS CAN support the continued recommendation of HPV vaccination for adolescents.
Specifically, ACS's guideline adaptation of the current ACIP recommendations is:

The ACS recommends routine HPV vaccination between ages 9 and 12 years to achieve higher on-time vaccination rates, which will lead to increased numbers of cancers prevented. Health care providers are encouraged to start offering the HPV vaccine series at age 9 or 10 years. Catch-up HPV vaccination is recommended for all persons through age 26 years who are not adequately vaccinated. Providers should inform individuals aged 22 to 26 years who have not been previously vaccinated or who have not completed the series that vaccination at older ages is less effective in lowering cancer risk. Although the ACIP recommended shared clinical decision making for some adults aged 27 through 45 years who are not adequately vaccinated, the ACS does not endorse this recommendation because of the low effectiveness and low cancer prevention potential of vaccination in this age group, the burden of decision making on patients and clinicians, and the lack of sufficient guidance on the selection of individuals who might benefit.[i]

Achieving optimal HPV vaccination is a cancer prevention priority.

HPV vaccination provides an opportunity to prevent cancer outright. HPV infections are responsible for 37,000 cancers in the U.S. each year, including virtually all cervical cancers, 90% of anal cancers, and 60-70% of oropharyngeal, vaginal, vulvar and penile cancers.[ii] In 2024, an estimated 13,820 people are expected to be diagnosed with cervical cancer, and 4,360 will die from the disease.[iii] Oropharyngeal cancer (cancer of the back of the throat, tonsils and base of the tongue) is the most common HPV-

related cancer diagnosed in people assigned male at birth, with a 12,900 estimated cases expected this year.[iv] HPV vaccination is associated with a reduction of CIN2+, and is expected to prevent other HPV-related cancers along with their associated human and financial costs; yet, even 18 years since its introduction, HPV vaccination rates still lag behind other child and adolescent immunizations. This will leave future generations of children and adolescents at risk of developing a preventable cancer during their lifetime.

Since its introduction in 2006, HPV vaccination has already led to substantial population-wide decreases in cervical precancers, and cervical cancers.[v,vi,vii,viii] A 2024 analysis of almost 3.5 million people in the U.S. confirmed that HPV vaccination lowers the chances of developing HPV-caused cancers, including head and neck cancers in men and women and cervical cancer in women.[ix] Most recently, a February 2025 study found an 80 percent decrease in cervical cancer precursors among screened women aged 20-24, the age group most likely to have received the HPV vaccination.[x]

The HPV vaccine is safe and effective.

HPV vaccines went through extensive safety testing before becoming available. The safety, effectiveness and quality of all vaccines are regulated by the U.S. Food and Drug Administration (FDA). The FDA provides scientific advice to vaccine manufacturers seeking approval, evaluates the safety and effectiveness of every vaccine and oversees the manufacturing process to ensure safety and consistency. FDA's oversight starts with a review of laboratory and preclinical data to assess whether a vaccine is ready to be tested on people based on its quality, safety, and process to manufacture and test it. FDA can then grant an Investigational New Drug approval. This allows the vaccine manufacturer to begin the clinical phase of testing with people. Clinical trials designs are typically developed with FDA input and test the safety and effectiveness of a vaccine by examining the relationship between dose and immune response.

Once a vaccine has proven safe and effective in the clinical phase and the manufacturing process has been assessed, the vaccine manufacturer may submit a Biologics Licensing Application which includes all preclinical and clinical data, as well as manufacturing and facilities processes. FDA then evaluates the application to determine whether the vaccine's safety and effectiveness has been demonstrated and whether the manufacturing and facility information assure product quality and consistency.

Both the FDA and the Centers for Disease Control and Prevention (CDC) provide ongoing surveillance of FDA-approved vaccines to identify uncommon adverse events, long-term complications, and monitor effectiveness. These surveillance systems include the Vaccine Adverse Event Reporting System (VAERS), the FDA Biologics Effectiveness and Safety (BEST) program and the FDA Sentinel Program, the FDA and Centers for Medicare & Medicaid Services (CMS) partnership, and CDC's Vaccine Safety Datalink. All clinicians have access to VAERS and report adverse events for any vaccine into the system, for the purpose of identifying unexpected patterns of adverse events. The VAERS cannot determine whether a vaccine is the cause of a health problem. FDA's BEST and Sentinel program provide post-market active surveillance of all biological products, including vaccines, to ensure safety and effectiveness.

The HPV vaccination has proven safe and effective for preventing infections of the types of HPV that cause most cancers.

Role of ACIP

ACIP performs a critical public health and health care function by providing CDC, the leading federal public health agency, recommendations on the use of vaccines approved by FDA as safe and effective for the control of vaccine-preventable diseases in the U.S. For each vaccine, ACIP must consider both the population and the circumstances in which vaccination is warranted for the protection of public health. As part of its recommendations, ACIP provides information on contraindications, precautions for use, and any known adverse events. In making its recommendations, ACIP must consider the disease epidemiology and burden and of disease, vaccine safety, vaccine efficacy and effectiveness, the quality of evidence reviewed, economic analysis and implementation issues.

The CDC uses ACIP's recommendations to set child, adolescent, and adult immunization schedules, which are used by health care providers to properly administer routinely recommended vaccines for the protection of public health. The child and adolescent schedules are also approved by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG).[xi] The adult schedule is also approved by AAFP, ACOG, the American College of Physicians, and the American College of Nurse-midwives.

HPV Vaccine Recommendation History

The HPV vaccine was first licensed in the U.S. in June 2006 and ACIP first recommended HPV vaccination in March 2007 for girls and expanded the recommendation to include boys in December 2011 based on the evidence. In its 2007 recommendation, ACIP stated, "The availability of a quadrivalent HPV vaccine offers an opportunity to decrease the burden of HPV infection and its sequelae, including **cervical cancer precursors, cervical cancer, other anogenital cancers**[emphasis added], and genital warts in the United States.[xii]" In December of 2016, ACIP revised its recommendation to reduce the 3-dose schedule to 2-doses for children who initiate the vaccine series between the ages of 9 and 14 after the FDA approved the new 2-dose series. ACIP reiterated in its recommendation "HPV vaccines are highly effective and safe, and a powerful prevention tool for reducing HPV infections and **HPV-associated cancers** [emphasis added].[xiii]"

ACS was among the organizations that were the earliest advocates of cervical cancer screening and first recommended regular Pap tests in 1957. ACS has introduced and periodically updated guidelines or guidance related to screening and/or informed decision-making about tests for early detection of cancers (and, in some cases, precursor lesions). These guidelines have evolved with new scientific data, as new technologies became available, and as standards for creating guidelines changed. ACS published its first guideline for HPV vaccination to prevent cervical cancer and its precursors in 2007, with an endorsement of the ACIP guideline starting in 2016 to include boys and the new recommended dosage schedule. The ACS concluded that ACIP's evidence review methods and findings were clearly presented, and the evidence regarding individual benefit and risk applied to recommendations formulation was well described. In the 2020 guideline update, ACS stated it "adapted the ACIP recommendation for routine HPV vaccination at age 11 or 12 years, with a statement that routine HPV vaccination between ages 9 and 12 years is expected to achieve higher on-time vaccination rates, **resulting in increased numbers of cancers prevented** [emphasis added].[xiv]"

Specific Workgroup Recommendations:

Evidence in Support of Starting at Age 9

ACS and ACS CAN are committed to implementing evidence-based interventions, including clinical and public policy interventions to reduce barriers and increase vaccination rates. The scientific evidence shows that implementing HPV vaccination at age nine, before adolescence, provides a clear benchmark for initiating vaccination, produces a strong immune response, offers more time to complete the series by age 13, and can help improve overall vaccine uptake. Adolescence is generally defined as ages 10-19, a period in which exposure to HPV increases with age and the protection of the HPV vaccination initiated in later adolescence is lower. Ellingson, et al. conducted a systematic review of HPV vaccine effectiveness by age at vaccination and observed that highest vaccine effectiveness in the youngest age groups, ranging from 74% to 93% in adolescents aged 9-14, and from 12% to 90% for adolescents ages 15-18 years.[xv] A new study published this year by Saxena, et al. demonstrated the opportunities to increase vaccination uptake by starting the recommendation at age 9.[xvi] The study found that more than one-third of children who have a well visit at age 9, did not have a well visit at age 11 and 12 – highlighting the missed benefit of routine vaccination at age 9. Additionally, modeling studies also show declining effectiveness of HPV vaccination at later ages in adolescence.[xvii]

There also are important practical reasons to initiate the vaccination series earlier.

- Adolescents initiating HPV vaccination at 9-10 years were more likely to be fully up to date by 13.5 years of age compared to those initiating at 11 to 12 years (97.5% versus 78%, respectively).[xviii]
- Quality improvement initiatives, including changing electronic medical record prompts to alert providers of the need for HPV vaccination starting at 9 years rather than 11 years, led to an 8-fold increase in vaccination prior to 11 years of age (4.6% to 35.7%).[xix]
- A provider-focused multi-level intervention in pediatric offices that agreed to initiate HPV vaccination at 9-10 years of age resulted in a 13-percentage point increase in vaccination among 9-10-year-olds, which was not only sustained but increased in the post-intervention period (27 percentage point increase).[xx]

<u>Need for an Updated Recommendation Statement</u>

The wording of the ACIP recommendation presents a barrier to initiating routine vaccination at age 9, even though this was not the intent of the ACIP. Furthermore, advising the initiation of HPV vaccination within a range of ages increases the likelihood of starting vaccination later in the range, which could result in completing the series at a point where the vaccine's effectiveness is diminished. It is well established in guideline development that recommendations should be as specific as possible regarding the age to begin, the interval to follow, and the age to discontinue. Updating the recommendation language would reduce confusion among providers and parents as to when to start routine vaccination and would align the ACIP recommendation with that of ACS.[xxi] The current wording does not clearly indicate that payers should cover the HPV vaccine at no cost to patients and families starting at age 9.

<u>Dosing Schedule Recommendation</u>

ACS and ACS CAN encourage ACIP to consider the following issues in their deliberations on potential changes to the dosing of the HPV vaccine:

- Availability of data and evidence on one dose, including but not limited to long term efficacy and immunogenicity, protection against cancers other than cervical, and efficacy and immunogenicity in males.
- FDA-approval for a vaccine(s) with a different dosing schedule, including the potential consequences of off-label use on clinical practice and public perception.

Importantly, the safety and effectiveness of the two-dose recommendation is well established by sound scientific evidence and should remain ACIP's recommendation and on CDC's immunization schedule while alternative dosing schedules are deliberated.

Conclusion

ACS and ACS CAN look forward to the important work of ACIP and the HPV Vaccine Workgroup specifically. For additional information from our groups, please contact Laura Makaroff, DO, Senior Vice President, Cancer Prevention, ACS at Laura.Makaroff@cancer.org, Deana M. Baptiste, MPH, PhD, Senior Director, Guidelines Development, ACS at Deana.Baptiste@cancer.org, and Katie McMahon, Policy Principal, ACS CAN at Katie.McMahon@cancer.org.

Thank you.

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