Addressing the Challenges of Adult and Adolescent Vaccinations: Improving Clinical and Economic Outcomes in Immunizations

A CME/CNE Approved Activity

This activity is supported by an educational grant from Merck & Co.
Addressing the Challenges of Adult and Adolescent Vaccinations: Improving Clinical and Economic Outcomes in Immunizations

Instructions for CME/CNE: Activity is valid from December 1, 2018 to November 30, 2020. A score of 70% must be achieved on the post-test to receive continuing education credits. Read the monograph, answer the post-test, complete the evaluation form, and send completed post-test and evaluation to:

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Learning Objectives:
1. Describe adolescent vaccine-preventable conditions.
2. Examine guidelines and recommendations about adolescent immunizations.
3. Assess the latest clinical guidelines regarding the timing of HPV immunizations in preteens and teens.
4. Discuss the prevalence of HPV infection, the types of cancers it causes and the economic impact of HPV vaccination.
5. Integrate strategies to overcome perceived barriers to HPV vaccination in the adolescent setting.
6. Describe common barriers to effective immunization practices among diverse patient populations.
7. Examine current adolescent vaccination recommendations for the influenza, pneumococcal, tetanus toxoid, reduced diphtheria toxoid, acellular pertussis (Tdap), and herpes zoster vaccines.
8. Provide recommendations for vaccinations in adult immunocompromised patients.
9. Employ the recommendations for the influenza vaccine to optimize immunization efforts and decrease the cost burden of influenza and its complications.
10. Identify strategies to address common barriers and misperceptions to effective immunization practices.

Faculty Disclosure:
Dr. Caskey has no financial relationships to disclose.
Dr. Weber serves on an advisory panel or group for Merck and Pfizer and as a consultant for Merck and Pfizer. He is on the Speaker’s Bureau for Merck.
All material has been peer reviewed for bias.

Planning Committee Disclosure
Bill Williams, MD; Jacqueline Cole, RN, CPHQ, CMCN; and Jeremy Williams have no relevant financial relationships to disclose.

Accreditation and Designation
The National Association of Managed Care Physicians (NAMCP) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. NAMCP designates this enduring material for a maximum of 1 AMA PRA Category 1 credits™. Each physician should claim credit commensurate with the extent of their participation in the activity.
The American Association of Managed Care Nurses is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation. Nurses who complete this activity and achieve a passing score will receive 1 hour in continuing nursing credit. This activity has been approved by the American Board of Managed Care Nursing for 1.0 contact hours toward CMCN recertification requirements.

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Addressing the Challenges of Adult and Adolescent Vaccinations: Improving Clinical and Economic Outcomes in Immunizations

Post-Test Questions

1. What is the major reason for the success of mass vaccination in U.S.?
   a. ACIP recommendations  b. School-mandates  
c. Medicare requirements  d. Consumer education

2. Every dollar spent on childhood vaccination results in _______ in cost savings.
   a. $1  b. $5  c. $10  d. $50

3. Which of the following groups provides the CDC with advice regarding immunizations and their final recommendations are official CDC recommendations?
   a. Food and Drug Administration  b. American Medical Association  
c. American Society of Pediatrics  d. Advisory Committee on Immunization Practices

4. Which of the following is NOT an accurate best practice guideline?
   a. Missed dose(s) require a restart of a given vaccine series.
   b. Inactivated vaccines are safe for immunocompromised and pregnant persons.
   c. Influenza and Tdap are specifically indicated for pregnant women.
   d. Vaccine doses can be provided at intervals beyond those recommended but intervals cannot be shortened.

5. Optimally, when should influenza vaccinations start?
   a. End of September  b. End of October  
c. Beginning of December  d. Beginning of January

6. Administration of either PPSV23 or PCV13 is recommended for adults greater than 65 years of age.
   a. True  b. False

7. Which of the following is preferred in the guidelines for the prevention of herpes zoster and related complications in those 50 and older?

8. Which of the following vaccines prevents certain types of cancer?
   a. Tdap  b. Yellow fever  c. HPV  d. Rubella

9. Which of the following is the best strategy for improving HPV vaccination rates in adolescents?
   a. Discuss the sexual transmission of the virus with parents
   b. Present information on the benefits of vaccination and low risk of adverse effects.
   c. Require HPV vaccination for high school attendance.
   d. Give less information rather than more and announce that vaccination will occur.

10. In general, which of the following is effective for increasing community demand for vaccination?
    a. Financial incentives  b. Feedback on prescriber performance  
c. Client reminder systems  d. Enhanced access at schools

Activity Evaluation and Improvement Process

Please rate this activity on the following scale: 4 - Excellent  3 - Good  2 - Fair  1 - Poor

1. Based on the content presented, I am better able to:
   b. Examine guidelines and recommendations about adolescent immunizations.
   c. Assess the latest clinical guidelines regarding the timing of HPV immunizations in preteens and teens.
   d. Discuss the prevalence of HPV infection, the types of cancers it causes and the economic impact of HPV vaccination.
   e. Integrate strategies to overcome perceived barriers to HPV vaccination in the adolescent setting.
   f. Describe common barriers to effective immunization practices among diverse patient populations.
   g. Examine current adult vaccination recommendations for the influenza, pneumococcal, tetanus toxoid, reduced diphtheria toxoid, acellular pertussis (Tdap), and herpes zoster vaccines.
   h. Provide recommendations for vaccinations in adult immunocompromised patients.
   i. Employ the recommendations for the influenza vaccine to optimize immunization efforts and decrease the cost burden of influenza and its complications.
   j. Identify strategies to address common barriers and misperceptions to effective immunization practices.

2. The activity and presenters were free of bias.

3. The activity was applicable to my position.

4. How confident are you in managing patients based on this activity? (4 very confident - 1 not confident)

5. Do you plan to change management strategies or patient care in your organization or practice based on the content presented?
   a. Yes  b. No

6. If yes, what changes do you plan to implement in management strategies or patient care in your organization or practice?

7. Did the content of the activity help in meeting your above goal?
   a. Yes  b. No
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# JOURNAL OF MANAGED CARE MEDICINE

The Official Journal of the NAMCP MEDICAL DIRECTORS INSTITUTE

A Peer-Reviewed Publication

**Immunizations Monograph**

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<td>Rachel N. Caskey, MD, MPP; David Jay Weber, MD, MPH</td>
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Vaccination programs are among the most widely used and cost-effective public health interventions in the United States (U.S.). Vaccinations were named the number one greatest public health achievement in both periods 1900 to 1998 and 2001 to 2010 by the Centers for Disease Control and Prevention (CDC). Mass vaccination has led to control of multiple infectious diseases. Exhibit 1 illustrates the dramatic decrease in vaccine-preventable diseases in the U.S.

The major reason for the success of mass vaccination in the U.S. stems from school mandates; there is now a growing trend toward workplace mandates, which should help improve adult vaccination rates.

Vaccines are not only effective in reducing morbidity and mortality, they are also cost effective. In an analysis of a birth cohort of 4.2 million children, routine childhood immunization prevented 20 million vaccine-preventable diseases and 42,000 deaths due to vaccine-preventable disease. Vaccinating these 4.2 million children cost approximately $7.5 billion; however, the savings are estimated to be over $76 billion (direct and indirect costs). Importantly, every dollar spent on childhood vaccination results in $10 in cost savings (a benefit to cost savings of 10 to 1). Few other medical interventions have this degree of benefit to cost savings. Adult and adolescent vaccine programs have also been shown to be cost saving.

The ideal vaccine is potent, inexpensive to produce, stable at room temperature, and safe. Ideally, vaccines would have few or no systemic adverse effects, a long shelf life, and would be safe for use in pregnant women. Other factors that would make an ideal vaccine are a known correlate of immunity, an easily measured correlate of immunity, long-lived immunity – with no need for boosters – and efficacy not affected by circulating immunity. Lastly, an oral vaccine, rather than an intramuscular or subcutaneous route of administration, would be desirable. Unfortunately, there are no ideal vaccines; however, some of them are close.

Exhibit 2 lists the many goals of vaccination and a single vaccine can have multiple goals. For example, measles vaccine can prevent disease pre-exposure and post-exposure, provide herd protection, and eliminate or eradicate disease. Another example is influenza vaccine. In a given season, the vaccine might be 50 percent effective in preventing infection, but 70 percent effective for reducing severity (i.e., preventing hospitalization and death).

In the U.S., the FDA approves vaccines based on data submitted by manufacturers after review of efficacy and safety. The Advisory Committee on Immunization Practices (ACIP) is the committee that provides the CDC with advice regarding immunizations; final recommendations from the ACIP are official CDC recommendations. The committee has 15 members, who meet three times annually, and includes liaisons from government agencies (e.g., Health and Human Services, Department of Defense) and professional organizations (e.g., American Medical Association). FDA approval is required prior to ACIP recommendations and the ACIP is not bound by the approved FDA label. The Affordable Care Act included a stipulation that ACIP recommendations trump FDA label with regard to insurance coverage. The ACIP recommendations are published in the Morbidity and Mortality Weekly Report (MMWR).

ACIP recommendations are now developed using an explicit evidence-based method based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Category A recommendations are made for all persons in an age- or risk-factor-based group. Category B recommendations are made for individual clinical decision making. The GRADE approach relies on randomized controlled trials and observational studies only and considers strengths (strength of study, dose-response) and weaknesses (risk of bias, inconsistency, indirectness, imprecision and publication bias) of each study. The ACIP, unlike the FDA, also relies on cost-benefit analyses in making recommendations.

The ACIP publishes best practice guidelines for immunization. Some key recommendations are provided in these guidelines which are summarized here. Inactivated vaccines are safe for immunocompromised and pregnant persons;
However, the human papillomavirus (HPV) vaccine is not recommended for use in pregnant women. Influenza and tetanus/diphtheria/acellular pertussis (Tdap) are specifically indicated for pregnant women. Live-attenuated vaccines are contraindicated in immunocompromised and pregnant individuals, but there are exceptions for mild immunocompromising states. Breastfeeding is only a contraindication for smallpox and yellow fever vaccination. The guidelines state that vaccine doses can be provided at intervals beyond those recommended, but intervals cannot be shortened. In the case of missed dose(s) in a vaccine series, there is never a need to restart the series; clinicians should just provide additional vaccines as per the series recommendations. Simultaneous administration of vaccines is acceptable in most cases; there are a few exceptions which are detailed in the guidelines. Household contacts and other close contacts of individuals with altered immune competence should receive all age- and exposure-appropriate vaccines, with the exception of the smallpox vaccine. When assessing a patient’s vaccine

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### Exhibit 1: Impact of Vaccines in the U.S.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Maximum Cases per Year</th>
<th>2015 Cases</th>
<th>Percentage Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>206,939 (1921)</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Invasive Hib (&lt; 5 yrs)</td>
<td>20,000 (1984)</td>
<td>29</td>
<td>99.96%</td>
</tr>
<tr>
<td>Measles</td>
<td>894,135 (1941)</td>
<td>188</td>
<td>99.98%</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209 (1968)</td>
<td>1,329</td>
<td>99.13%</td>
</tr>
<tr>
<td>Meningococcal ACWY</td>
<td>330 (2008)</td>
<td>120</td>
<td>68.19%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>265,269 (1934)</td>
<td>20,762</td>
<td>92.17%</td>
</tr>
<tr>
<td>Polio</td>
<td>21,269 (1952)</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>57,686 (1969)</td>
<td>5</td>
<td>99.99%</td>
</tr>
<tr>
<td>Rubella (congenital)</td>
<td>20,000 (1964 - 1965)</td>
<td>1</td>
<td>99.99%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>601 (1948)</td>
<td>29</td>
<td>95.17%</td>
</tr>
</tbody>
</table>

^Indigenous 162, Imported 26  
Hib – Hemophilus influenza type B vaccine  
ACWY – Serogroups A, C, W, and Y

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### Exhibit 2: Goals of Vaccination

- **Prevent colonization**  
  - Conjugate vaccines for H. influenza, meningococci, pneumococci
- **Prevention infection (pre-exposure)**  
  - Live-attenuated polio vaccine  
  - Inhaled influenza vaccine
- **Prevent disease (pre-exposure)**  
  - Hepatitis A and B, tetanus, measles, mumps, rubies, rubella, others
- **Prevent disease (post-exposure)**  
  - Measles, varicella, smallpox, hepatitis A & B, tetanus, rubies
- **Reduce disease severity**  
  - Influenza, pneumococcal, varicella
- **Prevent reactivation**  
  - Zoster
- **Provide herd protection**  
  - Measles, mumps, rubella, varicella, polio, pneumococcal, others
- **Disease elimination** (Incidence of 0 in a selected area)  
  - Polio (Americas), measles (US)
- **Disease eradication** (Worldwide eradication)  
  - Smallpox, type 2 and 3 polio virus
- **Reduce incidence of infections due to multi drug resistant pathogens** (MRSA, Group A strep)  
  - Influenza, pneumococcal, varicella/zoster
- **Prevent cancer**  
  - Hepatitis B (liver), HPV (cervical, anal, vaginal, vulvar, oral)
Exhibit 3: Recommended Adult Immunization Schedule, 2018

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19 - 21 years</th>
<th>22 - 26 years</th>
<th>27 - 49 years</th>
<th>50 - 64 years</th>
<th>&gt; 65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tdap or Td</td>
<td></td>
<td>1 dose Tdap then Td booster every 10 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>1 or 2 doses depending on indication (if born in 1957 or later)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAR</td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RZV or ZVL</td>
<td></td>
<td></td>
<td>2 doses RZV (preferred)</td>
<td></td>
<td>or 1 dose ZVL</td>
</tr>
<tr>
<td>HPV - Female</td>
<td>2 or 3 doses depending on age at series initiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV - Male</td>
<td>2 or 3 doses depending on age at series initiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV13</td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
<td></td>
</tr>
<tr>
<td>PPSV23</td>
<td>1 or 2 doses depending on indication</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HepA</td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HepB</td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MenACWY</td>
<td>1 or 2 doses depending on indication, then booster every 5 years if risk remains</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MenB</td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib</td>
<td>1 or 3 doses depending on indication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection.

Recommended for adults with other indications

No recommendations

Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine
Td = tetanus and diphtheria toxoids
MMR = measles, mumps, and rubella vaccine
VAR = varicella vaccine
RZV = recombinant zoster vaccine
ZVL = zoster vaccine live
HPV vaccine = human papillomavirus vaccine

PCV13 = 13-valent pneumococcal conjugate vaccine
PPSV23 = 23-valent pneumococcal polysaccharide vaccine
HepA = hepatitis A vaccine
HepB = hepatitis B vaccine
MenACWY = serogroups A, C, W, and Y meningococcal vaccine
MenB, serogroup B meningococcal vaccine
Hib, Haemophilus influenzae type b vaccine

history, self-report is acceptable for influenza and pneumococcal but not any other vaccinations. Documented immunization for measles/mumps/rubella (MMR) and varicella trumps serology because serology values are not perfect. Finally, immunized individuals should be observed for 15 minutes after administration; the most common adverse effect is fainting.

Adult Immunization

Exhibit 3 shows the 2018 recommendations for adult immunization. Information to note on selected vaccinations is covered below. The guidelines contain additional specific recommendations for pregnancy, HIV infected, immunocompromised, asplenia, complement deficiencies, end-stage renal disease on hemodialysis, heart disease, lung disease, liver disease, alcoholism, diabetes, health care personnel, and men who have sex with men.

Influenza

Optimally, influenza vaccination should occur before the onset of influenza activity in the community. Health care personnel should offer vaccination by the end of October, if possible. Available influenza vaccines include trivalent and quadrivalent inactivated (IIV3 and IIV4), cell culture-based quadrivalent (cIIV4), adjuvanted trivalent (aIIV3), high dose trivalent inactivated (HD-IIV3), intradermal quadrivalent (ID4), recombinant quadrivalent (RIV4), and live...
attenuated intranasal quadrivalent (LAIV4). Trivalent influenza vaccine is being replaced by quadrivalent vaccines. RIV, which does not contain any egg protein, may be administered to persons aged 18 years and older with egg allergy of any severity. IIV may be used with additional safety measures for persons with hives-only allergy to eggs. For the 2018 to 2019 influenza season, providers may choose to administer any licensed, age-appropriate influenza vaccine (IIV, RIV4, or LAIV4). No preference is expressed for any influenza product in the ACIP guidelines. Some studies, but not all, have shown that high-dose IIV3 is better at reducing illness rates in the elderly, compared with standard-dose IIV3, but adverse effects are higher with the higher dose.7-11

Pneumococcus

Two pneumococcal vaccines are available: 23-valent pneumococcal polysaccharide vaccine (PPSV23) and 13-valent pneumococcal conjugate vaccine (PCV13). The additional strains covered by PPSV23 provide coverage for an additional 20 to 30 percent of infecting organisms. Both vaccines work to prevent invasive disease. The conjugate vaccine prevents pneumonia better, and the polysaccharide vaccine helps prevent meningitis better. The PCV13 has one strain – 6A – which is not included in PPSV23. The differences in the vaccine benefits are why giving both vaccines is recommended in certain cases (Exhibit 4). Administration of both PPSV23 and PCV13 are recommended for adults greater than 65

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Exhibit 4: Adult Pneumococcal Vaccine Timing

**Age 65 Years and Older**

*If PCV13 was given before age 65, no additional PCV13 is needed.

- No history of pneumococcal vaccine
  - PCV13 (Prevnar 13®)
  - 1 Year (8 weeks for groups B and C as defined below)
  - PPSV23 (Pneumovax 23®)

- Received PPSV23 before age 65
  - 1 year
  - PCV13
  - 1 Year (8 weeks for groups B and C as defined below) and 5 years after prior dose of PPSV23

- Received PPSV23 at age 65 or older
  - 1 year
  - PCV13

**Age 19 - 64 years with Underlying Medical Condition(s)**

- A. Smoker, long-term facility resident, or chronic conditions:
  - Heart Disease (excluding hypertension)
  - Lung Disease (including Asthma)
  - Liver Disease (including cirrhosis)
  - Diabetes
  - Alcoholism
  - PCV13
  - 8 Weeks

- B. Immunocompromised
  - HIV Infection
  - Chronic Renal Failure
  - Nephrotic Syndrome
  - Asplenia
  - PCV13
  - 8 Weeks

- C. CSF Leaks or Cochlear Implants
  - PCV13
  - 8 Weeks

*For further information, see: [http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm](http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm)*
years of age and for selected adults 19 to 64 years of age with immunocompromised states, cochlear implants, and cerebrospinal fluid leaks. PPSV23 alone is recommended for adults 19 to 64 years of age with certain chronic diseases (heart or lung disease, diabetes mellitus, alcoholism, liver disease, smoking). Booster doses are not recommended for PCV13; however, for PPSV23, up to three total doses may be provided per ACIP guidelines.

**Pertussis**

The majority of serious cases of pertussis are in infants and young children. There has been an increase in cases of pertussis in the U.S. since 2000. Infants aged less than 12 months accounted for 145 (93%) of 156 pertussis-related deaths reported to the CDC for 2000 to 2006. To protect infants until they are old enough to have immunizations, pregnant women should receive a dose of Tdap vaccine during each pregnancy (preferably during 27–36 weeks’ gestation) regardless of the interval since the prior Td or Tdap vaccination. Tdap immunization of pregnant women has been shown to transfer pertussis antibodies to the newborn and to be very effective in reducing cases of pertussis from birth to 18 months of age. Individuals aged 11 and older who have not received Tdap vaccine, or for whom vaccine status is unknown, should receive a dose of Tdap followed by tetanus and diphtheria toxoids (Td) booster doses every 10 years thereafter. Tdap can be administered regardless of the interval since the most recent tetanus or diphtheria toxoid-containing vaccine. In cases of wounds, Tdap or Td should be provided as prophylaxis.

**Zoster**

Zostavax® is a live attenuated vaccine indicated to prevent herpes zoster was originally licensed in the U.S. in 2006. It has been recommended for all adults over 60 years of age. In 2017, a new recombinant vaccine, Shingrix®, was approved; it is recommended for the prevention of herpes zoster and related complications for immunocompetent adults aged 50 years and older. Shingrix® is recommended for the prevention of herpes zoster and related complications for immunocompetent adults who previously received Zostavax® two months or longer ago. Screening for a history of varicella (either verbally or via laboratory serology) before vaccination for herpes zoster is not recommended. Adults with a history of herpes zoster should receive Shingrix®. Although not specifically indicated in immunocompromised patients, the recombinant vaccine is safe to use in those patients. Shingrix® has a higher efficacy rate (90-97% vs 51–64%), but it causes a higher rate of severe injection site reactions and systemic reactions than Zostavax®.

Overall, Shingrix® is preferred over Zostavax® for the prevention of herpes zoster and related complications.

**Meningococcus**

There are two different vaccine types to prevent meningococcal infections – meningococcal serogroups A, C, Y, W (MenACWY, Menactra®, Menveo®) and meningococcal serogroup B vaccines (MenB). Menactra® is recommended for ages 9 months to 55 years and Menveo® for ages 2 to 55 years. Meningococcal polysaccharide vaccine (MPSV4, Menomune®) is recommended for ages 56 and older. Meningococcal serogroup B vaccines (MenB) vaccines include Trumenba®, indicated for ages 10 to 25 years (given at 0, 6 months or 0, 1 – 2, 6 months) and Bexsero®, indicated for ages 10 to 25 years (2 doses at least 1 month apart). MenB vaccination is a Category B recommendation for adolescents because incidence of meningococcal disease is decreasing, meningococcus serogroup B disease is uncommon in adolescents and adults, and the duration of protection is unknown. However, outbreaks continue to occur and there is substantial morbidity and mortality with meningococcal disease.

**Hepatitis B**

The rate of hepatitis B virus (HBV) infection has dramatically declined since the introduction of the vaccine. Strategies to eliminate HBV transmission in the U.S. include screening of all pregnant women, prophylaxis (HBV vaccine and hepatitis B immune globulin) for infants born to hepatitis B surface antigen (HBs-Ag) positive women, universal vaccination of infants beginning at birth, and routine vaccination of previously unvaccinated children less than 19 years of age. Vaccination of at-risk adults is recommended in those with intravenous drug use, individuals who have unprotected sex, household contacts of persons with chronic HBV, health care personnel, hemodialysis patients, hepatitis C virus-positive persons, persons with chronic liver disease, HIV-positive individuals, diabetics, and travelers to endemic countries. HBV vaccines (Engerix-B®, Recombivax-HB®) are given on a 0, 1, and 6 month schedule. A high-dose formulation is available for hemodialysis patients. Post-exposure prophylaxis is given to children born to HBV-positive women, health care providers exposed to blood or potentially infectious material, and in cases of sexual assault.

Heplisav-B® is a yeast-derived vaccine prepared with a novel adjuvant and administered as a two-dose series (0, 1 month) for persons aged 18 and older. It was approved by the FDA in 2017 and
recommended by the ACIP in 2018. It can be used for revaccination of health care providers, in immunocompromised persons, and for patients on hemodialysis. In a comparison trial, two doses of this vaccine achieved seroprotective anti-hepatitis B levels in 90 to 100 percent of subjects, compared with 70.5 to 90.2 percent of subjects receiving three doses of Engerix-B. Similar rates of adverse effects were seen with each vaccine.

Multiple outbreaks of HBV associated with blood glucose monitoring plus inadequate infection control practices in health care settings have occurred. Thus, HBV vaccination should be administered to unvaccinated adults with diabetes who are aged 19 through 59 years (Category A recommendation) and may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes who are 60 years of age or older (Category B).

**Immunocompromised Patients**

All recommended vaccines should be provided as early in the course of immunosuppressive disease as possible. Vaccines given prior to immunosuppressive therapy result in immunologic memory and patients do not require revaccination (except when stem cell transplantation occurs). Certain types of corticosteroid therapies are not a contraindication to live virus vaccine. This includes short-term regimens (i.e., < 14 days); chronic low- to moderate-dose regimens (< 20 mg prednisone or equivalent per day); long-term, alternative-day therapy with short-acting preparations; maintenance physiologic doses (replacement therapy); and topical, inhaled, or by intra-articular, bursal, or tendon injection regimens. All inactivated vaccines (killed whole cell, recombinant, subunit, toxoid, and polysaccharide) can be administered safely, regardless of immune compromise. Live vaccines should not be administered for at least three months after immunosuppressive therapy has been discontinued. Patients vaccinated within 14 days before starting immunosuppressive therapy should be considered unimmunized and should be revaccinated at least three months after therapy is discontinued, if immune competence has been restored.

**Childhood Immunization**

For infants and children, the U.S. primarily has a culture of vaccination. Providers expect to administer vaccines and parents expect their children to receive vaccines. Except for the small portion of the population that refuses vaccination for their children, for the most part vaccines are part of pediatric care across the country. The ACIP guidelines provide recommendations for childhood immunization.

**Adolescent Immunization**

The culture of immunization is not as prevalent in adolescent care. For many years, families have considered vaccination as something that started in infancy and ended at school age. The number of recommended vaccines for adolescents has increased from one (Td booster) to four (Tdap, HPV, meningitis, influenza) between 2000 and 2010 (Exhibit 5). Today’s parents of adolescents did not receive these vaccines as teenagers and many are not aware of the need for vaccination. As shown in Exhibit 6, the rates of Tdap and meningitis vaccination in 2016 were much higher than those for HPV. This data shows that school mandates work; in many states Tdap and meningitis are mandated for school enrollment in sixth grade or ninth grade, but HPV is not. Access does not appear to be the issue with the low HPV rates because most insurance plans cover its use. It appears likely to be a combination of providers not recommending the HPV vaccination, and families choosing only to have state mandated vaccinations.

**HPV**

Clinicians and managed care need to work to increase HPV vaccination rates because it is the most

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<table>
<thead>
<tr>
<th>Exhibit 5: Adolescent Immunizations⁶</th>
</tr>
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<tbody>
<tr>
<td><strong>Tdap (tetanus, diphtheria, acellular pertussis)</strong></td>
</tr>
<tr>
<td>- First dose at 11 - 12 years old, then every 10 years</td>
</tr>
<tr>
<td><strong>HPV (Gardasil9)</strong></td>
</tr>
<tr>
<td>- Two doses, 6+ months apart, if started before age 15</td>
</tr>
<tr>
<td>- Three doses (0, 2, 6 months) if started 15+ years old</td>
</tr>
<tr>
<td><strong>Meningitis</strong></td>
</tr>
<tr>
<td>- Meningitis conjugate (MenACWY)</td>
</tr>
<tr>
<td>- First dose 11 - 12 years old</td>
</tr>
<tr>
<td>- Booster dose at 16 years old</td>
</tr>
<tr>
<td><strong>Meningitis B vaccine</strong></td>
</tr>
<tr>
<td>- Dose at 16 - 23 years old</td>
</tr>
<tr>
<td><strong>Influenza (annually)</strong></td>
</tr>
</tbody>
</table>
common sexually transmitted infection in the U.S., with more than 6.2 million new genital infections every year. Nearly three-quarters of new infections are in the 15 to 24-year-old age group. By 50 years of age, greater than 80 percent of Americans will have acquired at least one genital HPV infection. Although the peak age of infection is 20 to 24 years of age, women still have a significant risk of HPV infection throughout their lifetime. The peak age for men to have high-risk HPV (more likely to cause cancer) is 30 to 34 years and, as with women, risk for infection continues throughout their lifetime.

HPV is responsible for over 90 percent of cervical, 70 percent of oropharyngeal, 91 percent of anal, 75 percent of vaginal, 69 percent of vulvar, and 63 percent of penile cancers. Some researchers believe that all anogenital cancers are caused by HPV, but that has not yet been proven. Overall, most infected people will not go on to develop HPV-related cancer, but because it is such a prevalent infection and there is the risk of cancer, vaccination is important.

HPV is now a recognized cause of oropharyngeal cancer (OPC). The incidence of HPV-related OPC is increasing, particularly among males. From 1988 to 2004, there was a 225 percent increase in HPV-related OPC in the U.S. By 2030, half of all head and neck cancer cases will be HPV related. Tobacco and alcohol use remain major risk factors for OPC; however, the increase in OPC has occurred, despite a decrease in tobacco use. Many HPV-positive cancers occur among never smokers. If the trend continues, HPV-related OPC will exceed the incidence of cervical cancer in coming years; there are already more men with HPV-related cancer than women.

Unfortunately, from a public health perspective, calling HPV infection a sexually transmitted disease (STD) is an issue because the term STD is fraught with stigma and judgment. This virus is so prevalent that the mode of transmission becomes irrelevant. HPV is transmitted by any surface to surface contact, which is why it is so prevalent. It can be transmitted by finger to genital contact, and condoms are only partially effective prevention (~70%). Some adolescents have tested positive for vaginal HPV prior to their first vaginal sexual intercourse. Additionally, the virus can spread across the anogenital region. For example, this can increase risk of anal cancer in someone who has only had vaginal intercourse.

The HPV vaccine has been available for over 10 years and has been demonstrated to be safe and effective. Greater than 350 million doses have been given worldwide. The most common adverse effects with this vaccine are arm soreness and myalgias. The safety of HPV vaccine is similar to the safety of all
Within six years of vaccine approval in the U.S., there was an 89 percent reduction in HPV 6, 11, 16, and 18 infections in females 14 to 24 years of age who received one or more doses, compared to unvaccinated females.29 Interestingly, there was a 17 to 49 percent reduction of HPV infection in unvaccinated females, which is potentially an indicator of herd immunity. A 72 percent decline in HPV 16 and 18 precancerous cervical lesions was seen four years after vaccination in women given one or more doses. Because it can take many years to develop some of the cancers from HPV (such as OPC), the full cancer prevention benefit of this vaccine will not be seen for decades.

In terms of giving the HPV vaccine, only the 9 strain vaccine (Gardasil9®) is currently marketed in the U.S. The 2 and 4 strain products have been discontinued. The two or three doses (depending on age at start) should be given at least six months apart, but the interval can be as long as one year. Delaying the time between doses delays full immunity; however, the vaccine series does not have to be restarted if the patient is late getting a dose. Under spacing is more of a concern than over spacing. As of today, there is no recommendation for booster injections of HPV vaccine. It will take time to fully understand how long immunity lasts from the initial vaccine series.

**Strategies to Increase HPV Vaccination**

Specifically for HPV vaccination, there are challenges to vaccinating adolescents. Parents do not want to think about their children being sexually active, but vaccines can only prevent disease to which you have not yet been exposed. It is important to immunize before exposure to HPV, but most parents do not know how immunizations work. Many clinicians initially took the wrong approach when talking with parents about this vaccine by focusing on sexual transmission, and they scared parents with too much information. The approach to consider is less information is more. Clinicians can just state that the patient will be getting routine vaccines which include HPV. This is how clinicians approach vaccination for infants. HPV vaccine needs to be treated just like all other vaccines, with an announcement that vaccination will occur rather than a conversation about whether to vaccinate.30-32 An example would be “Today your son is due for three routine vaccines which include HPV, meningitis vaccine, and Tdap (which is tetanus), diphtheria, and whooping cough. Someone will be right in to administer those vaccines, and I look forward to seeing you next year.” If questions arise about the HPV vaccine, clinicians can focus their discussion on why we have a HPV vaccine (cancer prevention) and not the mode of transmission. Example statements can include “We can reduce the chances of your son having a cancer experience. Do you want to reduce the chances of your son having cancer?”

Parents may not be thinking about cancer in their adolescents. The median age of cervical cancer diagnosis is 47; more than 14 percent occur before age 35.33 The oropharynx cancer median age of diagnosis is 62 years, but 30 percent occur before age 50. HPV-related OPC typically occurs in those 50 or younger.34,35 The median age for anal cancer is 60 years, and more than 30 percent of cases occur before the age of 55.33

Overall, HPV is a life course infection. It requires prevention during adolescence, can cause disease during adulthood, and importantly infection can occur throughout the lifetime. HPV disease prevention requires an all-out effort by everyone involved. A clinician’s recommendation is most effective for vaccination to occur.

**Overcoming Barriers to Vaccination**

In addition to the issues related to HPV vaccination in adolescents discussed previously, there are numerous other barriers to vaccination in general (Exhibit 7). In one study, the most common physician explanations for why adults did not receive pneumococcal vaccine...
were lack of well visits, concern about adverse effects, lack of knowledge, and fear of needles. Patients said that they were healthy and did not need the vaccine, their doctor had not recommended it, or they were worried about adverse effects. To help increase vaccination rates in all populations, health care providers and systems need to make vaccinations available, assess a patient's vaccine status at every visit, educate patients about the risks and benefits of vaccination, administer and document vaccinations properly, and develop procedures for vaccinations. Strategies to improve vaccination rates can include patient reminders, and health systems and providers partnering with the community for education and vaccination programs. Client reminder systems, multicomponent interventions including education, and requirements for entry to schools, childcare facilities, and colleges are all proven interventions for increasing community demand for vaccination. All types of reminders (postcards, letters, and telephone or autodialed calls) are effective; telephone calls are most effective, but are most costly. Recommended strategies to enhance access to vaccine services include reducing out-of-pocket costs; enhancing access through the U.S. Department of Agriculture Women, Infants, and Children program; home visits, outreach, and case management; and enhanced access at schools. Strongly recommended strategies to help providers improve their vaccination rates include automated recall/reminder systems, assessment and feedback on performance, and standing orders. Exhibit 8 lists some patient-related barriers and solutions to overcome those barriers.

**Conclusion**

Overall, vaccines reduce morbidity and mortality and are cost effective. Increasing rates of HPV vaccination among adolescents and continuing to push for improvements in adult vaccination rates should both be missions for providers, health systems, and managed care. Although there are barriers to vaccination in all patient populations, these can be overcome with proven strategies.

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**References**


