Vaccination of Adults in General Medical Practice

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Abstract

In vaccinating adults, clinicians face 2 types of challenges: (1) staying current on recommendations for influenza, pneumococcal, hepatitis A and B, zoster, and other vaccines and (2) addressing systemic barriers to implementing practices that increase vaccination rates. Although adult immunization rates remain suboptimal, there has been much good news in adult vaccination recently. New high-dose and adjuvanted influenza vaccines help improve immune response and may reduce influenza complications in older adults. The new recombinant zoster vaccine offers significantly more efficacy against zoster outbreaks and postherpetic neuralgia than zoster vaccine live. Pertussis vaccine given during the third trimester of pregnancy may prevent between 50% and 90% of pertussis infections in infants. Shorter time for completion (1 vs 6 months) of new, adjuvanted hepatitis B vaccine may increase adherence. Clinicians can address systemic barriers to increasing vaccination rates in their clinics and health care systems by following the Centers for Disease Control and Prevention's Standards for Adult Immunization Practice. Clinicians can help increase vaccination rates by writing standing orders and by advocating for nurses or medical assistants to receive training and protected time for assessing and documenting vaccination histories and administration. Strong recommendations that presume acceptance of vaccination are effective with most patients. Communication techniques similar to motivational interviewing can help with vaccine-hesitant patients. Clinicians, as experts on providing preventive services, can educate community leaders about the benefits of immunization and can inform vaccine experts about challenges of implementing vaccination recommendations in clinical practice and strategies that can work to raise vaccination rates.

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In vaccinating adults, clinicians face 2 types of challenges: (1) staying current on recommendations for influenza, pneumococcal, hepatitis A and B, zoster, and other vaccines and (2) addressing systemic barriers to implementing practices that increase vaccination rates. Although adult immunization rates remain suboptimal, there has been much good news in adult vaccination recently. As experts on providing preventive services, clinicians can educate community leaders about the benefits of immunization and can inform vaccine experts about challenges of implementing vaccination recommendations in clinical practice and strategies that can work to raise vaccination rates.

VACCINE-PREVENTABLE DISEASE

Public health experts rank the reduction in vaccine-preventable diseases as one of the top 10 public health achievements in the 21st century.[1] In addition to seeing tremendous advances in childhood and adolescent vaccinations, the past 2 decades witnessed substantial advances in adult vaccinations. In the last review of adult vaccines in *Mayo Clinic Proceedings* in 1999, Reid et al[2] emphasized that "In the United States, between 50,000 and 90,000 adults die each year from pneumococcal disease, influenza, and hepatitis B infection," highlighting the need to focus on adult vaccinations. Indeed, over the past 2 decades, new recommendations for adults have been issued for vaccines targeting influenza, pneumococcal infection, pertussis, hepatitis A, hepatitis B, human papillomavirus (HPV), and herpes zoster, among other infections. These vaccines are recommended for large numbers of patients aged 18 years and older seen by clinicians

For Limelight, see page 29

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in family medicine and general internal medicine practices. Vaccine recommendations for patients younger than 18 years, most risk-based vaccine recommendations (especially for immunocompromised patients), and vaccines for international travel, health care workers, and emerging infections are topics for other articles in this *Mayo Clinic Proceedings* series of Thematic Reviews on Vaccines. In particular, vaccines for measles, mumps, rubella, varicella, *Hemophilus influenzae* type B, and meningococcal disease are not included in this article.

In addition to keeping up with advances in vaccines and new immunization recommendations, clinicians face many challenges to delivering immunizations to adults, as demonstrated by suboptimal immunization rates (Table 1).[3] For example, in 2016, influenza immunization rates were only 43% for adults over 18 years and only 70% for adults over 65 years. Less than 10% of adults received hepatitis A vaccine. For pneumococcal, pertussis, hepatitis B, HPV, and zoster, only 25% to 67% of adults received these vaccines. In addition, only about 50% of pregnant women receive influenza or tetanus, diphtheria, and acellular pertussis vaccine (Tdap) vaccinations, and only about 33% receive both.[4]

On a positive note, strong evidence shows that increasing immunization rates reduces morbidity and mortality via both direct and indirect protection. Even though its effectiveness is less than perfect, influenza vaccine still directly protects adults who receive it,[5] although season-to-season variations make calculating deaths from influenza difficult. Estimates put the death toll of the 2017-2018 influenza season at about 80,000, making it one of the deadliest since 1976.[6] Complex modeling, however, suggests that prior to the 2017-2018 season, recent annual deaths related to influenza usually range from 4000 to 20,000.[7]

Decreases in pneumococcal disease and acute hepatitis B infections in adults seem to have resulted mainly from indirect effects of herd immunity from childhood vaccinations rather than increased vaccination of adults. From 1998 to 2016, rates of invasive pneumococcal disease (IPD) in adults decreased by 50% following introduction of 7-valent conjugate vaccine in children in 2000 and its replacement by 13-valent vaccine in 2010.[8] From 2000 to 2014, rates of reported acute hepatitis B in younger adults (20-49 years) also decreased by 50%.[9]

Recent encouraging evidence supports some strategies for raising adult immunization rates, including changes that clinicians can make in communication with patients, practice-based improvements, health care system changes, and policies. Raising adult immunization rates will require scaling up these evidence-based strategies in clinics, health care systems, and communities everywhere.

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES RECOMMENDATION PROCESS

The 15 members of the Advisory Committee on Immunization Practices (ACIP) meet 3

TABLE 1. Adult Vaccination Rates[a]

Vaccine	Age (y)			
	>18	19-49	50-64	>64
Influenza	43.5%	32.1%	46.4%	70.4%
Pneumococcal	NA	24.0%[b]	24.0%[b]	66.9%[b]
Tdap	26.6%	28.0%	28.0%	20.4%
Hepatitis A	9.5%	13.4%	5.4%	5.4%
Hepatitis B	24.8%	32.9%	15.9%	15.9%
ZVL	NA	NA	23.9%	37.4%
HPV, 1 dose	19-26 y: female, 48.5%; male, 13.5%			

[a]HPV = human papillomavirus vaccine; NA = not applicable; PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; Tdap = tetanus, diphtheria, and acellular pertussis vaccine; ZVL = zoster vaccine live.

[b]PPSV23 and/or PCV13 as recommended by age and medical condition.

Data from the Centers for Disease Control and Prevention.[3]

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times yearly to vote on recommendations for use of vaccines in general medical practice (Table 2). The director of the Centers for Disease Control and Prevention (CDC) reviews and approves ACIP recommendations before they become official CDC guidance with publication in the *Morbidity and Mortality Weekly Review*. Inclusion of liaisons from the American Academy of Pediatrics, American College of Physicians, American Academy of Family Physicians, American College of Obstetricians and Gynecologists, American Medical Association, and other professional societies in ACIP deliberations promotes harmonization of those groups' recommendations with the ACIP's recommendations.[10,11] One of the authors of this review (S.A.F.) is the American Medical Association liaison to the ACIP. The other 2 authors of this article (P.H., P.G.S.) are ACIP voting members. The CDC annually updates the adult immunization schedule, which summarizes current ACIP recommendations for all vaccines for routine medical practice.[12]

Part 1 of this article summarizes current recommendations for and clinical challenges with influenza, pneumococcal, pertussis, hepatitis A and B, HPV, and zoster vaccines. Part 2 describes how clinicians can address systemic barriers to increasing vaccination rates in their clinics and health care systems by following the CDC's Standards for Adult Immunization Practice (Table 3).[13]

TABLE 2. Advisory Committee on Immunization Practices

ACIP makes recommendations about:
Age for administration
Number of doses
Dosing interval
Precautions and contraindications
Goals:
Decrease disease
Increase safety
Members:
14 Medical experts
1 Consumer representative
4-Year terms
Recommendation process:
Votes in February, June, and October
Approval by CDC director
Publish in *MMWR* later
Recommendations differ from:
FDA indications
State-mandated school requirements

ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; FDA = Food and Drug Administration; *MMWR* = *Morbidity and Mortality Weekly Review*.
Data from the Centers for Disease Control and Prevention.[10]

PART 1: CURRENT CHALLENGES IN CLINICAL IMMUNIZATION PRACTICE

Influenza

Epidemiology, Disease Burden, and Vaccine Choices. Universal influenza vaccine would ideally prevent all strains of both types A and B, with efficacy potentially lasting multiple years. However, the quest for a universal influenza vaccine faces very significant technical challenges.[14,15] Current influenza vaccines are either trivalent or quadrivalent. Trivalent influenza vaccines contain 3 antigens: 2 type A lineage (usually H3N2 and H1N1) and 1 of 2 type B lineages (Victoria or Yamagata). Influenza B lineages in trivalent vaccines did not match circulating lineages in 6 of 12 seasons between 2000 and 2011.[16] Because quadrivalent influenza vaccines contain both B lineages, mismatch with circulating B strains is less likely with quadrivalent than with trivalent vaccines. Current vaccines include inactivated influenza vaccine (IIV), recombinant influenza vaccine (RIV), and live attenuated influenza vaccine (LAIV). Virus for one version of IIV is grown in cell culture.

Since 2010, to prevent complications of influenza, especially pneumonia, the ACIP has recommended immunizing all patients 6 months and older annually with vaccines appropriate for their ages and medical conditions.[17] However, there are significant

TABLE 3. Centers for Disease Control and Prevention's Standards for Adult Immunization Practice

1. Assess adults' vaccination status at every clinical encounter
2. Strongly recommend needed vaccines
3. Either offer needed vaccines or refer patients to another provider who can administer the recommended vaccine
4. Document the vaccines administered in the state's immunization information system[13]

challenges to achieving high annual vaccination rates. Younger adults, 19 to 49 years old, have lower rates of influenza vaccination (32.1%) and fewer complications, but infected, healthy, younger adults may feel well enough to continue to interact socially and professionally with and transmit influenza to older adults, 65 years and older.[18]

Because older adults have development of more influenza complications and less immunity after vaccination, manufacturers created high-dose and adjuvanted vaccines specifically for older adults. Intradermal influenza vaccine is not being marketed in the United States, apparently because of low demand. Adjuvanted vaccines generally have significantly higher rates of local reactions, especially pain, swelling, and redness.[19] High-dose IIV contains 4 times as much antigen as standard-dose IIV. One study found that 1.4% of older adults vaccinated with high-dose vaccine had development of laboratory-detected influenza infections vs 1.9% of those receiving standard-dose vaccine.[20] In other words, vaccinating 200 older adults with high-dose rather than standard-dose vaccine may prevent one additional influenza infection. The ACIP has not made preferential recommendations for trivalent high-dose or adjuvanted influenza vaccines over quadrivalent, standard-dose, nonadjuvanted influenza vaccines. However, with the US Food and Drug Administration (FDA) approval of a quadrivalent version of high-dose influenza vaccine in November 2019,[21] the ACIP may intensify its ongoing review of comparative effectiveness of influenza vaccines.

Live attenuated influenza vaccine can be used in nonpregnant, healthy persons from ages 2 through 49 years. The effectiveness of LAIV, acceptability of intranasal vs intramuscular route, and LAIV as a percentage of total vaccine administered all decrease as the ages of the vaccinated persons increase.[22,23] Between 2014 and 2018, changes in the ACIP recommendations about LAIV—from preferred for young children to recommended against for all ages and back to routinely recommended—had limited effects on adults because of its limited use in young adults. For the 2018-2019 influenza season, the ACIP recommended that LAIV be added back to the list of recommended influenza vaccines (without a preferential recommendation for any vaccine) based on data showing similar effectiveness against H3N2 and B strains, as well as data on the new H1N1 vaccine strain showing improved replicative fitness.[24] However, based on ongoing concern about past decreased effectiveness against the H1N1 strain, the American Academy of Pediatrics and the American Academy of Family Physicians currently recommend using IIV and RIV preferentially over LAIV for 2018-2019.

Efficacy, Timing, and Interchangeability. Influenza vaccine efficacy varies significantly from season to season based in part on how well vaccine strains match circulating strains. Annually, epidemiologists recommend vaccine strains for the Northern Hemisphere based on strains circulating recently in the Southern Hemisphere because these strains tend to foreshadow strains in other parts of the world. Choice of vaccine strains occurs early in the calendar year because of production issues such as virus growing slowly in chicken embryos. Although cell culture and recombinant methods make influenza vaccine supplies more resilient, neither method has so far produced vaccine dramatically faster than egg-based methods. Because of slow manufacturing processes, most influenza vaccine must be ordered by "prebooking" at least several months before delivery.

Timing influenza vaccination efforts challenges clinicians and public health professionals. Because antibodies develop over 2 weeks and then wane over several weeks and because dates of peak influenza activity vary widely year to year, predicting the best times to vaccinate is nearly impossible. The ACIP recommends that adults should be offered influenza vaccination (appropriate for age and health status) by the end of October.[24] Many health care systems and health departments already have a practice of scheduling large vaccination events in late October. However, the logistics of vaccinating many patients in narrow time frames challenges practitioners and public health leaders. In addition, the

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ACIP recommends using IIV and RIV interchangeably and as licensed by age.[24]

Egg Allergy Is Not a Contraindication. Severe allergic reaction to any component of any vaccine contraindicates repeating that vaccine. Because studies indicate that severe allergic reactions in people with egg allergies are unlikely, the ACIP no longer considers egg allergy as a contraindication to influenza vaccination. However, for patients with egg allergy symptoms other than hives (such as angioedema, respiratory distress, lightheadedness, recurrent emesis, or requiring epinephrine or another emergency medical intervention), the ACIP recommends vaccinating under supervision of "a health care provider who is able to recognize and manage severe allergic conditions."[25] The amount of egg protein in influenza vaccines grown in eggs is very small. Recombinant influenza vaccine (RIV) and the updated formulation of IIV grown in cell culture (ccIIV) do not contain any egg protein.

Pneumococcal Vaccines

Two pneumococcal vaccines are currently available: 23-valent pneumococcal polysaccharide vaccine (PPSV23) and 13-valent pneumococcal conjugate vaccine (PCV13). The PPSV23 has antigens from 11 strains of *Strepococcus pneumoniae* that are not in PCV13.

Pneumococcal vaccines prevent invasive disease, especially meningitis in young children and bacteremia in older adults. The FDA licensed PPSV23 in 1983 to replace the 14-valent vaccine licensed in 1977.[26] In 1989, the ACIP recommended PPSV23 for adults with certain medical conditions.[27] In 1997, the ACIP started recommending PPSV23 for everyone 65 years and older.[26] The FDA licensed PCV13 in 2010, replacing a 7-valent formulation licensed in 2000. Since 2000, the ACIP has recommended 4 doses of pneumococcal conjugate vaccine before age 6 years for all healthy children.[28] Because vaccinating children with PCV13 prevents much of the pneumococcal disease in adults via herd immunity, European countries did not add PCV13 to their adult schedules.[29]

In contrast, in 2012 the ACIP recommended PCV13 in addition to PPSV23 for immunocompromised adults and in 2014 for all adults 65 years and older. The 2014 recommendation also called for reviewing data in 2018. In 2019, ACIP completed this data review and debated whether vaccinating immunocompetent adults 65 years and older has significant direct effects on reducing pneumococcal disease.[30] This review was complicated by the difficulty in determining how well pneumococcal vaccines prevent community-acquired (nonbacteremic) pneumonia.[31] In June 2019, ACIP voted to remove the routine recommendation to vaccinate immunocompetent adults 65 years and older with PCV13 and replace it with a recommendation for vaccinating this group based on shared clinical decisionmaking. This involves clinicians and patients discussing specific medical conditions and patient values regarding the benefits and risks of vaccination.[30]

The complexity of pneumococcal recommendations—which combine 2 different vaccines and both risk- and age-based schedules that changed multiple times in recent years—have created significant challenges to accurate implementation in clinical practice. Should manufacturers produce conjugate vaccines that cover additional pneumococcal strains, incorporating such new vaccines into recommendations for adults may be just as challenging as PCV13 in 2014.

Pertussis and Tdap Vaccination

The ACIP recommends that Tdap be given once to adolescents and adults at age 11 years or older. Although adults can experience severe complications from pertussis (seizures, fractures, and syncope from weeks of severe coughing), outside of infancy pertussis infections usually cause mild, nonspecific respiratory symptoms. However, children (especially siblings) and adults transmit infections to very young infants, who may be incompletely vaccinated and who can experience severe illness and death from pertussis.[32] Among other barriers, billing issues make it very difficult to vaccinate adults who have frequent contact with newborns. Consequently, efforts to prevent pertussis in infants emphasize Tdap

given during each pregnancy (preferably from 27 through 36 weeks' gestation) to prevent pertussis in newborns via passage of antibodies from mother to baby through the placenta and in breast milk.[33] This practice is an off-label use of Tdap, recommended by the ACIP but not licensed by the FDA. Prenatal maternal vaccination with Tdap may prevent between 50% and 90% of pertussis infections in infants.[34]

In January 2019 the FDA approved a second dose of Tdap (Adacel brand) to be given 8 years after the first.[35] In October 2019, the ACIP voted to recommend Td and Tdap to be used interchangeably for the booster every ten years for adults, for tetanus prophylaxis for wound management, and for catch-up immunization schedule for persons age 7 and older, including pregnant women.[36] This was based on reassuring safety data on multiple Tdap doses and overwhelming use of Tdap relative to Td in clinical practice.

The association of whole-cell vaccine with rare cases of intractable seizures in young children spurred the switch from whole-cell to acellular pertussis vaccine in the 1990s. Immune responses to acellular pertussis vaccine are initially equal those of whole-cell vaccines.[37] However, immunity wanes rapidly after acellular vaccines.[38] Development of a vaccine with more durable effectiveness does not appear imminent.[39]

Hepatitis A

Vaccination of 1-year-olds for hepatitis A (starting in 1996 with high-risk groups and routinely in 2006) has resulted in a cohort of adolescents and young adults with reduced lifetime exposure to hepatitis A compared with older adults. To prevent acute liver failure, the ACIP recommends vaccinating adults who are more likely to have exposure to or complications from hepatitis A. This group includes users of injection and noninjection drugs, men who have sex with men (MSM), patients with chronic liver disease, certain travelers, and others[40] and a recently added group, persons experiencing homelessness[41] and people living with HIV.[42] Recently, several outbreaks have had sustained person-to-person transmission, especially among adults experiencing homelessness and with substance use disorders. These outbreaks have resulted in higher rates of hospitalization and death than typical of foodborne clusters.[43] The limited supply of vaccine has complicated public health responses to recent hepatitis A outbreaks.[44]

Hepatitis B

Routine hepatitis B vaccination of infants starting in 1991 has resulted in a cohort of younger adults with higher rates of immunity compared with older adults. To prevent chronic liver failure and hepatocellular carcinoma, the ACIP recommends vaccinating adults who are more likely to have exposure to, or complications from, hepatitis B. This group includes users of injection drugs, MSM, patients seeking evaluation or treatment for a sexually transmitted infection, patients with chronic liver disease, all persons with diabetes aged 19 to 59 years, persons with diabetes aged 60 years or older at the discretion of the treating clinician, certain travelers, and others.[45]

Recent introduction of a hepatitis B vaccine with novel adjuvant (Heplisav-B® [HepB CpG]) for adults allows for rapid completion of a 2-dose series over 1 month, rather than at least 6 months for the older 3-dose vaccine series. Shorter time for completion may increase adherence, especially among patients temporarily in treatment for substance use disorder or incarcerated in correctional facilities. However, the new adjuvanted vaccine produces more local swelling and pain than standard hepatitis B vaccines.[46] The new vaccine can be used as a substitute dose in a 3-dose series of another hepatitis B vaccine, but because it currently costs about 35% more,[47] this may not be cost effective.

Hepatitis B surface antibody titers increase quickly after vaccination but then decrease over time—sometimes to levels below cutoff values between "immune" and "nonimmune" statuses—despite usually maintaining clinical protection from cell-mediated immunity.[48] Patients with a questionable history of vaccination may prefer determination of titers to vaccination but should realize that titers sometimes show lack of immunity despite previous disease or vaccination. The ACIP generally does not recommend postvaccination titers

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for hepatitis B, with the notable exception in health care workers at 1 to 2 months after the last dose.[45]

Human Papillomavirus Vaccine

Prior to June 2019, the ACIP recommended HPV vaccine through age 26 years for all females as well as for MSM and immunocompromised males. The ACIP also recommended HPV vaccine for all other males through age 21 years. For males aged 22 to 26 years who are immunocompetent and not MSM, the ACIP recommended HPV vaccine based on individual clinical decision making.[49]

In October 2018, the FDA approved expanded age indications for HPV vaccine for adults 27 to 45 years old.[50] In 2019 the ACIP reviewed data on young and middle-aged adults and voted to simplify the routine recommendation to include all adults through age 26. In addition, ACIP voted to recommend HPV for 27 through 45 year olds based on shared clinical decision making.[51] Because insurance coverage for vaccines follows ACIP recommendations rather than FDA approvals, it may take months before new vaccines or new indications for vaccines (such as these for HPV) are implemented in clinical practice.

The only HPV vaccine currently available in America is the 9-valent vaccine. The ACIP currently has no recommendation regarding revaccinating patients with 9-valent HPV vaccine if they previously completed HPV vaccination with 2- or 4-valent vaccines, which cover cancer-causing strains 16 and 18. As stated in the 2015 ACIP recommendation, "9vHPV [9-valent HPV] targets five additional cancer causing types [31, 33, 45, 52, and 58], which account for about 15% of cervical cancers."[52] Because rates of HPV vaccine completion in adolescents are low (48.6% in 2017) and the vast majority of HPV-related cancers are due to HPV infection acquired during adolescence or young adulthood, completing the HPV vaccine series as a young adult is the best strategy to prevent HPV-related cancers.[53,54]

Zoster

The ACIP preferentially recommends recombinant zoster vaccine (RZV; 2 doses, intramuscular, 2-6 months apart) over zoster vaccine live (ZVL; 1 dose, subcutaneous). Because its protection wanes within a few to several years, the ACIP recommends ZVL starting at age 60 years (even though the FDA licensed ZVL for adults 50 years and older). In contrast, the ACIP recommends RZV be given starting at age 50 because modeling suggests its efficacy persists 19 years compared with 4 to 12 years for ZVL. The ACIP also recommends RZV for those previously given ZVL.[55]

Recombinant zoster vaccine offers more efficacy against zoster cutaneous eruptions (97% vs 38% to 70%) and postherpetic neuralgia (80% to 91% vs 66% to 67%) than ZVL. Compared with ZVL, RZV causes more adverse reactions (pain, myalgia, and fatigue), sometimes severe enough to affect activities of daily living.[56]

Initial shortages of RZV may resolve in 2019 as production catches up to unexpectedly early and high demand.[57] Recombinant zoster vaccine errors in storage (refrigerated, not frozen as with ZVL) and route of administration (intramuscular, not subcutaneous) may continue to occur.[58]

Because RZV recommendations start at age 50 years and ZVL starts at age 60, insured patients now have 15 years (age 50-64), rather than 5 years (age 60-64), to get RZV before Medicare Part D rules make administering vaccines in medical clinics exceedingly cumbersome.[59]

PART 2: IMPLEMENTING VACCINATION RECOMMENDATIONS IN CLINICAL PRACTICE

Low vaccination rates (Table 1) among adults reflect a multitude of challenges in implementing vaccination recommendations. As researchers and manufacturers work to increase vaccine effectiveness, health care professionals and public health staff can collaborate to prevent more illness and premature deaths by increasing vaccination rates. Addressing disparities with lower vaccination rates in African Americans and Hispanics (by differences of up to 26%) is particularly difficult. Vaccination rates for all adults increased only slightly from 2010 to 2016. For influenza, although

three-quarters of older adults get vaccinated, only half of middle-aged adults and one-third of younger adults do. For pneumococcal disease, two-thirds of older adults receive vaccines, but only one-quarter of younger and middle-aged adults with increased risk do. For hepatitis A, only 9% of adults at increased risk received the vaccine.[3]

Four Standards for Adult Immunization Practice

In 2014, the National Vaccine Advisory Committee (NVAC) recommended comprehensive Standards for Adult Immunization Practice, which outline how to increase adult vaccination rates through individual and collaborative activities of nurses, medical assistants, clinicians, pharmacists, clinic managers, health care systems, health departments, and community organizations.[60] Table 3 lists 4 of the NVAC's Standards for Adult Immunization Practice that the CDC highlights as activities individual nurses, medical assistants, and clinicians can implement to increase immunizations in their adult patients. Implementing these standards in clinical practice requires augmenting them with evidence-based practices recommended by the Community Preventive Services Task Force, such as reminders and recalls.[61,62]

Standard 1—Assess Vaccination Status.- Assessing adults' vaccination status at every clinical encounter lays the foundation for implementing vaccination recommendations. Assessing vaccination status requires that physicians, nurses, and medical assistants all spend significant time reviewing the medical record, state registry, and sometimes personal notes from patients and even calling pharmacies in order to compile vaccination histories for adults.[63] Collating data from these multiple sources is needed because the percentage of adults with vaccine histories entered into state registries, while increasing in recent years, lags behind data for children.[64] The average of 3 medical problems that family physicians address at each encounter exemplifies the challenges clinicians face in implementing preventive services including immunizations.[65] Rather than relying solely on clinicians to assess vaccination status, training nurses and medical assistants, and supporting them working to the full extent of their licensing, can result in increased rates of preventive services including immunizations.[66,67]

Algorithmic Vaccine Forecasting. Determining which vaccines to administer requires comparing vaccination histories to vaccines recommended for patients' ages and medical conditions. Some electronic medical records and many statewide immunization registries generate forecasts of which vaccines patients need using algorithms based on logic from the CDC's Clinical Decision Support for Immunization.[68] Algorithmic forecasting functions most easily for age-based recommendations.[69] Algorithms based on medical conditions do not function as effectively. Few state registries have the resources needed, and few health care systems have the incentives, to collect diagnoses and generate forecasts for medically indicated vaccines.[70] Unexpected vaccination forecasts sometimes occur when ambiguous terms in the ACIP recommendations do not correlate to specific medical diagnosis codes.[71] Algorithms yield unreliable forecasts when vaccine and medical histories are incomplete.

Many states recognize that nurses and medical assistants using algorithmic forecasts and following standing orders can safely and accurately administer vaccines without consulting clinicians. However, for some patients, clinicians will need to apply generic wording of ACIP recommendations to patients' specific medical and vaccination histories.[72]

Individualized Vaccination Determinations. When lack of data entry precludes algorithmic forecasting, clinicians need to quickly determine which vaccines are medically indicated for their adult patients so that medical assistants and nurses can administer vaccines before patients leave the clinic. Software applications for handheld electronic devices, such as Shots Immunizations by the American Academy of Family Physicians and the Society of Teachers of Family Medicine (available at www.stfm.org/Resources/

Shots)[73] or the CDC's Vaccine Schedules app (www.cdc.gov/vaccines/schedules/hcp/schedule-app.html),[74] can help busy clinicians by providing easy access to ACIP recommendations by age and medical conditions. The ACIP compiles all its current recommendations annually into 2 schedules: one for adults (available at www.cdc.gov/vaccines/schedules/hcp/adult.html)[12] and one for children and adolescents. Before this annual compilation occurs, up-to-date recommendations appear on the ACIP website (www.cdc.gov/vaccines/hcp/acip-recs).[75]

Clinicians needing more information about immunization practices have several options. To answer nurses' and medical assistants' questions about situations not explicitly addressed by ACIP recommendations, guidance often appears in the ACIP's General Best Practices Guidelines (www.cdc.gov/vaccines/hcp/acip-recs/general-recs)[76] or in "Ask the Experts" on the Immunization Action Coalition website (www.immunize.org/askexperts).[77] Emailing CDC immunization experts directly at nipinfo@cdc.gov can help answer difficult vaccination questions not covered elsewhere. Table 4 lists these and other helpful resources.[12,61,73-89]

TABLE 4. Vaccine Recommendation Resources

Mobile apps
Shots by AAFP/STFM - www.stfm.org/Resources/Shots[73]
CDC immunizations - www.cdc.gov/vaccines/schedules/hcp/schedule-app.html[74]
Advisory Committee on Immunization Practices
Adult schedule - www.cdc.gov/vaccines/schedules/hcp/adult.html[12]
Vaccine-Specific ACIP Recommendations - www.cdc.gov/vaccines/hcp/acip-recs[75]
General Best Practice Guidelines - www.cdc.gov/vaccines/hcp/acip-recs/general-recs[71]
Immunization Action Coalition Web pages
Ask the Experts - www.immunize.org/askexperts[77]
Vaccinating Adults: A Step-by-Step Guide - www.immunize.org/guide[78]
Laminated schedules - www.immunize.org/shop/laminated-schedules.asp[79]
Standing orders - www.immunize.org/standing-orders[80]
Guide to Community Preventive Services
www.thecommunityguide.org/content/task-force-findings-increasing-vaccination[61]
CDC Pink Book: *Epidemiology and Prevention of Vaccine-Preventable Diseases*
www.cdc.gov/vaccines/pubs/pinkbook/index.html[81]
CDC Immunization Education and Training
Pink Book Webinars - www.cdc.gov/vaccines/ed/webinar-epv[82]
You Call the Shots - www.cdc.gov/vaccines/ed/youcalltheshots.html[83]
Clinical Vaccinology Courses by the National Foundation for Infectious Diseases
In-depth, clinically focused, 2-day in-person courses offered at least annually.
www.nfid.org/professional-education/conferences/cvc[84]
Vaccine Education Center in Philadelphia
"Current Issues in Vaccines" Webinar: Paul Offit reviews latest ACIP recommendations
www.chop.edu/centers-programs/vaccine-update-healthcare-professionals[85]
American College of Physicians
Numerous webinars, videos, and guidelines
www.acponline.org/clinical-information/clinical-resources-products/adult-immunization[86]
American Academy of Family Physicians
Comprehensive resources including coding and "Office Champions"
www.aafp.org/patient-care/public-health/immunizations.html[87]
American College of Obstetricians and Gynecologists
Clinical guidelines, practice management toolkits including billing and coding guidance
http://immunizationforwomen.org/providers/resources/default.php[88]
National Adult and Influenza Immunization Summit
Annual meeting of representatives of >130 health care and public health organizations
Goal of resolving systemic barriers to increasing adult vaccination rates
https://www.izsummitpartners.org/about[89]

AAFP = American Academy of Family Physicians; ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; STFM = Society of Teachers of Family Medicine.

Standard 2—Strongly Recommend Needed Vaccines. As Reid et al[2] stated in *Mayo Clinic Proceedings* in 1999, "physicians' attitudes and practices about vaccination greatly influence the actions of their patients." Clinicians' recommendations are the factor most strongly associated with patients getting vaccinated.[90] Pediatric literature suggests that beginning vaccine conversations with presumptive statements may increase patient acceptance of immunization recommendations. A simple, clear message—"These are the vaccines you need today"—presumes patients will accept vaccination. In contrast, an invitation to participate in a discussion such as "What do you think about getting vaccinated today?" may lead to vaccine refusal.[91,92]

The CASE Method. If patients hesitate accepting presumptive vaccine recommendations, many pediatric experts advise approaches similar to the CASE (corroborate, about me, science, explain/advise) method.[93] Acknowledging and corroborating (C in CASE) patients' concerns may create a respectful tone. Alternatively, expressing surprise when confronted with vaccine hesitance may

demonstrate that accepting vaccines is the social norm.[94] Clinicians describing their own expertise about vaccines (A or About me in CASE) may enhance trust in recommendations to vaccinate. Carefully listening to patients can help focus discussion of scientific (S in CASE) evidence on specific concerns, rather than introducing myths not previously considered. Clinicians can explain (E in CASE) benefits and risks of immunization by reading from and commenting on Vaccine Information Statements, which summarize efficacy, safety, and adverse effects.[95] Understanding how to submit reports to the Vaccine Adverse Event Reporting System and recognizing its role in identifying rare sequelae may increase clinicians' confidence in reassuring patients that vaccines are safe.[96-98]

Some key lessons from motivational interviewing can be incorporated easily into the CASE structure: (1) hear and affirm patients' concerns, (2) ask patients for permission to share the provider's perspective (to reduce pushback), (3) ask gentle, open-ended questions about patients' desire to prevent disease, rather than getting into an argument about the vaccine itself, and (4) support patients' power to say no, thereby allowing patients to openly consider vaccination, reflect, reconsider if they initially decline, and maintain a strong bond with clinicians.[99] For patients who persist in refusing vaccination, after documenting the refusal to vaccinate in the medical record, promising to continue conversations at future visits may reinforce the strength of recommendation. Some experts recommend requiring vaccine-hesitant patients to sign statements similar to Michigan's "Refusal to Consent to Vaccination (Adult)."[100]

Reminders and Recalls. Although helpful, opportunistically vaccinating patients only when they come to the clinic will not by itself raise adult vaccination rates to target levels. Reminding and recalling patients due and overdue for immunizations can increase "demand" for vaccinations and result in more patients receiving routinely recommended immunizations.[101] After receiving reminders/recalls, patients who did not remember, know about, or desire needed vaccinations may be influenced to schedule health care visits or request vaccination during a visit. Most state registries and some electronic medical records allow standard reports of patients due and overdue for vaccination. Often, these reports require curation to eliminate previous patients who no longer actively visit the practice. Reminders/recalls can increase immunization rates across many (but not all) settings, vaccines, and age groups.[101] Health systems might reduce staff time needed to implement reminders/recalls by centralizing curation of active patient lists and the notification of patients.[102]

Standard 3—Offer Needed Vaccines. Increasing adult vaccination rates will require that clinic processes for scheduling and administering vaccines be convenient for patients and staff. Vaccinating at all appointment types and all hours of operation can increase access to vaccination services. Some practices have found it helpful to offer evening or weekend flu vaccine clinics during peak influenza vaccination seasons. Standing orders allow nurses and medical assistants to vaccinate patients without consulting clinicians and can increase rates of adult vaccination, especially in clinics that fully implement policies, have strong quality improvement processes, and have an effective clinical leader who is passionate about immunization issues.[103]

Storing vaccines requires purchasing specialized refrigerators and freezers with continuous temperature monitoring linked to alarms for when vaccines get too warm (power outages) or cold (thermostat malfunctions). Clinics often purchase insurance to protect large financial investments in vaccines. Vaccine administration requires staff time to order vaccines, track inventory, document doses administered in records and registry, and submit billing. Specialty clinics are unlikely to stock and administer the vaccines their patients need.[104]

Small, independent clinics often find the costs of administering vaccines too high and

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refer patients to pharmacies and health departments. Large up-front investments by clinics and health care systems require timely clinical reimbursement. Recouping this investment requires efficiently determining patients' insurance coverage before administering vaccines.[105] For example, patients who have Medicare Part D may be referred to a pharmacy to get Tdap, but patients with other insurances may be vaccinated in the clinic. In the past, local health departments often vaccinated these adults regardless of their insurance status. With implementation of the Affordable Care Act, the CDC more strictly enforced limiting the use of federally subsidized "section 317" vaccines at local health departments solely for uninsured adults.[106,107] Most communities have lacked the political will for increasing funding to allow the local health department to vaccinate more adults. Pharmacies provide increasing portions of all administered doses of vaccines with age-based recommendations for adults.[108] However, unlike clinics and health departments, pharmacies often do not stock vaccines with indications for medical conditions or as catch-up doses for incomplete childhood series.

Standard 4—Document Vaccines Administered. Documenting the administration of vaccines in state registries helps clinics know which vaccines patients have had at any clinic, pharmacy, or health department. Clinicians should advocate for their medical records to automatically upload vaccination records in their states' registries because manual double-entry into both systems is inefficient and error prone. Clinicians should also ask their pharmacist colleagues to similarly upload vaccination records into state registries and check such registries before vaccinating in order to make assessing vaccination status at every clinical encounter (Standard 1) more accurate and efficient. Increased accuracy and completeness of vaccination histories helps clinicians to make strong recommendations (Standard 2) and to administer vaccinations (Standard 3) that patients have not received elsewhere already. Vaccines documented in state registries facilitate generation of accurate patient lists for reminder/recall notification and calculation of immunization coverage rates by clinic or individual clinician, which can guide quality improvement activities.

Overcoming Systemic Barriers in Clinics, Health Care Systems, and Communities

Systemic barriers to increasing vaccination rates limit the benefits of vaccines.[109,110] At the clinic level, individual clinicians, nurses, and medical assistants must work together to increase vaccination rates by combining patient education with decreasing inconveniences to vaccination.[111] These efforts function best when coordinated as clinic-wide quality improvement programs that include assigning a champion (often a nurse) or co-champions (nurse and physician), performing Plan-Do-Study-Act cycles to make small practice-based changes and measuring missed opportunities for vaccinations.[112] These quality improvement activities can become part of maintenance of certification activities.[113]

Implementing routine assessment of vaccine status by nurses and medical assistants requires training and encouragement. Improving clinicians' communication regarding vaccine recommendations is facilitated by small-group discussions of case scenarios.[114] Simplifying scheduling of vaccinations requires changing clinic policies that limit vaccinating to certain hours of service or types of visits.[78] Increasing the use of immunization registries may require nurses or medical assistants to receive training and protected time for documenting vaccinations administered.

Other barriers to adult vaccination require clinicians to advocate outside of health care systems. Immunization coalitions need clinicians to help develop community-wide messaging about vaccine safety and efficacy in order to address vaccine hesitancy and increase community demand for vaccination.[61] As administrators of, or consultants to, health insurance plans, clinicians can advocate for removing financial disincentives for vaccination. By representing health profession societies on local, state, and federal committees and work groups, clinicians can educate vaccine experts about challenges to implementing

complex vaccination recommendations in clinical practice.[115-117]

CONCLUSION

Clinicians making strong recommendations for immunizations may convince many patients to get vaccinated, but addressing systemic barriers is as important in increasing adult vaccination rates in clinical practice. Clinicians can apply best practices of vaccination in the examination room by rapidly accessing up-to-date national recommendations, applying those recommendations to the patient's medical conditions, and communicating clearly the benefits and adverse effects of vaccination. The CDC's version of the NVAC's Standards for Adult Immunization Practice provides a framework for clinicians and health care systems to develop policies to increase rates of vaccination and prevent disease in adults. Through professional societies, clinicians can advocate for recommendations that can be efficiently implemented in clinical practice. As consultants to community coalitions, clinicians can bring a lens of evidence-based public health practice to planning community-wide immunization messaging. Clinicians' actions—in examination rooms, within health care systems, via professional societies, and in community coalitions—can help increase low rates of adult vaccination and prevent illness and death from influenza, IPD, hepatitis A and B, zoster, and other vaccine-preventable diseases.

Abbreviations and Acronyms: **ACIP** = Advisory Committee on Immunization Practices; **CASE** = corroborate, about me, science, explain/advise; **CDC** = Centers for Disease Control and Prevention; **FDA** = Food and Drug Administration; **HPV** = human papillomavirus; **IIV** = inactivated influenza vaccine; **IPD** = invasive pneumococcal disease; **LAIV** = live attenuated influenza vaccine; **MSM** = men who have sex with men; **NVAC** = National Vaccine Advisory Committee; **PCV13** = 13-valent pneumococcal conjugate vaccine; **PPSV23** = 23-valent pneumococcal polysaccharide vaccine; **RIV** = recombinant influenza vaccine; **RZV** = recombinant zoster vaccine; **Tdap** = tetanus, diphtheria, and acellular pertussis vaccine; **ZVL** = zoster vaccine live

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The Thematic Review on Vaccines will continue in an upcoming issue.

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