Vaccinations for Adults and Adolescents: An Update



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Nothing to disclose....



Diseases/Pathogens with Vaccines Generally Available in the U.S.

- Tetanus
- Diphtheria
- Pertussis
- Measles
- Mumps
- Rubella
- Varicella
- Meningococcus
- Pneumococcus
- Hepatitis B

- Hepatitis A
- *Haemophilus influenzae* type B
- Human papillomavirus
- Polio
- Influenza
- Rabies
- Typhoid
- Yellow fever
- Japanese encephalitis
- Rotavirus
- Cholera



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Adult and adolescent vaccines to be covered

- New vaccine information or recommendations
- Epidemiologic concerns
- Complicated recommendations / questions are commonly asked

Outline

Briefly:

- Hepatitis A
- Yellow fever
- Measles
- Mumps
- New hepatitis B vaccine

- Pneumococcal
- Meningococcal
- Pertussis (Tdap)
- Influenza
- Varicella (Zoster)
- Human
 Papillomavirus

Key Resource

Centers for Disease Control and Prevention

http://www.cdc.gov/vaccines/

http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/index.html



Figure 1. Recommended immunization schedule for adults aged 19 years or older by age group, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

Vaccine	19–21 years	22–26 years	27–49 years	50–64 yea	rs	≥65 years
Influenza ¹	1 dose annually					
Tdap ² or Td ²		1 dose Tdap, then Td booster every 10 yrs				
MMR ³	1 or 2 doses depending on indication (if born in 1957 or later)					
VAR⁴		2 doses				
RZV⁵(preferred)					2 do	ses RZV (preferred)
ZVL ⁵						1 dose ZVL
HPV–Female ⁶	2 or 3 doses depending on age at series initiation					
HPV–Male ⁶	2 or 3 doses depending	on age at series initiation				
PCV13 ⁷	1 d <mark>ose</mark>					
PPSV237	1 or 2 doses depending on indication 1 dose			1 dose		
HepA ⁸	2 or 3 doses depending on vaccine					
НерВ°	3 doses					
MenACWY ¹⁰	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains					
MenB ¹⁰	2 or 3 doses depending on vaccine					
Hib''	1 or 3 doses depending on indication					



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 recommendation

February 6, 2018 - https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

Hepatitis A outbreak



 Outbreak in CA, mostly in persons who are homeless and/or use illicit drugs (injection and non-injection): final summary 4/11/18

Jurisdiction	Cases	Hospitalizations	Deaths
San Diego	587	402	20
Santa Cruz	76	33	1
Los Angeles	12	8	0
Monterey	12	10	0
Other	17	8	0
Total	704	461	21

- CDPH distributed ~ 123,000 doses hepatitis A vaccine to local health departments
- Recommended vaccination of occupational groups with close contact

Hepatitis A



• Expanded use of hepatitis A vaccine for post exposure prophylaxis if no immunocompromise

Age yrs	< 1	1 - 40	41 - 59	60 - 74	75+
	IG	Vaccine preferred	Vaccine	IG + vaccine	IG + vaccine

When immune globulin (IG) unavailable, may use vaccine for PEP ages 60 - 74 and > 6 months

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ Immunization/HepatitisA-PEPQuicksheet.pdf

Pending guidance from ACIP/CDC may be somewhat different

• When using IM immune globulin for pre or post exposure prophylaxis, use higher dose



Yellow fever vaccine shortage

- Due to manufacturing problems, currently using an imported vaccine Stamaril
- Available at fewer locations
- May resolve at the end of 2018
- Nearby clinics include
 - Passport Health, Oakland
 - AITC Immunization & Travel Clinic, San Francisco
 - Kaiser Permanente, several locations including Oakland

https://wwwnc.cdc.gov/travel/page/search-for-stamaril-clinics



ECDC map maker: https://emma.ecdc.europa.eu

Yellow fever in travelers

- Yellow fever outbreak ongoing in Brazil since December 2016
- Jan 1 March 15, 2018: ten cases of yellow fever in travelers to Brazil
 - All unvaccinated
 - Four deaths

Yellow fever vaccine now recommended in most areas of Brazil

https://www.cdc.gov/mmwr/volumes/67/ wr/mm6711e1.htm



Federal state

Measles

HEALTH ADVISORY Measles in San Francisco Bay Area April 5, 2018

Between 3/5/18 and 4/3/18, measles has been confirmed in six (6) unvaccinated patients who are residents of Santa Clara County (5) and Alameda County (1). One (1) additional linked case has been confirmed in Nevada. All cases are linked to an unvaccinated traveler who was exposed in Europe and developed measles after returning to the San Francisco Bay Area. Local health departments in the Bay Area are conducting contact investigations. Measles is very infectious, and airborne transmission can occur in settings with large numbers of people like healthcare facilities, schools, childcares, shopping centers, public transportation, airports, and amusement parks. Clinicians should be vigilant in identifying and appropriately managing suspected measles cases to avoid ongoing transmission and ensuring that their patients and staff are up-to-date with immunizations.

Measles

- Since 2000, annual number of cases in U.S. has ranged from 37 to 667
 - > 99% reduction from pre-vaccine era
- No longer endemic transmission in U.S.
 Cases related to importation
- Most cases occur in non-vaccinated persons
- Two doses of measles vaccine are about 97% effective
 - One dose is about 93% effective

California Senate Bill 277

- Went into effect July 1, 2016
- Prompted by Disneyland measles outbreak 2014-2015
- All children in public school, private school, daycare must be vaccinated against
 - Measles, mumps, rubella, pertussis, diphtheria, tetanus, *Haemophilus influenzae* type B, polio, hepatitis B, varicella
- No exemptions for personal or religious beliefs
- Allows medical exemptions
- Percentage of children in kindergarten with any type of exemption decreased by 1.4% in 2016-17 compared with 2015-2016

MMWR 2017;66(40):1073-80

Mumps

- > 99% decline from pre-vaccine era
- Several hundred to several thousand cases per year
- Outbreaks associated with people living in close proximity, including college campuses
- Spread is facilitated when vaccination rates are low
 - Vaccinated persons are also susceptible
- Two doses of vaccine are about 88% effective
 One dose is about 78% effective

Mumps vaccine - 3rd dose

- New ACIP "outbreak" recommendation 10/17
- If previously received two doses of mumpscontaining vaccine and at increased risk due to an outbreak, a 3rd dose is recommended
- Response to rising number of mumps outbreaks and outbreak-associated cases, most in young adults and many associated with universities

MMWR 2018;67(1):33-38

New hepatitis B vaccine for adults

HEPLISAV-B

- Recombinant, adjuvanted vaccine
- Contains recombinant hepatitis B surface antigen plus novel adjuvant CpG 1018 – oligodeoxynucleotide that enhances B cell and T cell responses
- Given as two doses, one month apart
 Hope for better completion of series
- Approved for 18 years and older
- Higher rates of seroprotection than Engerix-B
- Higher risk of MI in one study
 - Post marketing surveillance planned

New hepatitis B vaccine for adults

- Consider HEPLISAV-B with
 - Diabetes
 - Renal disease
 - Immunosuppression
 - Obesity
 - Older age
 - Smokers
 - Non-responders

Pneumococcal Vaccines

- Two vaccines now used routinely in adults 65 and older
- Pneumococcal polysaccharide vaccine
 - PPSV-23 (Pneumovax); 23 valent
 - In use since 1983
 - Efficacy against pneumonia in older adults is unclear
- Pneumococcal protein conjugate vaccine
 - PCV-13 (Prevnar); 13 valent
 - Recommended for selected adults in U.S. in 2012
 - Additionally recommended for 65 and older in 2014
 - In adults, only one-time dose indicated

Pneumococcal 13-Valent Conjugate Vaccine for Adults

- Clinical trial in the Netherlands: 84,496 adults > 65 randomized to PCV13 vs. placebo (CAPiTA trial)
 - 46% fewer first cases of vaccine type pneumococcal community acquired pneumonia (CAP) primary outcome
 - 75% fewer first cases vaccine type invasive pneumococcal disease
 - No difference CAP from any cause

New Engl J Med 2015; 372:1114-25

Single dose PPSV-23 (< age 65)

Condition	PCV-13 single dose	PPSV-23 single dose	PPSV-23 revaccinate 5 years after 1 st dose
Heart disease		Х	
Lung disease – including asthma		X	
Diabetes mellitus		X	
Alcoholism		X	
Cirrhosis		Х	
Cigarette smoking		X	
Long-term care resident		Х	
Native populations with high risk		Х	

Single dose PCV-13 and single dose PPSV-23 (< age 65)

Condition	PCV-13 single dose	PPSV-23 single dose	PPSV-23 revaccinate 5 years after 1 st dose
CSF leak	Х	Х	
Cochlear implant	Х	Х	

Single dose PCV-13 and repeat PPSV-23 five years after first dose (< age 65)

Condition	PCV-13 single dose	PPSV-23 single dose	PPSV-23 revaccinate 5 years after 1 st dose
Sickle cell disease	Х	Х	Х
Asplenia	Х	Х	Х
HIV	Х	Х	Х
Renal failure	Х	X	Х
Nephrotic syndrome	Х	Х	Х
Leukemia	Х	Х	Х
Lymphoma	Х	Х	Х
Multiple myeloma	Х	X	X
Hodgkin disease	Х	Х	Х
Generalized malignancy	X	X	X
Solid organ transplant	Х	Х	Х
Other immunosuppression	Х	Х	Х

Sequencing pneumococcal vaccines in adults

- If PCV-13 and PPSV-23 both indicated, give PCV-13 first
 - For 65 and older: wait at least one year before administering PPSV-23
 - Wait at least 8 weeks for less than age 65
- If PCV-13 and PPSV-23 both indicated and PPSV-23 has already been administered
 - Wait at least one year before PCV-13

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Meningococcal Vaccines -MenACWY

- Two tetravalent protein conjugate vaccines (Menactra, Menveo) covering strains A, C, Y, W-135
 - Menactra: 9 months 55 years; Menveo 2 months – 55 years
 - Advantages compared to polysaccharide vaccine which is no longer in use
 - Longer lasting antibody titers
 - Good antibody response to revaccination
 - Serogroup B not covered by tetravalent vaccines (B, C, and Y circulate in U.S.)

Who should get MenACWY vaccines?

- Recommended as routine for ages 11 18 ideally given at age 11-12 visit
- "Catch up" at high school or college entry if not given at age 11-12
- Second doses now routine for adolescent and teenage vaccinees

MenACWY vaccine - summary table

Risk group	Primary series	Booster dose
Age 11-18 *Also, 1 st yr. college students in residence halls up to age 21	1 dose, preferred age 11 or 12	 Age 16, if primary dose age 11 or 12 Age 16-18, if primary dose age 13-15 No booster if primary dose on or after age 16
Age 2-55 with complement deficiency or functional or anatomic asplenia	2 doses, 2 months apart	Every 5 years
Age 2 – 55 with prolonged increased risk of exposure	1 dose	Age 2-6: after 3 years Age 7 and older: after 5 years

MMWR. January 28, 2011;60:72-76

Who else should get MenACWY vaccine?

- Given to military recruits, travelers/residents with geographic risk, microbiologists
- Other notes:
 - Vaccination required for pilgrims going to Hajj or Umrah in Saudi Arabia

Who else should get MenACWY vaccine?

- In June 2016, ACIP voted to recommend MenACWY to all HIV-positive persons age 2 months and above
 - 5 24 fold increased risk invasive meningococcal disease
 - 2-dose primary series, doses given 8-12 weeks apart
 - Booster dose every 5 years
 - If Menactra will be used, give PCV-13 first and wait at least 4 weeks before MenACWY
 - Expert opinion data only in infants regarding immune interference with response to PCV-13

MMWR 2016;65(43):1189-94

Who else should get MenACWY vaccine?

 Clusters in New York City and Southern California among men who have sex with men – vaccine may be recommended before travel





 San Francisco Department of Public Health recommends MenACWY locally for MSM, especially if multiple partners, partners sought via websites or digital applications, visit crowded venues such as bars or parties, smoke, spend time in smoky settings

Epidemiology meningococcal disease United States

- Incidence of all serogroups has declined
 - Decline occurred prior to routine MenACWY vaccine
 - In 2013: 564 culture and PCR confirmed cases
 - Historically, only 2-3% of US cases occur in outbreaks, i.e. most cases are sporadic
 - Serogroup B now causes about 40% of cases in adolescents and young adults

Serogroup B outbreaks linked to college campuses

- Princeton 2013-2014
- UC Santa Barbara 2013
- University of Oregon 2015
- Santa Clara University 2016
- UMass Amherst 2017
- Oregon State University 2017-2018













Two meningococcal serogroup B vaccines available in US

- Both approved ages 10-25 years
- MenB-FHbp (Trumenba) approved Oct 2014
 - 2 or 3-dose series (high risk 3 doses preferred)
 - Contains two recombinant factor H binding protein antigens
 - One from each subfamily A and B
- MenB-4C (Bexsero) approved Jan 2015
 - 2-dose series
 - Contains four components
- Cover most but not all serogroup B strains
- Local and systemic reactions common
 - More common than with other adolescent vaccines

Recommendations for MenB vaccines

- Recommended for persons 10 years and older at elevated risk due to
 - Persistent complement component deficiencies
 - Including taking drug eculizumab
 - Anatomic or functional asplenia
 - Routine exposure (microbiologists)
 - Serogroup B outbreak

• Additional category B recommendation (individual decision making): MenB vaccine may be given to adolescents and young adults ages 16-23 to provide short-term protection; preferred age range 16-18

MMWR 2015. 64(22);608-612



Pertussis Vaccine

- Vaccine combinations:
 - Childhood DTaP: diphtheria toxoid, tetanus toxoid, and acellular pertussis
 - Adult/adolescent Td and Tdap: tetanus toxoid and reduced dose diphtheria toxoid +/reduced dose acellular pertussis antigens


Pertussis Vaccine

- Pertussis immunity wanes over time
- Peaks every 2-5 years in U.S., including
 - ^o 2005, 2010, 2012, 2014

Acellular pertussis vaccine in adults and adolescents - how well does it work?

- 2781 subjects 15 65 yrs received reduced dose acellular pertussis vaccine or hepatitis A placebo
- Followed for 2.5 yrs
- Based on primary pertussis definition, vaccine 92% effective

Ward et al, NEJM, Oct. 2005



Waning immunity after acellular vaccination

California outbreak 2010:

- Most pediatric cases were vaccinated as recommended
- High levels of disease in pre-adolescents, especially 10year-olds *J Pediatr 2012;161:1091-6*
- Kaiser Permanente study in CA kids: odds of pertussis increased by 42% per year in the 5 years after completing DTaP *New Engl J Med 2012;367:1012-19*
- Kaiser Permanente study:
 - 263,496 persons 8-20 years old who received acellular vs. whole-cell vaccine (at least one dose)
 - ~ 8.6 relative risk of pertussis for 5 doses acellular vaccine *Clin Infect Dis 2013;56:1248-54*

Why is acellular vaccine less protective?

Fewer antigens

- Acellular vaccines up to 5 antigens
- Whole cell vaccines ~ 3000 antigens
- Priming more robust with whole cell
- Different type of T cell response
- Antigen balance
 - High levels of antibody to pertussis toxin may have blocking effect on antibodies to other antigens
- Genetic changes in *Bordetella pertussis*
 - Pertactin deficiency



- Pertussis rates began increasing in 1980s
 - Well before acellular vaccines
- Rate today estimated 20-fold less than prevaccine era and reported rates influenced by
 - More testing
 - More sensitive tests PCR
 - False positives, e.g. due to other *Bordetella* species
- When acellular vaccine fails in children, illness less severe than in unvaccinated

Tdap - Recommendations

- For adolescents, give Tdap instead of Td at routine 11-12 yr visit
- For adults 19 and older, give single dose Tdap to replace a dose of Td
- Can be given at any interval from last tetanuscontaining vaccine
- Recommended for every pregnancy at 27 36 weeks

MMWR 2011 / 60(41):1424-26

Tdap - pregnancy

- Multiple studies showing Tdap is safe in pregnancy, including with short interval between vaccine doses
- Maternal immunization results in high levels of pertussis antibody in infants and does not impair response to DTaP
- High vaccine effectiveness (observational) when Tdap given at least 28 days before birth
- Some debate re exact timing recent data suggest targeting 27 weeks may be optimal
 - JAMA 2015;314(15):1581-7
 - JAMA 2014;311(17):1760-9
 - Lancet 2014;384(9953):1521-8
 - Clin Infect Dis 2016;62(7):829-36
- Clin Infect Dis 2017;64(1):3-8
- Clin Infect Dis 2017;64(1):9-14

Influenza Vaccine

- Indicated for all people older than 6 months
 - Unless there is a contraindication...
 - Egg allergy no longer a contraindication
 - Severe previous reaction
 - Guillain-Barre relative contraindication

Influenza Vaccine - egg allergy

- Only hives after exposure to egg any influenza vaccine appropriate for age and health status
- Other reactions to egg (including angioedema and respiratory distress) – any influenza vaccine appropriate for age and health status; administer in a medical setting with ability to treat allergic reactions
- No need to observe for 30 minutes
 - 15 minutes already recommended for all, especially adolescents (syncope)

MMWR 2016;65:1-54

2017-18 Influenza Vaccine

- A/Michigan/45/2015 (H1N1)pdm09-like (new)
- A/Hong Kong/4801/2014 (H3N2)-like (same)
- B/Brisbane/60/2008-like (B/Victoria lineage) (same)
- For quadrivalent vaccine add: B/Phuket/3073/2013-like (B/Yamagata lineage) (same)

2018-2019 influenza vaccine

- A/Michigan/45/2015 (H1N1)pdm09-like (same)
- A/Singapore/INFIMH-16-0019/2016 (H3N2)-like (new)
- B/Colorado/06/2017-like (B/Victoria/2/87 lineage) (new)
- For quadrivalent vaccine add B/Phuket/3073/2013-like (B/Yamagata/16/88 lineage) (same)

Recent Influenza Seasons

• 2016-17:

- Estimated vaccine effectiveness 48%
- Influenza A H3N2 (predominant virus): 43%
- Influenza B virus: 73%

• 2015-16: relatively mild

- Estimated vaccine effectiveness 59%
- Late peak (March), long duration
- Vaccine good match for circulating strains
- 2014-15: moderately severe
 - Rate of hospitalization for age 65+ highest since surveillance began 2005-6
 - Estimated vaccine effectiveness 19%

Interim estimate of effectiveness 2017-2018 influenza vaccine

- Based on data 11/2/17-2/3/18
 - □ H3N2 25%
 - □ H1N1 67%
 - Influenza B 42%
 - Overall 36%

https://www.cdc.gov/mmwr/volumes/67/wr/mm6706a2.htm

U.S. virus characterization 2017-2018

- Most influenza A viruses circulating are H3N2
 - H3N2 viruses show substantial genetic diversity but 98% of those tested are well inhibited by ferret antisera raised against the H3N2 virus in the vaccine, i.e. "a good match"
 - H1N1 viruses all belong to same clade and are similar to reference virus in vaccine



Challenges with influenza vaccine

- Correctly identifying strain(s) that will circulate
- Response affected by multiple factors
 - Age
 - First influenza strain encountered ("original antigenic sin")
 - Subsequent influenza strains encountered, including vaccine strains
- Growth of vaccine in eggs: egg-adapted H3N2 strain has a mutation that eliminates a glycosylation site found in circulating H3N2 strains in 2016-2017

PNAS 2017;114(47):12578-83

Influenza vaccines recommended in United States 2017-18

Inactivated, quadrivalent, standard dose

- Fluarix Quadrivalent
- Flulaval Quadrivalent
- Afluria Quadrivalent (adults by jet injector)
- Fluzone Quadrivalent
- Fluzone Intradermal Quadrivalent

Inactivated, quadrivalent, cell culture-based, standard dose

- Flucelvax Quadrivalent

Inactivated, trivalent, standard dose

- Afluria (adults by jet injector)
- Fluvirin

Adjuvanted, inactivated, trivalent, standard dose

- Fluad

Inactivated, trivalent, high dose

- Fluzone High-Dose

Recombinant

- Flublok Trivalent and Quadrivalent

Inactivated standard dose vaccines given IM

- Quadrivalent: 2 influenza A strains, 2 influenza B strains
- Trivalent: 2 influenza A strains, 1 influenza B strain



High-dose inactivated vaccine

- Trivalent
- Licensed for ages 65 and older
- 60 μg hemagglutinin per virus strain compared with 15 μg in regular dose
- Enhanced immune response in those 65 and older and other populations, including people living with HIV
- Local reactions (mild to moderate) more common

J Infect Dis 2009;200:161-3

High dose inactivated vaccine

Studies with clinical outcomes:

- 2-year study with 31,989 participants randomized to high dose vs. standard dose: 1.4% vs. 1.9% with confirmed influenza (relative efficacy 24.2%) *New Engl J Med 2014;371:635-45*
- Retrospective study at VA 2010-2011; 25,714 veterans high dose, 139,511 standard dose. No difference in hospitalization for influenza or pneumonia, except in those 85 and older Clin Infect Dis 2015;61:171-6
- Cluster randomized trial in 823 nursing homes 2013-2014; respiratory-related hospital admission 3.4% vs.
 3.9% Lancet Respir Med 2017 Jul 20 [epub]

Adjuvanted inactivated vaccine

- Trivalent
- MF-59 adjuvant: oil-in-water emulsion of squalene oil
- Has been used widely in Europe, licensed in Canada
- Licensed in U.S. November 2015 for ages 65 and older
- Approved based on safety and immunogenicity data
- Clinical trials in progress

Recombinant Influenza Vaccine

- Recombinant vaccine (Flublok) uses baculovirus vectors carrying genes that encode for hemagglutinin
- Vaccine with new antigens can be produced in 6 8 weeks
- 2014-2015 influenza season: 8855 participants 50 years and older received either quadrivalent recombinant vaccine (45 μ g HA per strain) or quadrivalent standard vaccine (15 μ g HA per strain)
- RT-PCR confirmed influenza attack rate 2.2% vs. 3.2%

Live Attenuated Influenza Vaccine (LAIV)

- Trade name FluMist
- Quadrivalent
- Heat sensitive and cold adapted
- Approved for healthy persons ages 2 49
- Not recommended 2016-17 or 2017-18
- Returning in 2018-19
 New H1N1 component



Additional influenza vaccines licensed in U.S.

- Cell culture derived vaccine using canine kidney cells (Flucelvax)
 - Quadrivalent; ages 4+
- One vaccine can be administered by jet injector (Afluria)
 - Ages 18-64
- Intradermal vaccine (Fluzone intradermal)
 - Quadrivalent; ages 18-64; needle one-tenth standard length; more local reactions

Influenza vaccination in pregnancy

- Multiple studies with reduction in infant influenza-like illness (ILI) and confirmed influenza after maternal vaccination in pregnancy
- Representative study:
 - Observational study of 249,387 infants in Utah for first 6 months of life
 - 658 infants with laboratory confirmed influenza:
 0.84/1000 if mother immunized, 2.83/1000 if mother not immunized
 - Risk reduction 64% ILI, 70% laboratory confirmed influenza, 81% influenza hospitalization

Pediatrics 2016;137(6):e20152360

Varicella Vaccine (Varivax)

- Recommended for all adults without immunity (history of varicella or laboratory evidence)
- Avoid in pregnancy and with most immunocompromise
- Given as 2 dose series for all ages
 Two doses 98% effective in children
- Average annual mortality has declined 88% overall and 96% under age 50

Shapiro et al, Journal Infect Dis 2011;203:312-15 Marin et al, Pediatrics 2011;128:214-20



Varicella Vaccine - Zoster (Zostavax)

Oxman et al, NEJM, June 2005

- Randomized trial 38,546 adults > age 60
 - Excluded if history of zoster, immunocompromise
- Potency much greater (at least 14x) than vaccine to prevent primary varicella
- Zoster incidence reduced by > 50%; post herpetic neuralgia reduced by > 65%
- Injection site reactions common



Varicella Vaccine - Zoster (Zostavax)

- Previously recommended as a single dose for adults age 60 and older
- Contraindicated in many, but not all, immunocompromised persons (e.g. okay in HIV if clinically well and CD4 count > 200)
- Follow up subjects in Shingles Prevention Study
 - Efficacy for zoster prevention estimated to last 8 years

Clin Infect Dis 2015;60(6):900-9

ORIGINAL ARTICLE

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

NEJM 2015;372:2087-96

- Phase 3 study; 7698 received vaccine, 7713 placebo
- Adults 50 and older stratified by age
- Two dose series
- 6 cases zoster in vaccine group, 210 in placebo group
 - Mean follow up 3.2 years
 - 97% efficacy
 - No difference in efficacy by age
- Mild-moderate systemic and local reactions common



Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older

- 13,900 participants age 70 and older
- 2 doses adjuvanted subunit vaccine or placebo
- Follow up 3.7 years
- Vaccine efficacy against zoster 89.8%
 - 23 cases vaccinated vs. 223 cases placebo
- No difference in efficacy by age
- More injection site and systemic reactions with vaccine
- Serious adverse events similar
- Long-term follow up both studies in progress

Zoster Vaccine Recombinant (Shingrix)

- FDA approved 10/20/17
- Contain recombinant glycoprotein E plus a novel adjuvant (AS01_B)
- Given as two doses, 2 to 6 months apart
- Recommended as a routine vaccine for ages 50 and older
 - Still give if history of zoster
 - Revaccinate those who received Zostavax has been studied after 5 years, wait at least 2 months

Zoster Vaccine Recombinant (Shingrix)

- No need to screen for history of chickenpox or to do laboratory testing
- Indicated with chronic medical conditions and low dose immunosuppressive therapy, e.g. < 20 mg prednisone daily
 - No current recommendations for other immunocompromise – pending data

https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html

https://www.cdc.gov/mmwr/volumes/67/wr/mm6703a5.htm



Human Papillomavirus (HPV) Vaccines

- Genital HPV most common sexually transmitted infection in the U.S.
- Quadrivalent HPV vaccine (Gardasil)
 - Contains major capsid protein L1 from types 6, 11, 16, 18
 - Phased out in 2016 replaced by nine valent vaccine
- Bivalent HPV vaccine (Cervarix) protects against types 16 and 18
 - Only licensed in females; no longer marketed in U.S.
- Types 16 & 18 associated with 66% cervical cancer
- Types 6 & 11 associated with 90% genital warts

Nine-valent HPV vaccine

- Protects against 6, 11, 16, 18 plus 31, 33, 45, 52, 58 (high risk types)
 - ~ 97% reduction in cervical, vaginal, vulvar precancers due to types 31, 33, 45, 52, 58 compared with quadrivalent vaccine
 - 5 additional types account for about 20% of cervical cancers

HPV Vaccines Recommendations for Use

- Routine vaccination beginning at age 11-12
 - Okay to start as young as age 9
- Females: vaccinate through age 26
- Males: vaccinate routinely through age 21
 Extend to age 26 for MSM or immunocompromise
- Okay to continue series with a different vaccine
 - No need to revaccinate with 9-valent vaccine if series previously completed

HPV vaccine: two dose series

- October 2016: ACIP and CDC recommended two-dose HPV series if started before age 15
 - 9 14 years olds should receive two doses at least 6 months apart
- If started at 15+ years, three doses still needed

HPV Vaccines



- Excellent efficacy in studies (nearly 100%) in preventing infection with HPV types included in vaccine, if not previously infected
- Prevent cervical and anal intraepithelial neoplasia
- Greatest benefit before onset of sexual activity / infection with HPV
- No protection against types with which already infected at time of vaccination
- Some partial cross protection against non-vaccine serotypes
HPV Vaccine: External Genital Lesions



Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males

- 4065 healthy men and boys ages 16 26
- Randomized, double-blind, placebo controlled
- 36 external genital lesions in vaccine group, 89 in placebo group (intent to treat efficacy 60%)
- In seronegative group with all doses received, vaccine was 90% effective against genital lesions due to HPV types 6, 11, 16, 18 (mostly 6 and 11)

HPV Vaccines - questions

- Relatively expensive
- Not clear what long-term effect will be on risk of cancer
 - No recommendation to change cervical cancer screening based on vaccination status

HPV Vaccines - uptake



- In 2016, 65% of girls and 56% of boys ages 13 17 had received one of more doses of HPV vaccine
 - Girls: small improvement; boys: greater increase from 2015
 - Lower than coverage with Tdap and MenACWY https://www.cdc.gov/hpv/hcp/vacccoverage/index.html
- HPV infections due to vaccine types are dropping in 14-19 year old girls even with limited uptake *J Infect Dis 2013;208:385-93*