2014 Immunization Recommendations an Update from the ACIP

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Immunization Symposium 2014
Coulee Region Immunization Coalition
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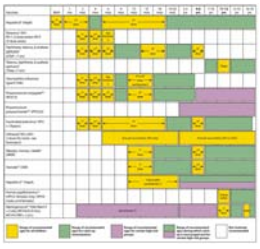
Objectives

- Recognized the ACIP Immunizations Schedules
- Review current ACIP recommendations
  - 10 key recommendations
  - understand the rationale and evidence used for recent vaccine recommendations
- Respond to patient concerns regarding vaccine safety and efficacy

ACIP Immunization Schedules

www.cdc.gov/vaccines/schedules/

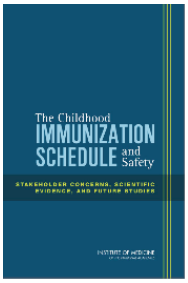


- Childhood (0 -- 18 years
- Adult
- Catch-up schedules
- Footnotes

ACIP Recommended Immunization Schedules are available at www.cdc.gov/vaccines/recs/schedules/default.htm

Why do we use the schedules?

- only schedule for which we have sufficient evidence for safety and efficacy
- Risk periods
  - rotavirus
- Response periods
  - immunogenicity
- Convenience
  - grouping immunizations with well care
- Collaborative Activity with Organizational Support



#1 Rotavirus vaccine

infants

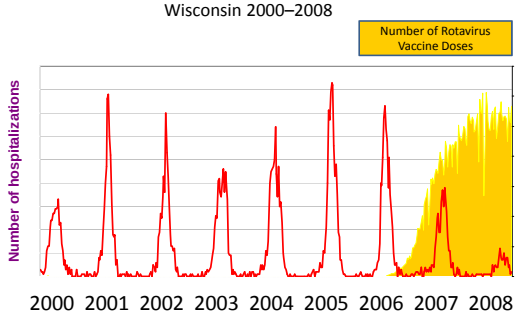
RV Vaccine in Practice

- Two options available:
  - Rotarix®—2 dose series at 2 and 4 months
  - RotaTeq®—3 dose series at 2, 4, and 6 months
- **Cochrane 2012: Vaccines are effective**
  - Prevention of rotavirus diarrhea, office visits, hospitalizations
- FPs are less likely to use RV vaccine than pediatricians

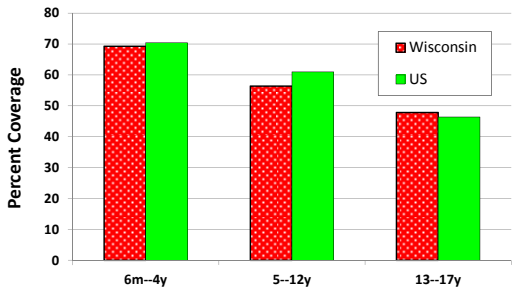
Soares-Weiser et al., Vaccines for preventing rotavirus diarrhea: vaccines in use. Cochrane Database Syst Rev 2012; Published Online: 15 FEB 2012 DOI: 10.1002/14651858.CD008521.pub2. Kempe et al., Adoption of rotavirus vaccination by pediatricians and family medicine physicians in the United States. Pediatrics 2009;134:e809-816.].

Weekly Rotavirus Hospitalizations

Wisconsin 2000–2008

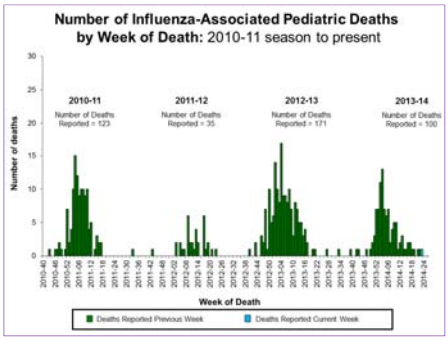


Wisconsin Influenza Coverage Rates



http://www.cdc.gov/flu/fluvaxview/reports/reporti1314/trends/index.htm.

Influenza-associated pediatric deaths



Source: http://www.cdc.gov/flu/weekly/

Influenza Vaccines

Image: CDC - Brian Judd

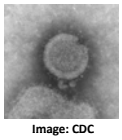


Image: CDC
Cynthia S. Goldsmith and Thomas Rowe

- **Recommended for all children**
  - 6 months through 18 years of age
- 2 doses at least 4 weeks apart
  - Children younger than 9 years of age
    - First time being vaccinated
    - Vaccinated in previous year with single dose
- Live attenuated influenza vaccine (LAIV) for children > 24 months of age
  - **When available, LAIV should be used for healthy children 2 through 8 years of age.**
  - **If LAIV is not immediately available, IIV should be used. Vaccination should not be delayed in order to procure LAIV.**
- Inactivated influenza vaccine (IIV) for children > 6 months of age

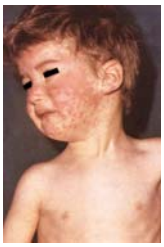
Influenza Vaccine Performance

- Number needed to vaccinate (NNV) to prevent
  - Hospitalization—age dependent
    - 6 to 23 months of age 1,031 to 3,050
    - 24 to 59 months of age 4,255 to 6,897
  - Outpatient Visits
    - Not age dependent 12 to 42

RCT: LAIV vs. IIV Outcomes	LAIV n=4179	IIV n=4173	Reduction (Influenza)	P
Total Influenza Cases	153	338	54.9%	0.001
Cases: Well-matched Virus	53	93	44.5%	0.001
Cases: Not Well-matched Virus	102	245	58.2%	0.001

Information from Lewis EN, Griffin MR, Szilagyi PG, et al. Childhood influenza: number needed to vaccinate to prevent 1 hospitalization or outpatient visit. *Pediatrics*. 2007;120(3):467-472; Belshe RB, Edwards KM, Vesikari T, et al; CAIV-T Comparative Efficacy Study Group. Live attenuated versus inactivated influenza vaccine in infants and young children. *N Engl J Med*. 2007;356(7):685-696. Erratum in: *N Engl J Med*. 2007;356(12):1283.

#3 MMR



all children at 12—15 months

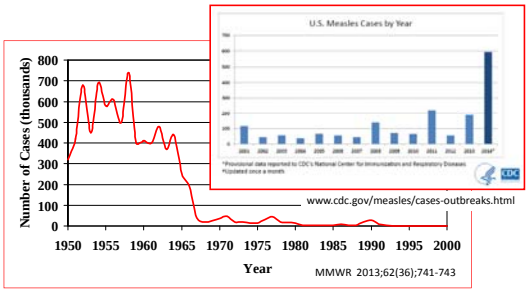
international travelers at 6 months

Measles Case Study

- Unvaccinated adult male presented to the ED with a rash illness, admitted and diagnosed empirically with a rickettsial illness
  - (+) measles serology reported by a commercial lab in Iowa 6 days later
  - Immediate serology available at Wisconsin State Laboratory of Hygiene
    - ½ mile away
- Exposed during those 6 days
  - 97 hospitalized patients
  - 105 visitors
  - 362 hospital employees were exposed
- Case-contact investigations in 18 of Wisconsin's 72 counties
  - 4 people were found to be at risk by serologic testing
    - including 1 infant, and 1 with an unknown serology

Changing Epidemiology of Measles

United States Elimination in 2000



2014 Measles Outbreak

- 593 cases (as of 8/29/2014)
  - 15% hospitalized
- 2 weeks to 65 years
  - 6% < 1 year
- 97% import-associated
  - 45 distinct importations
- 69% unvaccinated
- 20% unknown status
- Elimination Status Intact

- 89% were unvaccinated or had unknown vaccine status
  - **85% religious/personal belief waivers**
  - 6% missed opportunities
  - 5% too young to receive MMR
- Interactive GRAPHIC
  - Council on Foreign Relations
  - Vaccine-Preventable Outbreaks: www.cfr.org/interactives/GH_Vaccine_Map/#map

Centers for Disease Control and Prevention (CDC). Measles — United States, January 1–May 23, 2014. MMWR 2014;63(22);496-499

IGIM for postexposure prophylaxis

- The recommended dose of IGIM is 0.5mL/kg
  - Because concentrations of antibodies are lower, an increase in dose is needed.
- Postexposure use of IGIM might be limited because of volume limitations
  - The maximum dose by volume is 15 mL
- Persons who weigh >30 kg will receive less than the recommended dose and will have lower titers than recommended.

Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP) *MMWR Recommendations and Reports* June 14, 2013 / 62(RR04);1-34

Prevention of Measles:
Who should be vaccinated?

- **MMR is routinely recommended by ACIP**
  - age 12 through 15 months
  - age 4 through 6 years
- 1 dose is recommended for preschool-aged children ≥12 months and adults not at high risk for exposure/transmission
  - children aged 6 through 11 months who plan to travel or live abroad should receive MMR before travel
- 2 doses of MMR are recommended for school-aged children in kindergarten through grade 12 and adults at high risk for exposure/transmission
  - students attending colleges or other post-high school educational institutions, health-care personnel, and international travelers
  - minimum interval between the 2 doses is 28 days

#4 Hepatitis A

all children at 12—23 months

post-exposure prophylaxis

Hepatitis A Vaccine

- 2 doses recommended for all children
  - Age 12-23 months
- Post-exposure prophylaxis
  - vaccine can be used instead of Immunoglobulin for post-exposure prophylaxis
  - within 2 weeks of exposure
  - healthy persons
  - aged 12 months through 40 years
  - VFC approved
- Parents/caregivers of internationally-adopted children

#5 Meningitis

high risk infants

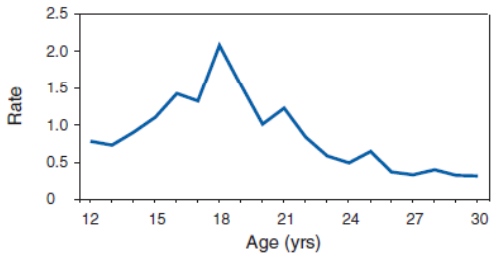
MenHibrix: Hib-Men-CY > 6 weeks

Menveo: MenACWY-CRM≥ 2 mos

Menactra: MenACWY-D >9 mo

Adolescent Peak of Meningococcal Disease

FIGURE 1. Rate* of meningococcal disease, by age — United States, 1991–2002



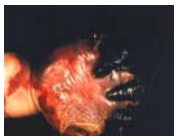
CDC. Prevention and Control of Meningococcal Disease Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54(No. RR-7):1-21.

Target groups

- **anatomic or functional asplenia** (including sickle cell disease):
  - 4-dose infant series of MenHibrix or Menveo at 2, 4, 6, and 12 through 15 months of age.
- **persistent complement component deficiency:**
  - 4-dose infant series of MenHibrix or Menveo at 2, 4, 6, and 12 through 15 months of age
- For children who **travel to or reside** in countries in which meningococcal disease is hyperendemic or epidemic administer an age appropriate formulation and series of Menactra or Menveo
  - Protection for serogroups A and W
- For children at risk during a **community outbreak** attributable to a vaccine serogroup, administer or complete an age- and formulation-appropriate series of any vaccine.

MCV4 - meningococcal

- Adolescent primary dose (MCV4) at age 11-12
  - Booster dose at age 16
- High Risk children: 2-dose primary series
  - administered at 9 and 12 months
    - persistent complement component deficiency and HIV
    - travel to endemic areas
  - 2 months apart for persons aged through 54 years
    - Functional or anatomic asplenia
  - Boost 3 years after primary until age 6
  - then boost every 5 years



Source: CDC/ Mr. Gust

Rabies
HDCV and PCECV

4-dose Post-exposure Prophylaxis for Unvaccinated Persons:

- Regimen of 4 one-mL vaccine doses of rabies vaccine (HDCV or PCECV) should be administered intramuscularly to previously unvaccinated persons with no immunosuppression
- The first dose of the 4-dose course should be administered as soon as possible after exposure. This date is considered day 0 of the post-exposure prophylaxis series
- Additional doses should then be administered on days 3, 7, and 14 after the first vaccination
- Considerations for the site of the intramuscular vaccination remain unchanged
- Rabies Immune Globulin Use: recommendations for use of immune globulin remain unchanged

ADULTS

Figure 1. Recommended adult immunization schedule, by vaccine and age group[1]

VACCINE ▼ AGE GROUP ►	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza [2]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) [3,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					Td/Tdap[3]
Varicella [4,*]	2 Doses					
Human papillomavirus (HPV) Female [5,*]	3 doses					
Human papillomavirus (HPV) Male [5,*]	3 doses					
Zoster [6]					1 dose	
Measles, mumps, rubella (MMR) [7,*]	1 or 2 doses				1 dose	
Pneumococcal (polysaccharide) [8,*]	1 or 2 doses					1 dose
Meningococcal [9,*]	1 or more doses					
Hepatitis A [10,*]	2 doses					
Hepatitis B [10,*]	3 doses					

*Covered by the Vaccine Injury Compensation Program

ACIP Recommended Immunization Schedule is available at www.cdc.gov/vaccines/recs/schedules/default.htm

#7 Tdap

all pregnancies

27 – 36 weeks gestation

Unexpected consequences of a safer vaccine

Vaccine Regimen	Rate Cases/100,000	Risk Ratio
Pure course DTwP	113.3	1 (reference)
Mixed – 1st dose DTwP	201.9	1.78
Mixed – 1st dose DTaP	409.0	3.61
Pure course DTaP	373.1	3.29

Sheridan SL, Ware RS, Grimwood K, Lambert SB. Number and order of whole cell pertussis vaccines in infancy and disease protection. JAMA. 2012;308(5):454-6. doi: 10.1001/jama.2012.6364.

Tdap

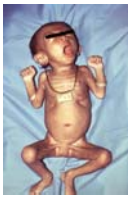


Image: CDC

- Pregnancy
  - Administer Tdap between 27 and 36 weeks gestation for each pregnancy
  - If not provided during pregnancy
    - administer Tdap immediately postpartum
- Adults 65 years and older
  - Now Routinely Recommended
  - Grandparents, child-care providers, and health-care practitioners who have/anticipate close contact with an infant less than 12 months of age and who previously have not received Tdap
- No indication for revaccination outside of pregnancy

Safety and Efficacy of Tdap in Pregnancy

- VAERS Study[1]
  - No new unexpected vaccine safety concerns
  - Limited number of pregnancy reports with repeat doses
  - CDC will continue to monitor
- VSD study[2]
  - Increased risk for chorioamnionitis
    - RR = 1.11 (1.03-1.21) 5.5% of unvaccinated; 5.6% of vaccinated
  - Decreased risk of pre-term labor
    - RR = 0.83 (0.77-0.90) 7.8% of unvaccinated; 5.3% of vaccinated
- Vaccine Effectiveness - UK evaluation[3]
  - Vaccine effectiveness estimated to be 91% (95% CI 84 to 95).

1. Moro P. Safety of Tdap vaccine during pregnancy: enhanced surveillance in VAERS. ACIP February 2014. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2014-02/02-Tdap-Moro.pdf 2. Kharbanda EO et al. Receipt of pertussis vaccine during pregnancy across 7 Vaccine Safety Datalink Sites. Prev Med. 2014. doi: 10.1016/j.ypmed.2014.05.025.
3. Amirthalingam G et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet. 2014; doi: 10.1016/S0140-6736(14)60686-3.

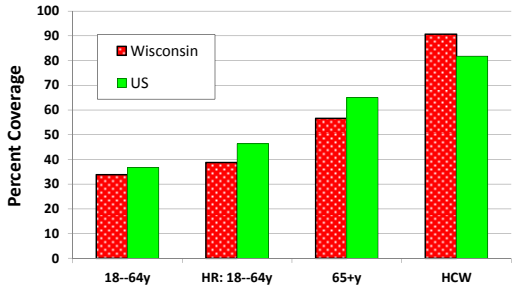
#8 Influenza

all adults

all pregnant women

any trimester

Wisconsin Influenza Coverage Rates



http://www.cdc.gov/flu/fluvaxview/reports/reporti1314/trends/index.htm.

IIV/LAIV

Influenza A and B

- Universal Recommendation
  - pregnant women (IIV only)
  - health-care workers
  - adults at high risk for influenza-related complications and severe disease
    - persons of any age with certain chronic medical conditions
    - adults who live with / care for HR persons
    - household contacts who have frequent contact with persons at high risk and who can transmit influenza to those persons at high risk

Benefit of Maternal Vaccination

Image: CDC/ James Gathany

- Randomized controlled study of 340 mothers (3rd Trimester)
- Infants of vaccinated mothers had less influenza
  - 6 cases vs. 16 cases
  - Vaccine effectiveness of 63% (95% CI, 5 to 85)
- Among mothers, reduction of 36% in respiratory illness with fever (95% CI, 4 to 57)

Information from Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med*. 2008;359(15):1555-1564.

Interesting Study

- UK study of 221 maternity hospitals
  - 256 pregnant women admitted with confirmed H1N1
  - 1220 pregnant women for comparison
- Perinatal mortality higher in infants of infected women
  - 39/1000 (95%CI: 19-71) for infected women
  - 7/1000 (95%CI: 3 -13) for uninfected
  - P < 0.001
- increase in the rate of stillbirth
  - 27/1000 vs. 6/1000 (P = 0.001)
- Increase in premature birth
  - (adjusted OR = 4.0, 95% CI 2.7 to 5.9)

Image: CDC

Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. BMJ. 201; 342:d3214.

Healthcare Worker Vaccination

- Pooled risk for all-cause mortality was 0.71
  - (95% confidence interval, .59–.85)
- Pooled risk for influenza-like illness was 0.58
  - (95% confidence interval, .59–.85)
- pooled estimates for all-cause hospitalization and laboratory-confirmed influenza were not statistically significant
- Using GRADE, the quality of the evidence for the effect of HCP vaccination on mortality was moderate

Ahmed F et al. Effect of Influenza Vaccination of Healthcare Personnel on Morbidity and Mortality Among Patients: Systematic Review and Grading of Evidence. Clin Infect Dis 2014; 58:50-7.

High Dose Influenza Vaccine

FDA licensure (on 12/23/2009)

- 4x-increase (60mcg) in the dose of hemagglutinin antigen for each of the three influenza strains
- A postlicensure study of effectiveness compared with standard dose TIV (Fluzone) was begun in 2009 and completed in 2013
- High dose showed ~25% relative risk reduction in influenza cases
  - Absolute RR = ~ 4 cases per 1000
    - Attack rate = 1.43% w/ high dose
    - Attack rate = 1.89% w/ regular dose

CDC/Richard Duncan

#9 Zoster

all adults

age 60 and older

Zoster/Varicella

Herpes zoster

- Vaccine licensed for use for age 50+ years
- Single dose of zoster vaccine is recommended for adults aged 60 years and older regardless of whether they report a history of chickenpox or a prior episode of herpes zoster
- Vaccinate persons with chronic medical conditions unless their condition is a contraindication
- No increase in HZ for individuals with immune mediated diseases

Source: CDC/ Judy Schmidt

Zhang J et al., Association between vaccination for Herpes Zoster and Risk of Herpes Zoster infection among older patients with selected Immune mediated diseases JAMA. 2012;308(1):43-9.

Post-licensure Assessment

Source: CDC

- retrospective cohort study of immunocompetent community-dwelling adults aged 60 years or older
  - Kaiser Permanente Southern California
  - 75,761 member vaccinated cohort
  - age matched (1:3) to 227,283 unvaccinated members
- 55% reduction in Shingles
  - 6.4 per 1000 person-years for vaccinated
  - 13.0 per 1000 person-years for unvaccinated
- 63% reduction in ophthalmic herpes zoster
- 65% reduction in herpes zoster hospitalizations

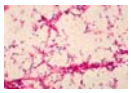
Tseng et al., Herpes Zoster Vaccine in Older Adults and the Risk of Subsequent Herpes Zoster Disease. JAMA. 2011;305(2):160-166.

#10 PCV-13/PPSV-23

65 years
immunocompromising conditions
medical conditions
smoking

PPSV-23 Indications

- Chronic lung disease
  - including asthma
- chronic cardiovascular diseases
- diabetes mellitus
- chronic liver diseases
  - cirrhosis
  - chronic alcoholism
- functional or anatomic asplenia
  - sickle cell disease
  - splenectomy
- immunocompromising conditions; including
  - chronic renal failure
  - nephrotic syndrome
- cochlear implants
- cerebrospinal fluid leaks
- HIV
- Residents of nursing homes or LTC facilities
- persons who smoke cigarettes



Revaccination with PPSV

- One-time revaccination after 5 years
  - for persons aged 19 through 64 years
  - with chronic renal failure or nephrotic syndrome;
  - functional or anatomic asplenia
    - (e.g., sickle cell disease or splenectomy)
  - persons with immunocompromising conditions.
- 65 years plus: one-time revaccination
  - if vaccinated 5 or more years previously and
  - less than 65 years at the time of primary vaccination

PCV-13 Immunocompromised Adults

- ACIP recommends routine use PCV13 for adults 19 years and older with:
  - immunocompromising conditions
  - functional or anatomic asplenia
  - cerebrospinal fluid (CSF) leaks
  - cochlear implants
- PCV13 is administered in addition to PPSV23
  - vaccine naïve individuals
    - PCV13 followed by PPSV23 at least 8 weeks later
  - previously been vaccinated with PPSV23
    - PCV13 one or more years after the last PPSV23 dose

Routine PCV-13 at age 65

- CAPiTA Trial
  - very large randomized, placebo-controlled trial
  - effects of PCV13 against pneumococcal pneumonia
  - over 80,000 participants in the Netherlands
- Effectiveness of PCV13 in prevention
  - 45% reduction in vaccine-type pneumococcal pneumonia
  - 75% reduction in (VT-PP) vaccine-type invasive pneumococcal disease
- Previous studies have shown significant boosting of "shared" antibodies when PCV13 is followed by PPSV23

PCV-13

New as of August 13, 2014

- ACIP recommends routine use PCV13 for adults 65 years and older
  - Pneumococcal vaccine naïve elders
    - PCV13, followed by PPSV23, 6 to 12 months later
  - Prior PPSV23 recipients at age 65+
    - PCV13 at least one year after the most recent PPSV23
  - When an additional dose of PPSV23 is indicated,
    - additional dose 6 to 12 months after PCV13
    - and at least 5 years after most recent dose of PPSV23.

Vaccine are Safe

- 2014: AHRQ-commissioned systematic review
  - *** **Rigorous lack of Conflict of Interest** ***
  - No association: MMR and autism spectrum disorder
  - high quality evidence
- 2013: Institute of Medicine Review

  *"Upon reviewing stakeholder concerns and scientific literature regarding the entire childhood immunization schedule, **the IOM committee finds no evidence that the schedule is unsafe.** The committee's review did not reveal an evidence base suggesting that the U.S. childhood immunization schedule is linked to autoimmune diseases, asthma, hypersensitivity, seizures, child developmental disorders, learning or developmental disorders, or attention deficit or disruptive disorders."*

Maglione et al. Safety of vaccines used for routine immunization of US children: a systematic review. Pediatrics 2014;134;325; DOI: 10.1542/peds.2014-1079.
The Childhood Immunization Schedule and Safety, Stakeholder Concerns, Scientific Evidence, and Future Studies
www.iom.edu/Reports/2013/The-Childhood-Immunization-Schedule-and-Safety.aspx

Vaccine are Effective

Among the 78.6 million children born during 1994–2013 routine childhood immunization was estimated to prevent:

- 322 million illnesses
  - (Average = 4.1 illnesses per child: NNV = 0.24)
- 21 million hospitalizations over the course of their lifetimes
  - (Average = 0.27 per child: NNV = 3.7)
- 732,000 premature deaths from vaccine-preventable illnesses
  - (Average = 0.01 per child: NNV = 107.4)

CDC. Benefits from Immunization During the Vaccines for Children Program Era — United States, 1994–2013. MMWR 2014; 63(16):352-5.

Vaccine are Effective

	Cases prevented (in thousands)		
Vaccine-preventable disease*	Illnesses	Hospitalizations	Deaths
Diphtheria	5,073	5,073	507.3
Tetanus	3	3	0.5
Pertussis	54,406	2,697	20.3
Haemophilus influenzae type B	361	334	13.7
Polio	1,244	530	14.8
Measles	70,748	8,877	57.3
Mumps	42,704	1,361	0.2
Rubella	36,540	134	0.3
Congenital rubella syndrome	12	17	1.3
Hepatitis B	4,007	623	59.7
Varicella	68,445	176	1.2
Pneumococcus-related diseases†	26,578	903	55.0
Rotavirus	11,968	327	0.1
Total	**322,089**	**21,055**	**731.7**

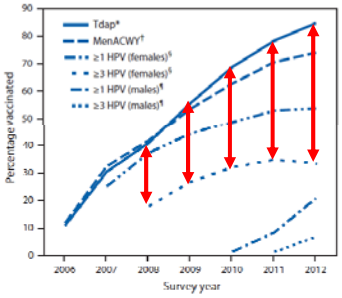
CDC. Benefits from Immunization During the Vaccines for Children Program Era — United States, 1994–2013. MMWR 2014; 63(16):352-5.

It's the message, stupid

- Messaging about routine use, safety, and effectiveness resonates with parents
  - MMR: parents reported increased vaccine acceptance with information emphasizing MMR's benefits
    - directly to the child
    - to both the child and society
    - but not to society alone
  - HPV: messaging about routine use, safety, and cancer prevention
- Provider Hesitancy
  - Become knowledgeable on vaccine safety and effectiveness

Hendrix KS. Vaccine Message framing and parents' intent to immunize their infants for MMR. Pediatrics 2014; DOI: 10.1542/peds.2013-4077.
Perkins et al. Missed opportunities for HPV vaccination in adolescent girls: a qualitative study. Pediatrics 2014;134:e666-674.

The HPV Dilemma



National and State Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2012. MMWR 2013; 62(34):685-693

HPV Effectiveness

- Between 2007-2010 and 2003-2006 vaccine-type HPV decreased by 56% in girls aged 14-19 years
- Risk for early sexual activity was not associated with vaccine receipt
  - pregnancy/STI testing/diagnosis/contraceptive counseling

Source: Markowitz LE, Hariri S, Lin C, Dunne EF, Steinau M, McQuillan G, Unger ER. Reduction in Human Papillomavirus (HPV) Prevalence Among Young Women Following HPV Vaccine Introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. J Infect Dis. 2013 Jun 19. [Epub ahead of print] Bednarczyk RA, Davis R, Ault K, Orenstein W, Omer SB. Sexual activity-related outcomes after human papillomavirus vaccination of 11- to 12-year-olds. Pediatrics. 2012;130(5):798-805.

Improving the message

HPV and the analogy of the bike helmet

- Most parent endorse the use of bike helmets
- When do you want your children to put on their bike helmets?
  - A. Before they get on their bike
  - B. When they are riding their bike
  - C. When they see the car heading directly at them
  - D. After the car hits them

Temte JL. Timing of HPV vaccine. [letter] Pediatrics 2014 http://pediatrics.aappublications.org/content/134/3/e666/reply#pediatrics_el_63882

Summary Points

- ACIP Immunization Schedules
  - Evidence-based
  - Constantly changing to address new needs
- Recommendations are constantly changing
  - New situations
  - New evidence
  - New vaccines
  - New indications
- Vaccines have been one of the most successful medical interventions
  - Highly effective
  - Excellent record of safety

Questions / Contact Information

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