Vaccines – Issues to Contemplate

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PEDIATRIC INFECTIOUS DISEASES

CHOC CHILDREN'S HOSPITAL

Disclosures

- I have no financial disclosures related to this presentation
- This talk is heavily plagiarized from Dr. Mark Sawyer's CIC presentation in April, 2019 (with his permission)

Confusing things in our current vaccine recommendations

- Influenza, LAIV- we used to love it, then we hated it, and now we like it again.
- PCV13-we started giving it to adults 65 and older in 2014. Now we are going to stop (sort of).
- Tdap-one of the Tdap vaccines is now licensed for a booster dose. Does that mean we should be giving more people booster doses?
- Meningococcal B vaccines…
- HPV is now recommended up to the age of 45. Does that mean we should be immunizing adults over 26 years of age?
- Do we still have to keep talking about measles?

Objectives

- Participants will be able to list the current recommendations regarding the return of LAIV in the US for the 2018-19 and 2019-20 seasons.
- Participants will be able to describe the factors being considered in deciding if non-pregnant individuals should get Tdap vaccine boosters.
- Participants will be able to explain why adults older than 26 years might benefit from HPV vaccine
- Participants will be able to explain the rationale for recommending meningococcal B vaccine to adolescents.
- Participants will be able to discuss common questions regarding measles vaccine and immunity given the current global outbreaks.

New Issues to Contemplate…

- Live attenuated influenza vaccine (LAIV) is back
- Continuing to give PCV13 to adults 65 and older is not uniformly recommended any longer.
- Tdap vaccine boosters may be recommended for non-pregnant individuals
- Meningococcal B vaccine boosters are recommended for high-risk individuals
- HPV vaccine now licensed by FDA up to age 45. The ACIP recommendations now harmonize male and female recommendations up to age 26y.

Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger

UNITED STATES 2019

Vaccines in the Child and Adolescent Immunization Schedule*

Vaccines	Abbreviations	Trade names
Diphtheria, tetanus, and acellular pertussis vaccine	DTaP	Daptacel Infanrix
Diphtheria, tetanus vaccine	DT	No Trade Name
Haemophilus influenzae type b vaccine	Hib (PRP-T) Hib (PRP-OMP)	ActHIB Hiberix PedvaxHIB
Hepatitis A vaccine	HepA	Havrix Vaqta
Hepatitis B vaccine	HepB	Engerix-B Recombivax HB
Human papillomavirus vaccine	HPV	Gardasil 9
Influenza vaccine (inactivated)	IIV	Multiple
Influenza vaccine (live, attenuated)	LAIV	FluMist
Measles, mumps, and rubella vaccine	MMR	M-M-R II
Meningococcal serogroups A, C, W, Y vaccine	MenACWY-D MenACWY-CRM	Menactra Menveo
Meningococcal serogroup B vaccine	MenB-4C MenB-FHbp	Bexsero Trumenba
Pneumococcal 13-valent conjugate vaccine	PCV13	Prevnar 13
Pneumococcal 23-valent polysaccharide vaccine	PPSV23	Pneumovax
Poliovirus vaccine (inactivated)	IPV	IPOL
Rotavirus vaccine	RV1 RV5	Rotarix RotaTeq
Tetanus, diphtheria, and acellular pertussis vaccine	Tdap	Adacel Boostrix
Tetanus and diphtheria vaccine	Td	Tenivac Td vaccine
Varicella vaccine	VAR	Varivax
Combination Vaccines *(Use combination vaccines instead of separate injections when appropriate)*		
DTaP, hepatitis B, and inactivated poliovirus vaccine	DTaP-HepB-IPV	Pediarix
DTaP, inactivated poliovirus, and *Haemophilus influenzae* type b vaccine	DTaP-IPV/Hib	Pentacel
DTaP and inactivated poliovirus vaccine	DTaP-IPV	Kinrix Quadracel
Measles, mumps, rubella, and varicella vaccines	MMRV	ProQuad

*Administer recommended vaccines if immunization history is incomplete or unknown. Do not restart or add doses to vaccine series for extended intervals between doses. When a vaccine is not administered at the recommended age, administer at a subsequent visit. The use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.

How to use the child/adolescent immunization schedule

1 Determine recommended vaccine by age **(Table 1)**

2 Determine recommended interval for catch-up vaccination **(Table 2)**

3 Assess need for additional recommended vaccines by medical condition and other indications **(Table 3)**

4 Review vaccine types, frequencies, intervals, and considerations for special situations **(Notes)**

Recommended by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/acip) and approved by the Centers for Disease Control and Prevention (www.cdc.gov), American Academy of Pediatrics (www.aap.org), American Academy of Family Physicians (www.aafp.org), and American College of Obstetricians and Gynecologists (www.acog.org).

Report

- Suspected cases of reportable vaccine-preventable diseases or outbreaks to your state or local health department
- Clinically significant adverse events to the Vaccine Adverse Event Reporting System (VAERS) at www.vaers.hhs.gov or (800-822-7967)

Download the CDC Vaccine Schedules App for providers at www.cdc.gov/vaccines/schedules/hcp/schedule-app.html.

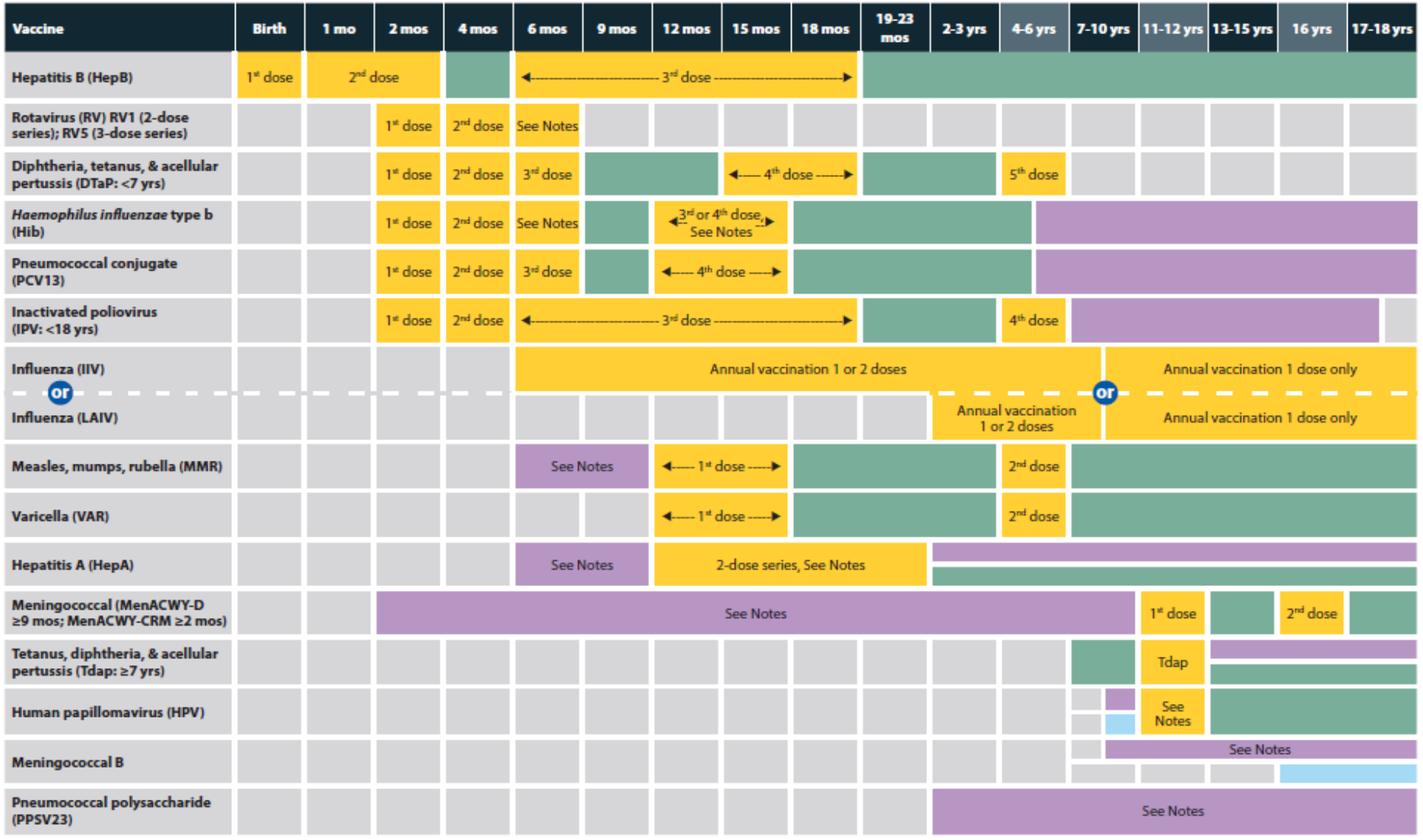
Helpful Information

- Complete ACIP recommendations: www.cdc.gov/vaccines/hcp/acip-recs/index.html
- General Best Practice Guidelines for Immunization: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
- Outbreak information (including case identification and outbreak response), see Manual for the Surveillance of Vaccine-Preventable Diseases: www.cdc.gov/vaccines/pubs/surv-manual

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger United States, 2019

These recommendations must be read with the Notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Table 1. To determine minimum intervals between doses, see the catch-up schedule (Table 2). School entry and adolescent vaccine age groups are shaded in gray.



Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision-making

No recommendation

Table 2 Catch-up immunization schedule for persons aged 4 months—18 years who start late or who are more than 1 month behind, United States, 2019

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Table 1 and the notes that follow.

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B	Birth	**4 weeks**	**8 weeks *and* at least 16 weeks after first dose.** Minimum age for the final dose is 24 weeks.		
Rotavirus	6 weeks Maximum age for first dose is 14 weeks, 6 days	**4 weeks**	**4 weeks** Maximum age for final dose is 8 months, 0 days.		
Diphtheria, tetanus, and acellular pertussis	6 weeks	**4 weeks**	**4 weeks**	**6 months**	**6 months**
Haemophilus influenzae type b	6 weeks	**No further doses needed** if first dose was administered at age 15 months or older. **4 weeks** If first dose was administered before the 1st birthday. **8 weeks (as final dose)** If first dose was administered at age 12 through 14 months.	**No further doses needed** if previous dose was administered at age 15 months or older. **4 weeks** If current age is younger than 12 months ***and*** first dose was administered at younger than age 7 months, ***and*** at least 1 previous dose was PRP-T (ActHib, Pentacel, Hiberix) or unknown. **8 weeks *and* age 12 through 59 months (as final dose)** If current age is younger than 12 months ***and*** first dose was administered at age 7 through 11 months; OR If current age is 12 through 59 months ***and*** first dose was administered before the 1st birthday, ***and*** second dose administered at younger than 15 months; OR If both doses were PRP-OMP (PedvaxHIB; Comvax) ***and*** were administered before the 1st birthday.	**8 weeks (as final dose)** This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal conjugate	6 weeks	**No further doses needed** for healthy children if first dose was administered at age 24 months or older. **4 weeks** If first dose administered before the 1st birthday. **8 weeks (as final dose for healthy children)** If first dose was administered at the 1st birthday or after.	**No further doses needed** for healthy children if previous dose administered at age 24 months or older. **4 weeks** If current age is younger than 12 months and previous dose given at <7 months old. **8 weeks (as final dose for healthy children)** If previous dose given between 7-11 months (wait until at least 12 months old); OR If current age is 12 months or older and at least 1 dose was given before age 12 months.	**8 weeks (as final dose)** This **dose** only necessary for children age 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus	6 weeks	**4 weeks**	4 weeks if current age is < 4 years. 6 months (as final dose) if current age is 4 years or older.	**6 months** (minimum age 4 years for final dose).	
Measles, mumps, rubella	12 months	**4 weeks**			
Varicella	12 months	**3 months**			
Hepatitis A	12 months	**6 months**			
Meningococcal	2 months MenACWY-CRM 9 months MenACWY-D	**8 weeks**	See Notes	See Notes	
Children and adolescents age 7 through 18 years					
Meningococcal	Not Applicable (N/A)	**8 weeks**			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis	7 years	**4 weeks**	**4 weeks** If first dose of DTaP/DT was administered before the 1st birthday. **6 months (as final dose)** If first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday.	**6 months** if first dose of DTaP/DT was administered before the 1st birthday.	
Human papillomavirus	9 years	**Routine dosing intervals are recommended.**			
Hepatitis A	N/A	**6 months**			
Hepatitis B	N/A	**4 weeks**	**8 weeks *and*** at least 16 weeks after first dose.		
Inactivated poliovirus	N/A	**4 weeks**	**6 months** A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.	A fourth dose of IPV is indicated if all previous doses were administered at <4 years or if the third dose was administered <6 months after the second dose.	
Measles, mumps, rubella	N/A	**4 weeks**			
Varicella	N/A	**3 months** if younger than age 13 years. **4 weeks** if age 13 years or older.			

Table 3 Recommended Child and Adolescent Immunization Schedule by Medical Indication United States, 2019

VACCINE	INDICATION										
	Pregnancy	Immunocompromised status (excluding HIV infection)	HIV infection CD4+ count[1]		Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease	CSF leaks/ cochlear implants	Asplenia and persistent complement component deficiencies	Chronic liver disease	Diabetes
			<15% and total CD4 cell count of <200/mm3	≥15% and total CD4 cell count of ≥200/mm3						
Hepatitis B										
Rotavirus		SCID[2]								
Diphtheria, tetanus, & acellular pertussis (DTaP)										
Haemophilus influenzae type b										
Pneumococcal conjugate										
Inactivated poliovirus										
Influenza (IIV)										
or										
Influenza (LAIV)						Asthma, wheezing: 2-4yrs[3]				
Measles, mumps, rubella										
Varicella										
Hepatitis A										
Meningococcal ACWY										
Tetanus, diphtheria, & acellular pertussis (Tdap)										
Human papillomavirus										
Meningococcal B										
Pneumococcal polysaccharide										

- Vaccination according to the routine schedule recommended
- Recommended for persons with an additional risk factor for which the vaccine would be indicated
- Vaccination is recommended, and additional doses may be necessary based on medical condition. See Notes.
- Contraindicated or use not recommended—vaccine should not be administered because of risk for serious adverse reaction
- Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction
- Delay vaccination until after pregnancy if vaccine indicated
- No recommendation

1 For additional information regarding HIV laboratory parameters and use of live vaccines, see the General Best Practice Guidelines for Immunization "Altered Immunocompetence" at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and Table 4-1 (footnote D) at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html.
2 Severe Combined Immunodeficiency
3 LAIV contraindicated for children 2–4 years of age with asthma or wheezing during the preceding 12 months.

Notes

Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019

For vaccine recommendations for persons 19 years of age and older, see the Recommended Adult Immunization Schedule.

Additional information

- Consult relevant ACIP statements for detailed recommendations at www.cdc.gov/vaccines/hcp/acip-recs/index.html.
- For information on contraindications and precautions for the use of a vaccine, consult the General Best Practice Guidelines for Immunization and relevant ACIP statements at www.cdc.gov/vaccines/hcp/acip-recs/index.html.
- For calculating intervals between doses, 4 weeks = 28 days. Intervals of ≥4 months are determined by calendar months.
- Within a number range (e.g., 12–18), a dash (–) should be read as "through."
- Vaccine doses administered ≤4 days before the minimum age or interval are considered valid. Doses of any vaccine administered ≥5 days earlier than the minimum age or minimum interval should not be counted as valid and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see Table 3-1, Recommended and minimum ages and intervals between vaccine doses, in General Best Practice Guidelines for Immunization at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html.
- Information on travel vaccine requirements and recommendations is available at wwwnc.cdc.gov/travel/.
- For vaccination of persons with immunodeficiencies, see Table 8-1, Vaccination of persons with primary and secondary immunodeficiencies, in General Best Practice Guidelines for Immunization at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and Immunization in Special Clinical Circumstances (In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:67–111).
- For information regarding vaccination in the setting of a vaccine-preventable disease outbreak, contact your state or local health department.
- The National Vaccine Injury Compensation Program (VICP) is a no-fault alternative to the traditional legal system for resolving vaccine injury claims. All routine child and adolescent vaccines are covered by VICP except for pneumococcal polysaccharide vaccine (PPSV23). For more information, see www.hrsa.gov/vaccinecompensation/index.html.

Diphtheria, tetanus, and pertussis (DTaP) vaccination (minimum age: 6 weeks [4 years for Kinrix or Quadracel])

Routine vaccination

- 5-dose series at 2, 4, 6, 15–18 months, 4–6 years
  - **Prospectively:** Dose 4 may be given as early as age 12 months if at least 6 months have elapsed since dose 3.
  - **Retrospectively:** A 4th dose that was inadvertently given as early as 12 months may be counted if at least 4 months have elapsed since dose 3.

Catch-up vaccination

- Dose 5 is not necessary if dose 4 was administered at age 4 years or older.
- For other catch-up guidance, see Table 2.

Haemophilus influenzae type b vaccination (minimum age: 6 weeks)

Routine vaccination

- **ActHIB, Hiberix, or Pentacel:** 4-dose series at 2, 4, 6, 12–15 months
- **PedvaxHIB:** 3-dose series at 2, 4, 12–15 months

Catch-up vaccination

- **Dose 1 at 7–11 months:** Administer dose 2 at least 4 weeks later and dose 3 (final dose) at 12–15 months or 8 weeks after dose 2 (whichever is later).
- **Dose 1 at 12–14 months:** Administer dose 2 (final dose) at least 8 weeks after dose 1.
- **Dose 1 before 12 months and dose 2 before 15 months:** Administer dose 3 (final dose) 8 weeks after dose 2.
- **2 doses of PedvaxHIB before 12 months:** Administer dose 3 (final dose) at 12–59 months and at least 8 weeks after dose 2.
- **Unvaccinated at 15–59 months:** 1 dose
- For other catch-up guidance, see Table 2.

Special situations

- **Chemotherapy or radiation treatment:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

  Doses administered within 14 days of starting therapy or during therapy should be repeated at least 3 months after therapy completion.
- **Hematopoietic stem cell transplant (HSCT):**
  - 3-dose series 4 weeks apart starting 6 to 12 months after successful transplant regardless of Hib vaccination history
- **Anatomic or functional asplenia (including sickle cell disease):**
  12–59 months
  - Unvaccinated or only 1 dose before 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before 12 months:1 dose at least 8 weeks after previous dose

  Unvaccinated persons age 5 years or older*
  - 1 dose
- **Elective splenectomy:**
  Unvaccinated persons age 15 months or older*
  - 1 dose (preferably at least 14 days before procedure)
- **HIV infection:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

  Unvaccinated persons age 5–18 years*
  - 1 dose
- **Immunoglobulin deficiency, early component complement deficiency:**
  12–59 months
  - Unvaccinated or only 1 dose before age 12 months: 2 doses, 8 weeks apart
  - 2 or more doses before age 12 months: 1 dose at least 8 weeks after previous dose

**Unvaccinated* = Less than routine series (through 14 months) OR no doses (14 months or older)

Influenza

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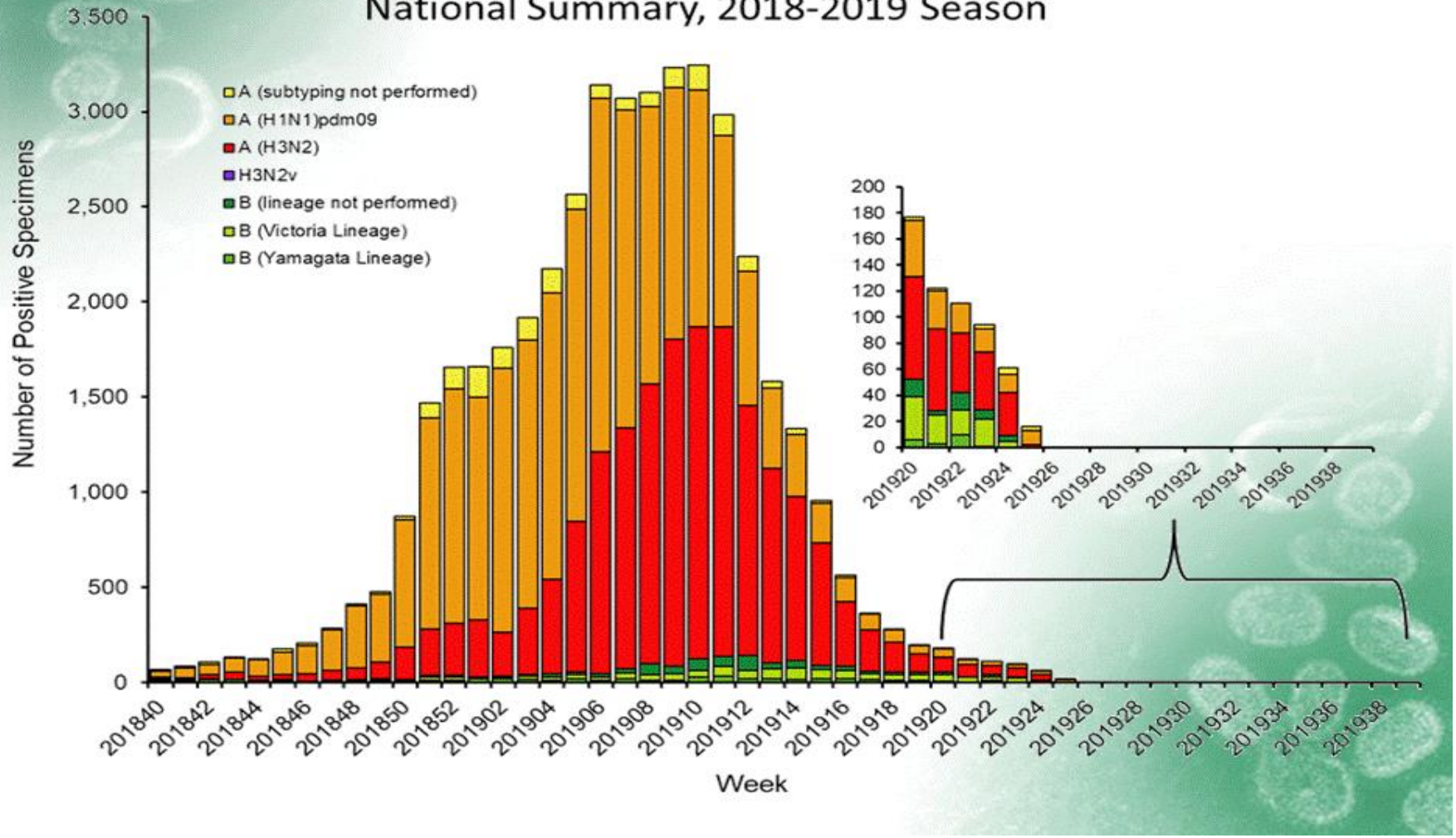
FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

CDC
Centers for Disease Control and Prevention

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2018-2019 Season



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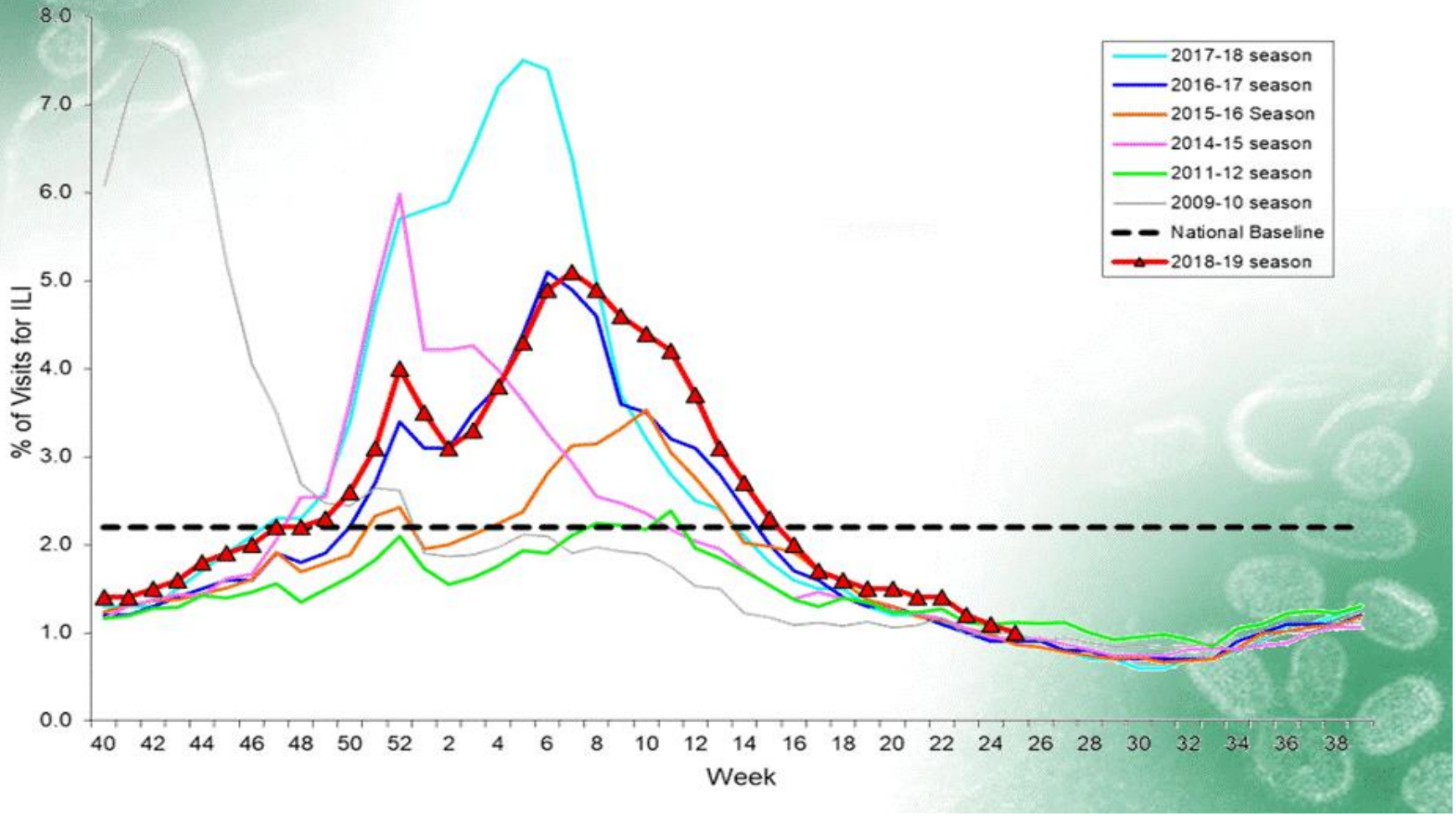
FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

CDC
Centers for Disease Control and Prevention

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2018-2019 and Selected Previous Seasons



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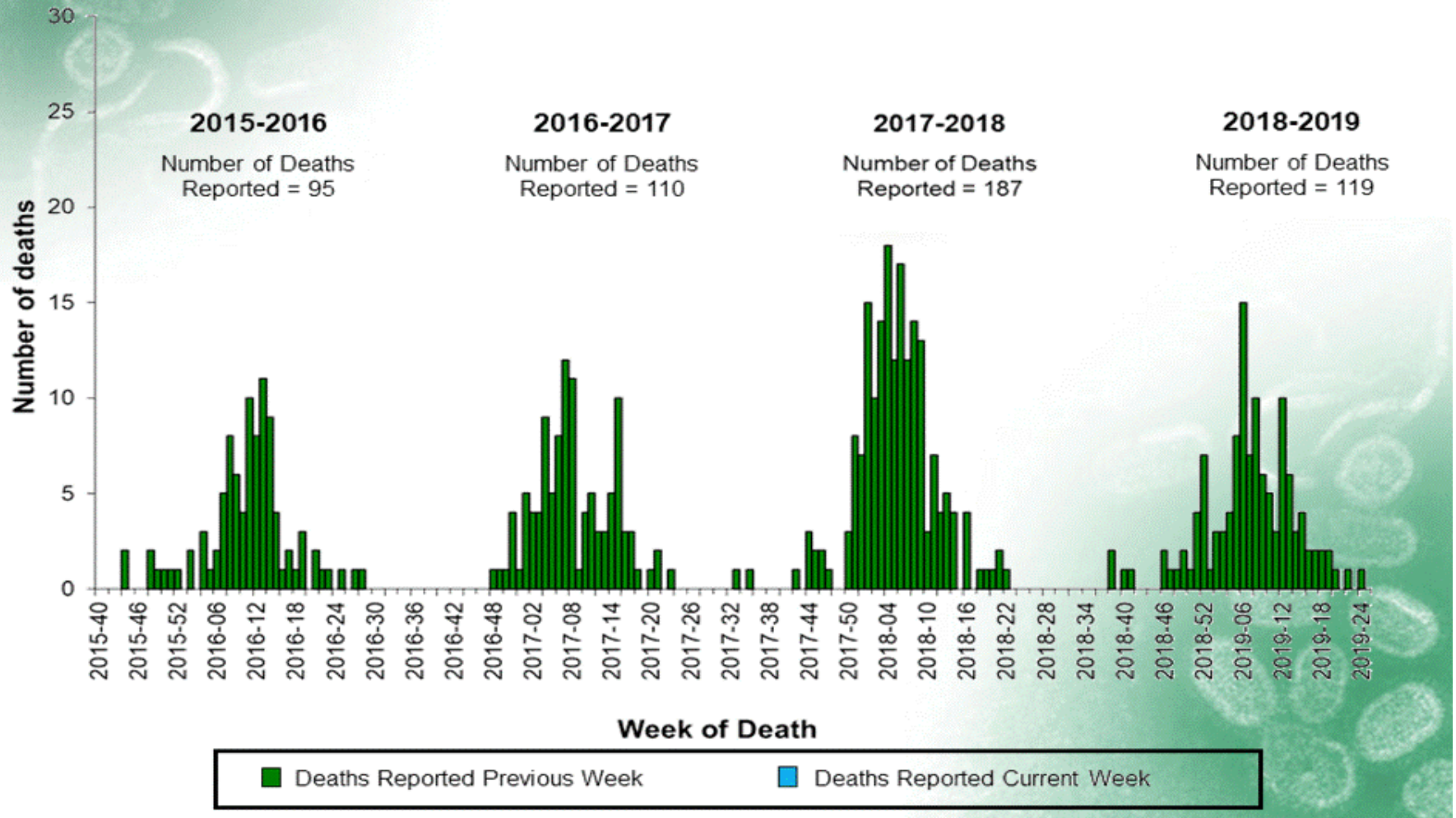
FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

CDC Centers for Disease Control and Prevention

Number of Influenza-Associated Pediatric Deaths by Week of Death: 2015-2016 season to present



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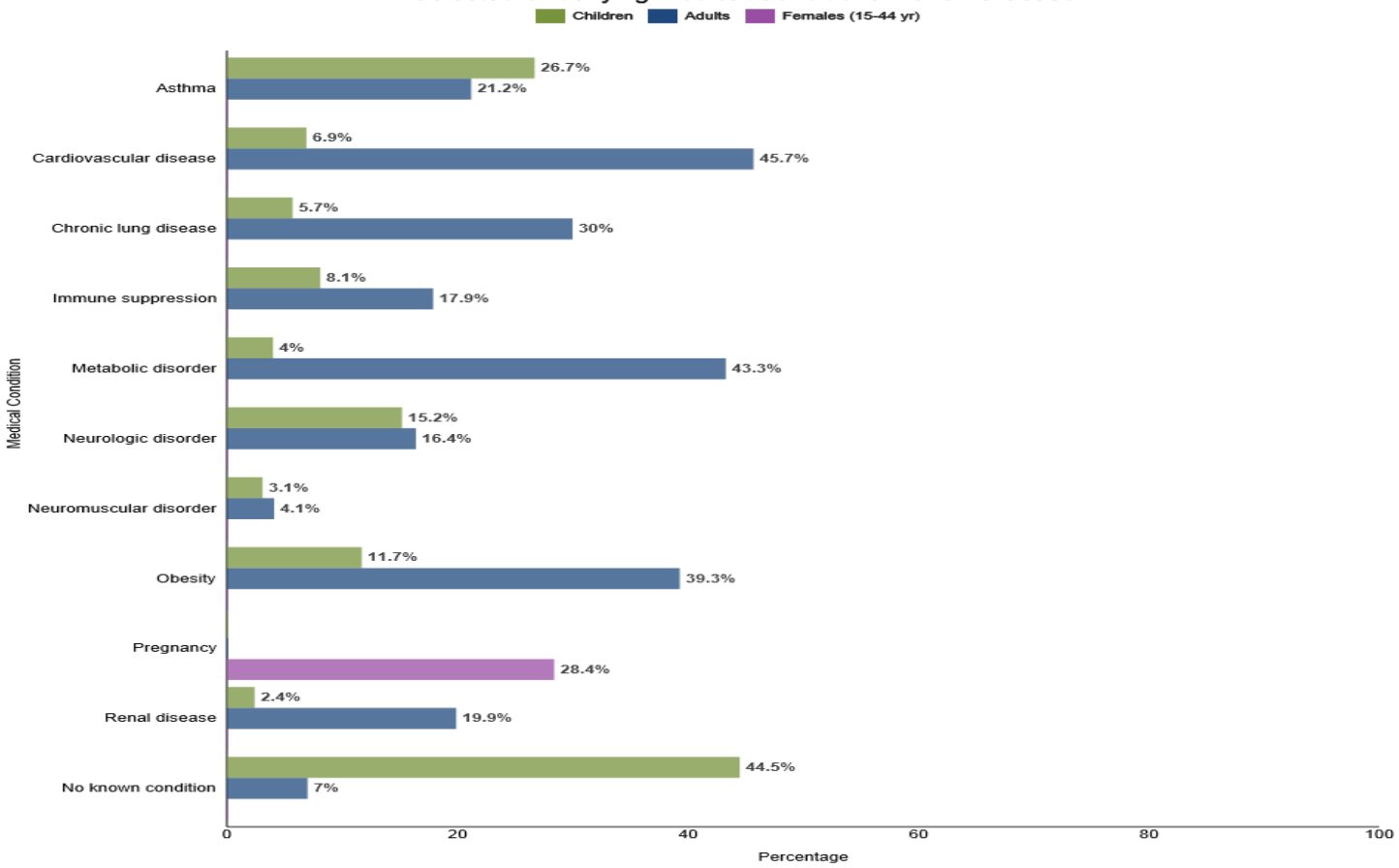
Laboratory-Confirmed Influenza Hospitalizations

Preliminary data as of Jun 22, 2019

Selected Underlying Medical Conditions: 2018-19 Season



FluSurv-NET data are preliminary and displayed as they become available. Therefore, figures are based on varying denominators as some variables represent information that may require more time to be collected.Data are refreshed and updated weekly.
Asthma includes a medical diagnosis of asthma or reactive airway disease.
Cardiovascular diseases include conditions such as coronary heart disease, cardiac valve disorders, congestive heart failure, and pulmonary hypertension; does not include isolated hypertension.
Chronic lung diseases include conditions such as chronic obstructive pulmonary disease, bronchiolitis obliterans, chronic aspiration pneumonia, and interstitial lung disease.
Immune suppression includes conditions such as immunoglobulin deficiency, leukemia, lymphoma, HIV / AIDS, and individuals taking immunosuppressive medications.
Metabolic disorders include conditions such as diabetes mellitus.
Neurologic diseases include conditions such as seizure disorders, cerebral palsy, and cognitive dysfunction.
Neuromuscular diseases include conditions such as multiple sclerosis and muscular dystrophy.
Obesity was assigned if indicated in patient's medical chart or if body mass index(BMI) > 30 kg / m2.
Pregnancy percentage calculated using number of female cases aged between 15 and 44 years of age as the denominator.
Renal diseases include conditions such as acute or chronic renal failure, nephrotic syndrome, glomerulonephritis, and impaired creatinine clearance.
No known condition indicates that the case did not have any known high risk medical condition indicated in medical chart at the time of hospitalization.

How did the 2018-19 Flu Season Go?

- The 2018-’19 season was moderate in severity but with activity above baseline for 21 weeks, the longest in a decade, due to separate waves of H1N1 and H3N2.
- Across all ages, vaccines were 29% effective in preventing illness requiring outpatient medical attention.
- Most effective for children ages 6 months to 8 years at 49%.
- However, this year’s vaccine did not provide significant protection against H3N2 due to the emergence of a different virus clade. The WHO delayed choosing an H3N2 strain for next season.
- Throughout the season, 119 children died of flu. Across all ages, the CDC estimates as many as 42.9 million people got sick, 647,000 were hospitalized and 61,200 died. Vaccines are estimated to have prevented 40,000 to 90,000 hospitalizations.
- Manufacturers plan to start distributing vaccines for the 2019-’20 season between mid-August and early September.

Influenza vaccine strains 2019-2020

- A/Brisbane/02/2018 (H1N1)pdm09-like virus (NEW);
- A/Kansas/14/2017 (H3N2)-like virus * (NEW);
- B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and
- B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).

* The A(H3N2) component was recommended on 21 March 2019.

Effectiveness of LAIV compared to IIV

TABLE 2 Vaccine Effectiveness Against any Influenza in Children, by Age and Vaccine Type

Season (Predominant Strain)	Age Range (y)	Adjusted VE % (95% CI)	
		LAIV4	IIV3/IIV4
2013–2014[a] (H1N1pdm09)	2–17	7 (−46 to 40)	60 (41 to 73)
	2–8	−36 (−151 to 27)	59 (30 to 76)
	9–17	41 (−21 to 72)	61 (27 to 79)
2014–2015[b] (H3N2)	2–17	9 (−18 to 29)	31 (16 to 44)
	2–8	9 (−28 to 35)	26 (2 to 44)
	9–17	17 (−27 to 46)	33 (9 to 51)
2015–2016[c] (H1N1pdm09)	2–17	5 (−47 to 39)	60 (47 to 70)
	2–8	0 (−75 to 43)	56 (42 to 71)
	9–17	17 (−84 to 63)	66 (44 to 80)

VE, vaccine effectiveness.

Reasons LAIV is back

- Good vaccine effectiveness in the UK in 2018-2019
- Small amount of nasopharyngeal shredding and serologic data that the current vaccine should work
- Historically better for H3N2 and influenza B
- Well accepted/ preferred by some families
- Easier to administer in non- medical settings

- WHAT'S MISSING?
- Effectiveness data in the U.S.

Flu Vaccine Recommendations 2019-2020

- ACIP is not making significant changes to its flu vaccine recommendations for 2019-'20 and is expected to be in harmony with AAP recommendations.
- Both are recommending everyone 6 months and older be vaccinated and will not have a preference between inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV). However, AstraZeneca, which manufactures LAIV vaccine FluMist Quadrivalent, has announced its supply will be limited due to manufacturing constraints.
- Four IIVs are expected to be available for children ages 6 through 35 months, and the CDC's policy will include a table summarizing dose volumes as they differ for each. The CDC also is clarifying that children needing two doses of flu vaccine still should receive the second dose if they turn 9 between doses, consistent with AAP guidance.

Influenza Vaccine Products for the 2018–2019 Influenza Season

Manufacturer	Trade Name (vaccine abbreviation)[1]	How Supplied	Mercury Content (mcg Hg/0.5mL)	Age Range	Vaccine Product Billing Code[2]	
					CPT	Medicare
GlaxoSmithKline	Fluarix (IIV4)	0.5 mL (single-dose syringe)	0	6 months & older	90686	90686
ID Biomedical Corp. of Quebec, a subsidiary of GlaxoSmithKline	FluLaval (IIV4)	0.5 mL (single-dose syringe)	0	6 months & older	90686	90686
		5.0 mL (multi-dose vial)	<25	6 months & older	90688	90688
MedImmune	FluMist (LAIV4)	0.2 mL (single-use nasal spray)	0	2 through 49 years	90672	90672
Protein Sciences Corporation, a Sanofi company	Flublok (RIV4)	0.5 mL (single-dose syringe)	0	18 years & older	90682	90682
Sanofi Pasteur, Inc.	Fluzone (IIV4)			gh 35 months	90685	90685
				& older	90686	90686
				& older	90686	90686
				gh 35 months	90687	90687
		5.0 mL (multi-dose vial)	25	3 years & older	90688	90688
	Fluzone High-Dose (IIV3-HD)	0.5 mL (single-dose syringe)	0	65 years & older	90662	90662
Seqirus	Afluria (IIV3)	0.5 mL (single-dose syringe)	0	5 years & older[3]	90656	90656
		5.0 mL (multi-dose vial)	24.5		90658	Q2035
	Afluria (IIV4)	0.5 mL (single-dose syringe)	0	5 years & older[3]	90686	90686
		5.0 mL (multi-dose vial)	24.5		90688	90688
	Fluad (aIIV3)	0.5 mL (single-dose syringe)	0	65 years & older	90653	90653
	Flucelvax (ccIIV4)	0.5 mL (single-dose syringe)	0	4 years & older	90674	90674
		5.0 mL (multi-dose vial)	25		90756	90756

Infant dose of Fluzone will be 0.5ml next year

Footnotes

1. IIV3/IIV4 = egg-based trivalent/quadrivalent inactivated influenza vaccine (injectable); where necessary to refer to cell culture-based vaccine, the prefix "cc" is used (e.g., ccIIV4); RIV4 = quadrivalent recombinant hemagglutinin influenza vaccine (injectable); aIIV3 = adjuvanted trivalent inactivated influenza vaccine.
2. An administration code should always be reported in addition to the vaccine product code. Note: Third party payers may have specific policies and guidelines that might require providing additional information on their claim forms.
3. Afluria is approved by the Food and Drug Administration for intramuscular administration with the PharmaJet Stratis Needle-Free Injection System for persons age 18 through 64 years.

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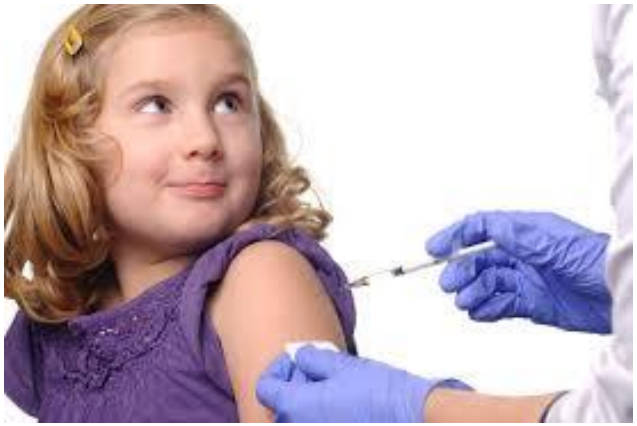
Timing for Flu Vaccine?

- CDC recommends getting vaccinated by the end of October.

- Evidence suggests decrease of VE by about 7% per month, with sharper decline for H3N2 strains.

- This has to be balanced against the logistical difficulty of getting everyone vaccinated in a short period of time, and the possibility of missed opportunities.

PCV13 for adults 65 years and older-do we still need this?



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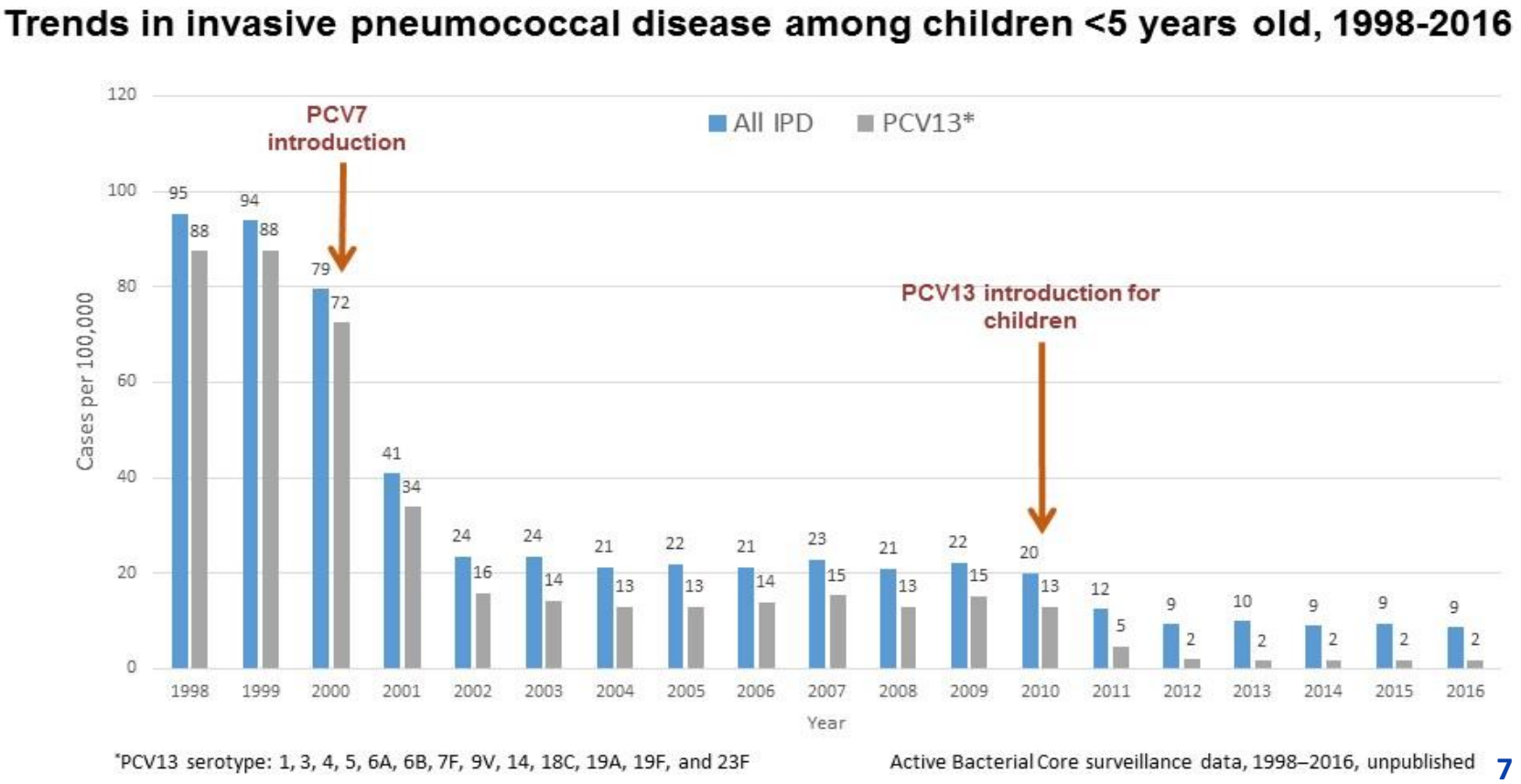
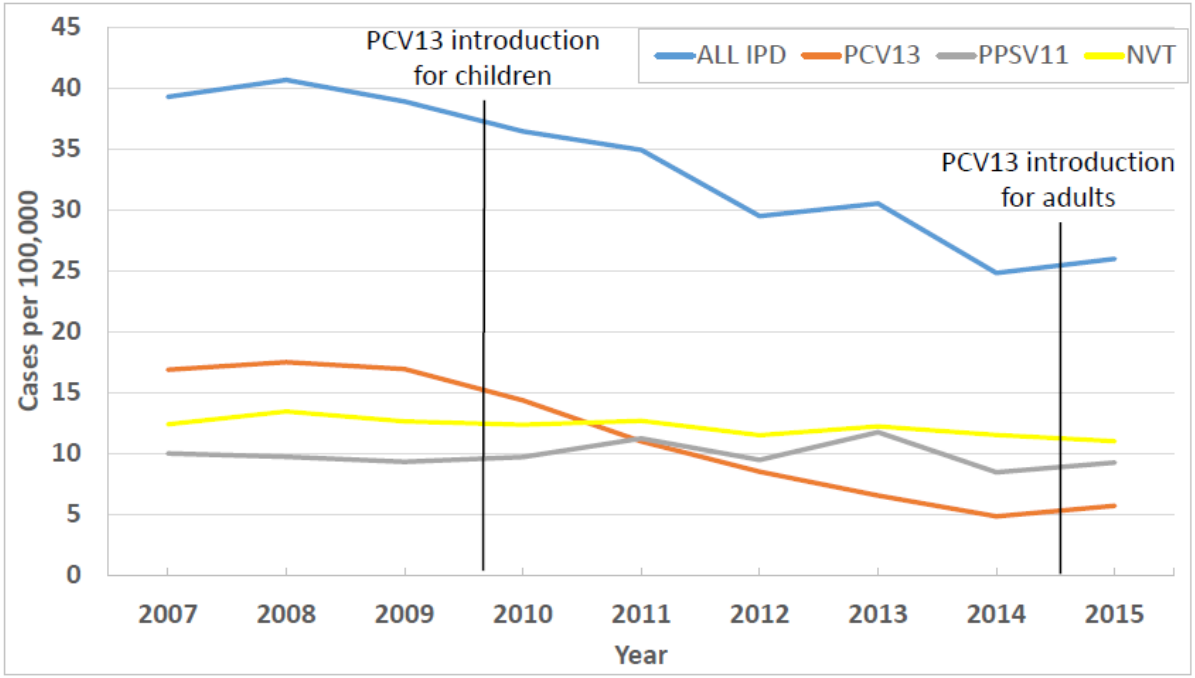
Protecting Children with Pneumococcal Conjugate Vaccines (PCV)



Source: Pneumococcal Disease Surveillance and Reporting. https://www.cdc.gov/pneumococcal/surveillance.html

Annual Trends in IPD Incidence by Serotype Groups, Adults ≥65 Years Old, 2007–2015



By immunizing children we prevent disease in adults!

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PCV13 for Adults >65y

Summary of Key Issues

Reasons Raised in Favor of <u>Continuing</u> Routine PCV13 Use	Reasons Raised in Favor of <u>Discontinuing</u> Routine PCV13 Use
• **PCV13 effective in preventing PCV13-type pneumococcal disease** • PCV13-type disease has been reduced through indirect effects, but not eliminated • Easier to adhere to universal prevention strategies than to risk-based ones • Frequent changes in recommendations may negatively impact the perceived importance of future adult vaccine recommendations and may present implementation challenges	• **Overall impact on PCV13-type disease from vaccinating older adults is minimal in the context of indirect effects from pediatric PCV use** • Low remaining burden of PCV13-type disease limits the potential benefit from direct effects • Lack of clear population-level impact on disease since 2014 • Judicious use of resources • Simplification of the recommendations

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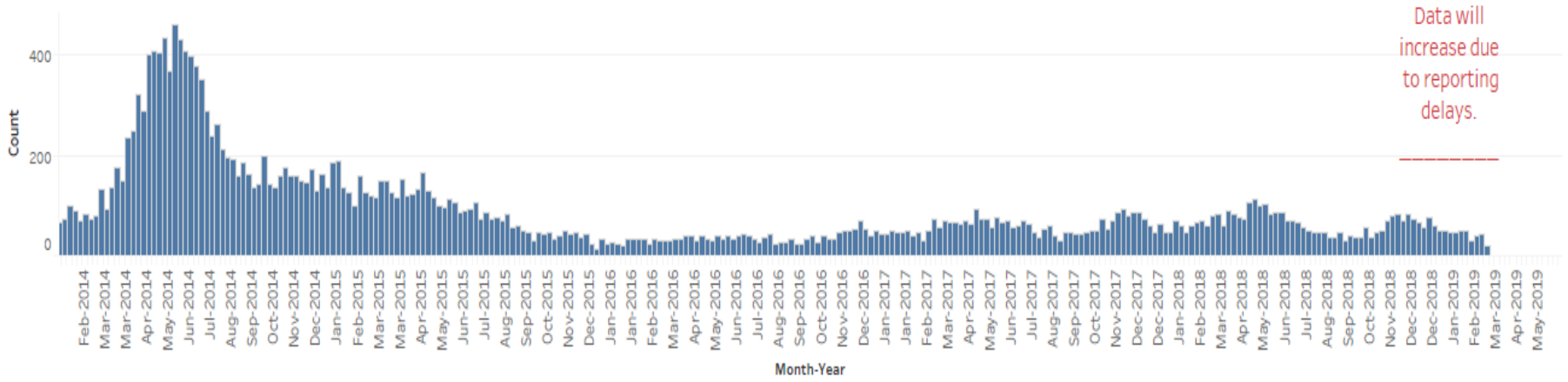
PCV13 for Adults >65y
ACIP June 2019:

- In a close vote, members decided not to recommend the PCV13 for all adults age 65 or older who have not previously received it, reversing a 2014 recommendation, following cont'd reductions in PCV13-type disease due to the indirect effects from pediatric PCV13 use.
- Voted 13-1 to recommend that PCV13 be administered "based on shared clinical decision making" in adults 65 years or older who do not have an immunocompromising condition and who have not previously received PCV13. It recommends that all adults 65 years or older receive a dose of the 23-valent pneumococcal polysaccharide vaccine (PPSV23).

Whatever happened to Pertussis?

Pertussis in California-CDPH

Figure 1. Year to date* pertussis case counts by week of onset -- California, 2014-2019



Varies by county

Historically has peaks every 3-5 years

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Tdap Vaccine Effectiveness

TABLE 3 Tdap VE by Year After Tdap Vaccination

Year After Tdap (Time Since Tdap)	HR (95% CI)	Tdap VE(95% CI)
Year 1 (8 d to <1 y)	0.31 (0.24 to 0.40)	68.8 (59.7 to 75.9)
Year 2 (1 to <2 y)	0.43 (0.32 to 0.59)	56.9 (41.3 to 68.4)
Year 3 (2 to <3 y)	0.75 (0.54 to 1.04)	25.2 (–4.3 to 46.4)
Year 4+ (≥3 y)	0.91 (0.64 to 1.31)	8.9 (–30.6 to 36.4)

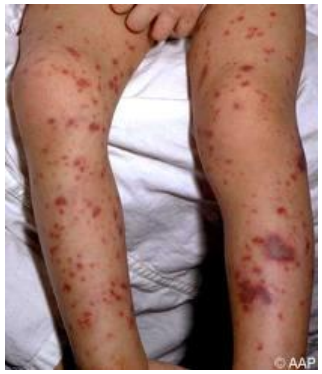
Tdap boosters

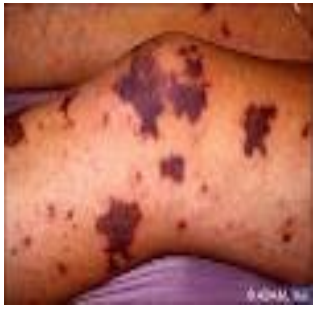
- Currently boosting pregnant woman with every pregnancy
- Boosters in pregnant women have been safe and effective
- Everyone else just gets one dose of Tdap
- Adacel licensed by FDA for a second dose in 2018 (dose interval=8 years)
- Now we need to decide who to give it to!

Tdap-Considerations for a booster dose

- Family members when a new baby comes into the household
- Healthcare workers who see young infants
- During outbreaks in defined settings (e.g. schools, geographic areas experiencing peaks in cases)
- To replace the every 10-year Td with a Tdap

Meningococcal Disease, College Outbreaks, Meningococcal Vaccines





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Meningococcal vaccines-Be careful!

- Two very different vaccine types
  - MenACWY (Menveo, Menactra)
  - MenB (Trumenba, Bexero)
- Two very different recommendations
  - Men ACWY-routine for adolescents and high-risk individuals **including infants**
  - Men B-routine only for a subset of high-risk individuals and not infants
- MenACWY products-difference in recommendations for use under 2 years of age due to vaccine interference (Menveo preferred over Menactra)
- MenB vaccines-two very different vaccines products (Bexero and Trumenba)
  - Different schedules and different intervals between doses
  - Can't be interchanged

Meningococcal B vaccine-issues

- The vaccine doesn't cover all circulating strains of Men B
- Immunity wanes over a few years
- May not reduce nasopharyngeal carriage
- Long-term safety unknown
- Epidemiology of meningococcal disease is changing

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MenB - Category B Recommendation

- The CDC estimates about 35,000 college students are exposed during campus outbreaks each year.

- People ages 16-23 years may choose to be vaccinated based on a conversation with their doctor, but vaccination isn't routine for this group.

New developments with MenB vaccine
ACIP June 2019

- Booster doses now recommended for individuals at high risk:
  - Complement deficiency
  - Monoclonal antibody
  - Asplenia
  - Microbiologists
  - During outbreaks
- A booster 1 year after primary series and then every 2-3 years based on evidence that MenB vaccine protection wanes after a year or two

MenB Vaccine Recommendations

- High Risk (asplenia, complement deficiency, outbreak settings)-immunize starting at age 10 with booster doses.

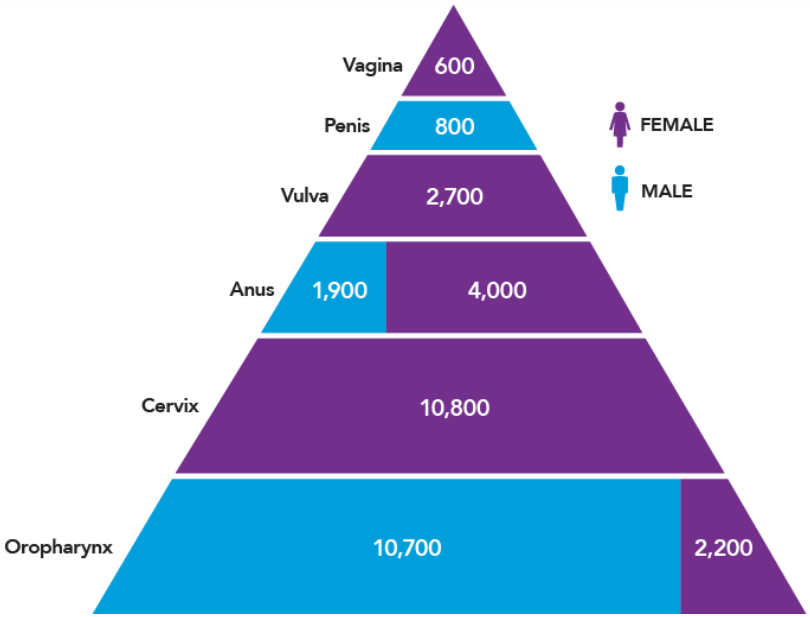
- Normal Risk: A Men B vaccine series MAY be administered to adolescents and young adults aged 16-23 years to provide SHORT-TERM protection against MOST strains of serogroup B meningococcal disease. The preferred age for Men B vaccination is 16-18 years.

So, which normal risk persons should you give MenB vaccine to?

- 16-23 year olds who request it
- Kids whose college or other institution requires it
- College students?
- Those living in dormitories or other crowded conditions?
- Those who smoke or drink alcohol?
- Everyone?
- No one?

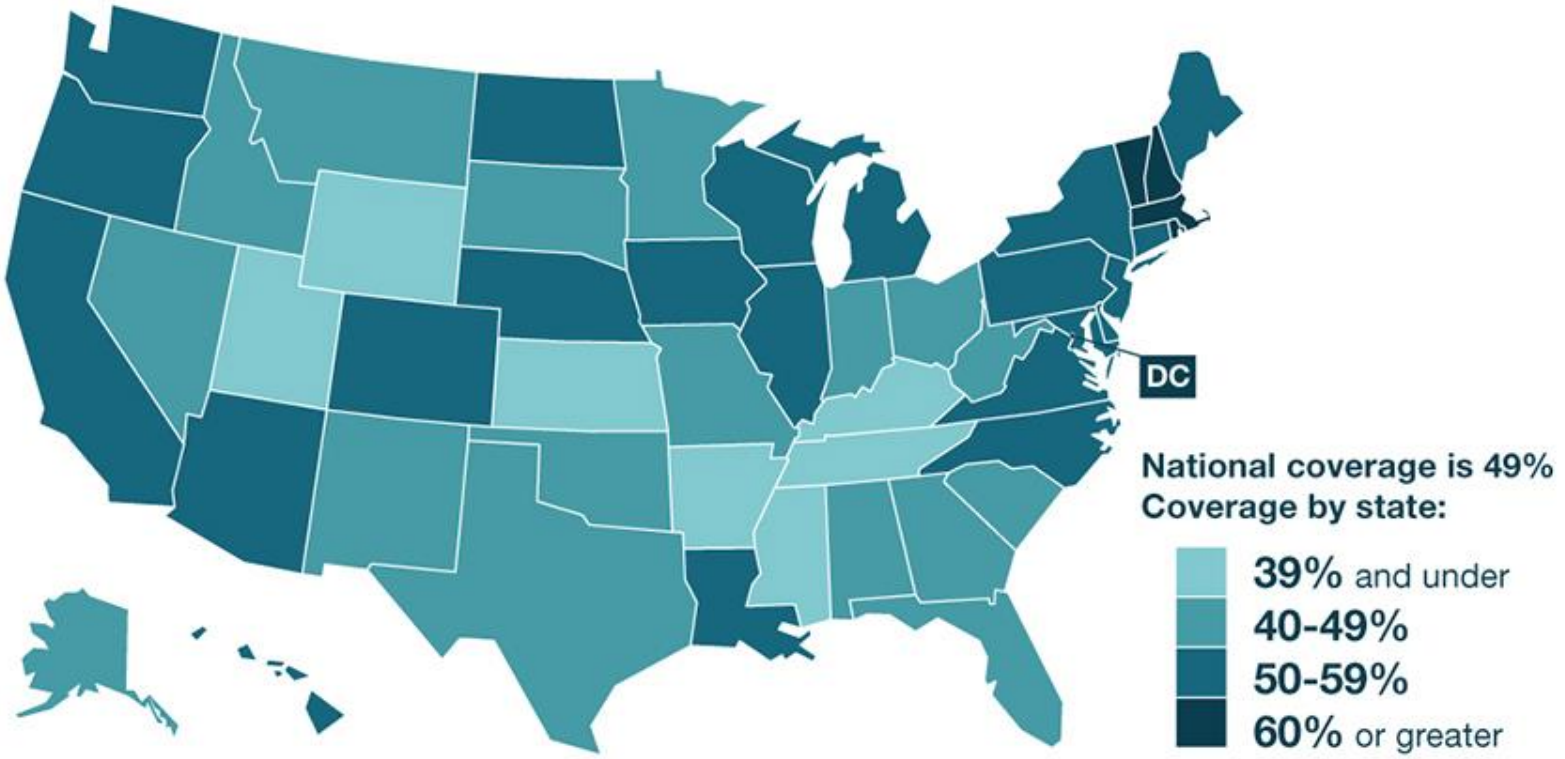
HPV vaccine-it shouldn’t be this hard!

Figure 1: Numbers of U.S. Cancers Caused by HPV



Source: HPV Vaccination for Cancer Prevention: Progress, Opportunities, and a Renewed Call to Action. A Report to the President of the United States from the Chair of the President's Cancer Panel. Bethesda (MD): President's Cancer Panel; 2018 Nov.
Data from: Centers for Disease Control and Prevention. How many cancers are linked with HPV each year? [Internet]. Atlanta (GA): CDC; [updated 2018 Aug 22; cited 2018 Aug 26]. Available from: https://www.cdc.gov/cancer/hpv/statistics/cases.htm

Percentage of adolescents who are up to date on HPV vaccination



Source: MMWR August 24, 2018

www.cdc.gov/hpv

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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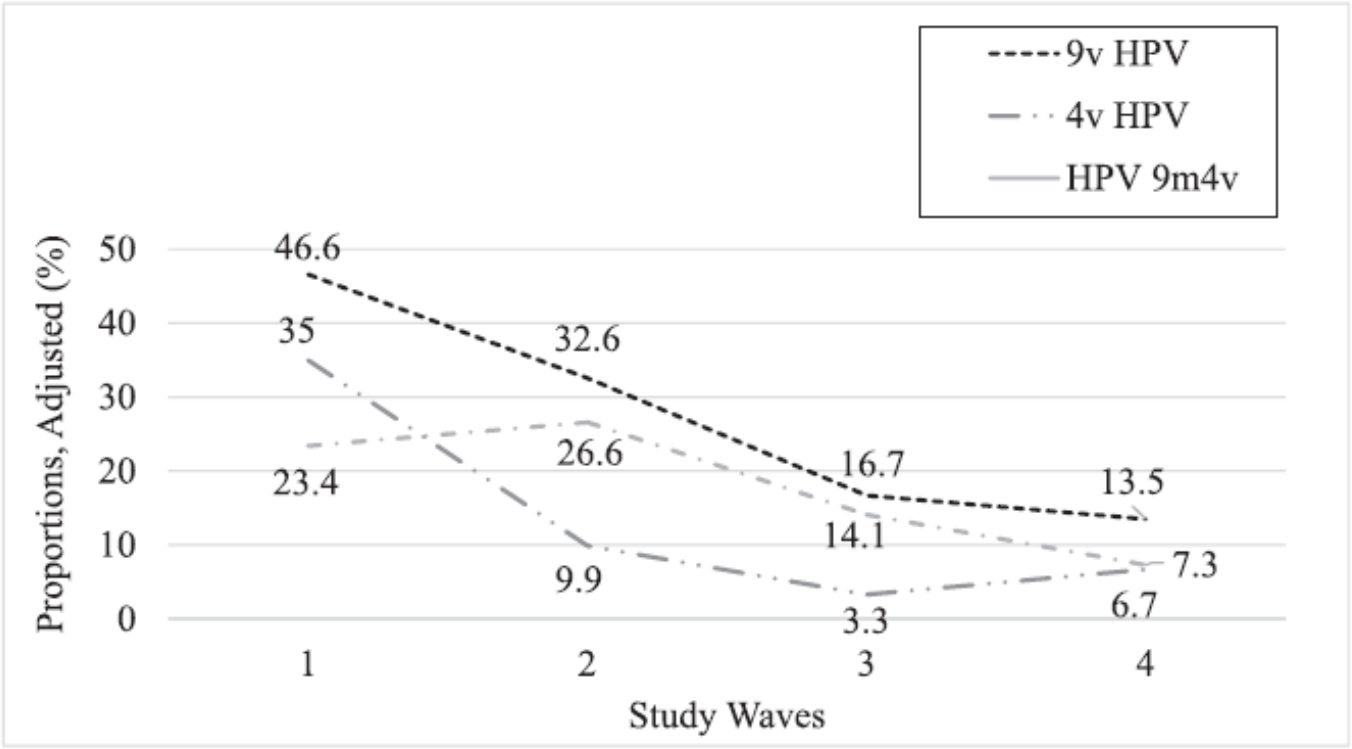
2-dose HPV Vaccine

vs.

- Age at dose #1 is key!
  - If dose #1 at 14 years of age or younger, then 2-dose regimen is OK
  - If dose #1 at 14 years of age or younger, then long intervals between doses doesn't matter (e.g. dose #2 could be at age 16)
  - If dose #1 at 15 years of age or older, then a 3-dose interval required
- Recommendation counts retrospectively
- 2-dose regimen not indicated for immunocompromised patients (congenital immunodeficiency, HIV infection, malignancy, transplant recipients, autoimmune disease)

HPV vaccine works!



Spinner C, Pediatrics 2019:143(2):e20181902

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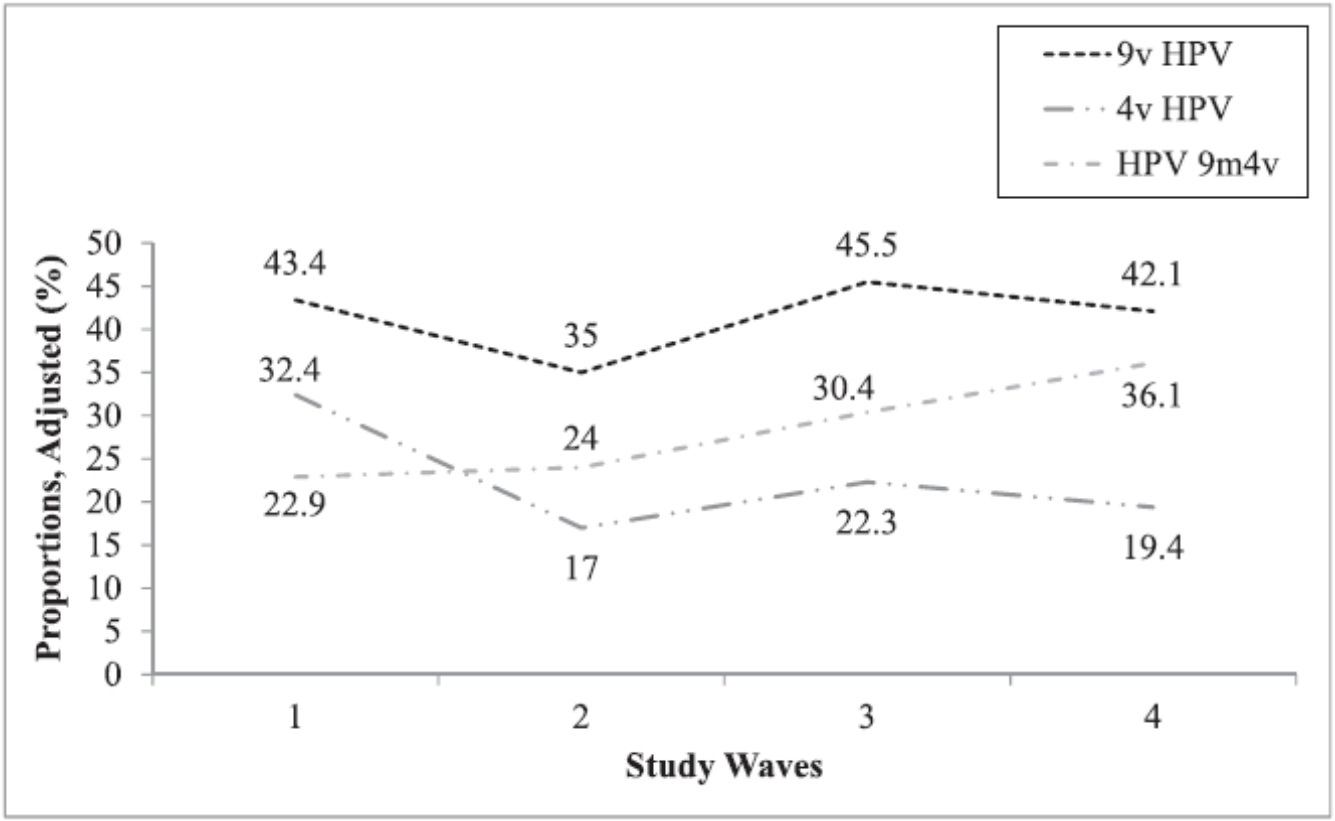
HPV vaccine even works if you are not vaccinated!!



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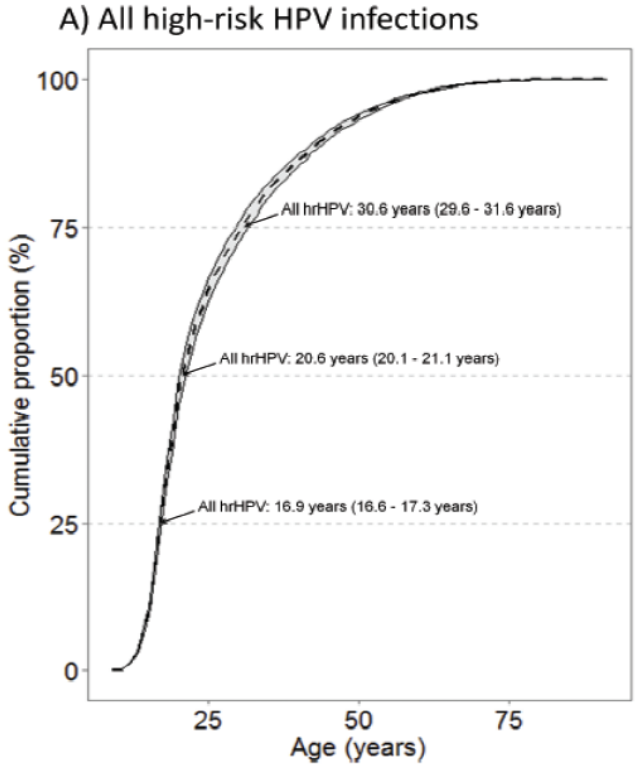
What proportion of cervical cancers are caused by HPV infections acquired by different ages?

Of women with cervical cancer, an estimated

- 50% of women acquired causal HPV infection by age 21 years
- 75% of women acquired causal HPV infection by age 31 years

Other modeling teams also working to estimate age at causal infection



In the context of no vaccination or screening
Burger at al. CID 2017

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FDA News Release

FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old

For Immediate Release

October 5, 2018

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HPV Immunization Recommendations

- Routine immunization at age 11-12 years for all
- Catch up for all Females aged 13-26 years
- Catch up for all Males aged 13-21 years
- Men who have sex with men aged 13-26 years

ACIP June 2019 meeting:

- Recommended harmonization of the upper age for catch-up vaccination for males and females through age 26 years, concluding that this would simplify the immunization schedule and communication
- A recommendation for individual clinical decision making for persons aged 27 through 45 years

Potential future HPV immunization recommendations

- Emphasis on getting 11 year olds immunized
- Possible encouragement from AAP to immunize starting at age 9 years:
  - We know the vaccine is more immunogenic.
  - Would this help with completing the series? Younger kids are more likely to still be coming in for yearly check-ups.
  - Potentially less discussion about HPV as an STI at this age, more discussion about HPV vaccine being an anti-cancer vaccine
  - MCV4 and Tdap still at 11-12y

What about catch up HPV9?

- No routine recommendation to revaccinate those who have already completed a series with HPV2 or HPV4
- Girls immunized 2007-2015 and boys immunized 2010-2015 only received HPV2 or HPV4
- HPV9 could potentially prevent 10-15% of the remaining HPV-related cancers
- Vaccine not licensed nor recommended for those who already completed a series with the HPV2 or PHV4 vaccines
- No safety concerns seen in studies of catch up vaccination
- Probably not cost effective
- OC Oral Health Initiative

Hexavalent Vaccine
ACIP June 2019

- DTaP-IPV-Hep B-Hib Hexavalent vaccine
- Joint venture between Merck and Sanofi. It is given as a three-dose series at 2, 4 and 6 months.
- Will be available in 2021.
- Experts say combination vaccines are beneficial because they reduce the number of injections needed and could improve coverage rates.

Hepatitis A Vaccine
ACIP June 2019

- As rates of hepatitis A continue to rise, ACIP voted for catch up vaccination for everyone ages 2-18 y
- 3,365 cases of acute hepatitis A were reported in 2017 and rates were the highest since 2007. Since 2016, there have been 20,512 cases reported in 24 states, which resulted in 11,776 hospitalizations and 194 deaths
- The vaccine provides long-term protection.
- ACIP also voted to add people with HIV to a list of people with special risk factors for hepatitis A

Looking further forward?

- Universal influenza vaccine
- Needle free delivery
- A better pertussis vaccine
- Men ACWYB
- PCV15 and PCV20
- RSV vaccine during pregnancy
- Ebola vaccine

Summary

- LAIV is an option for influenza vaccination in 2019-2020
- ACIP no longer recommends PCV13 for all >65y. We might even stop using PPSV23 in seniors if PCV20 is licensed
- Pertussis is still around and we may be using booster Tdap doses in the future
- Meningococcal B vaccine recommendations are challenging and booster doses are now recommended for high risk individuals
- HPV vaccination is important and should start at age 11
- Exciting future for vaccines

Other Fun Vaccine News…

Rotavirus Vaccine:

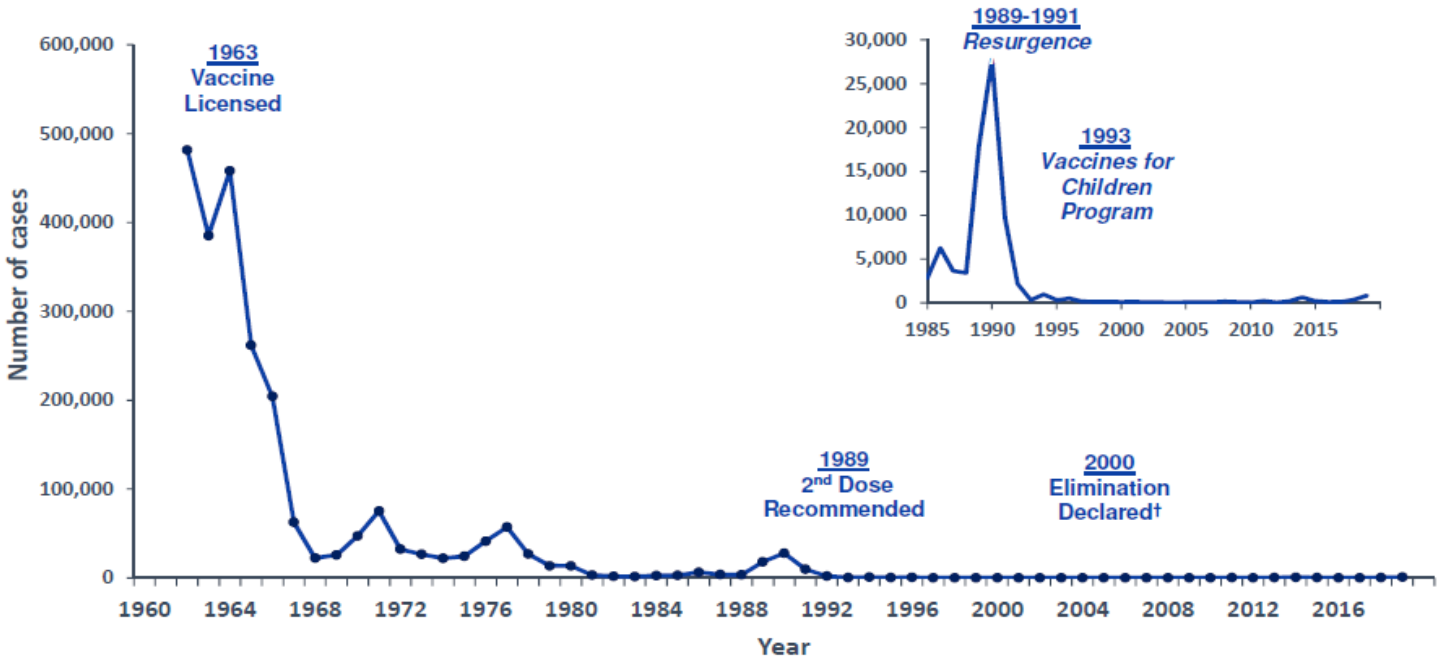
- 2 studies have shown decrease in T1DM
- No increase in intussusception

JAMA. 2019;321(13):1241-1242. doi:10.1001/jama.2019.0766

Suburban county outside New York City bars unvaccinated kids from public places to stem measles outbreak

Published: Mar 27, 2019 10:11 a.m. ET

Reported Measles Cases, United States, 1962–2019*



*2018 and 2019 data are preliminary and subject to change

†Elimination is defined as the absence of endemic measles transmission in a region for ≥ 12 months in the presence of a well-performing surveillance system

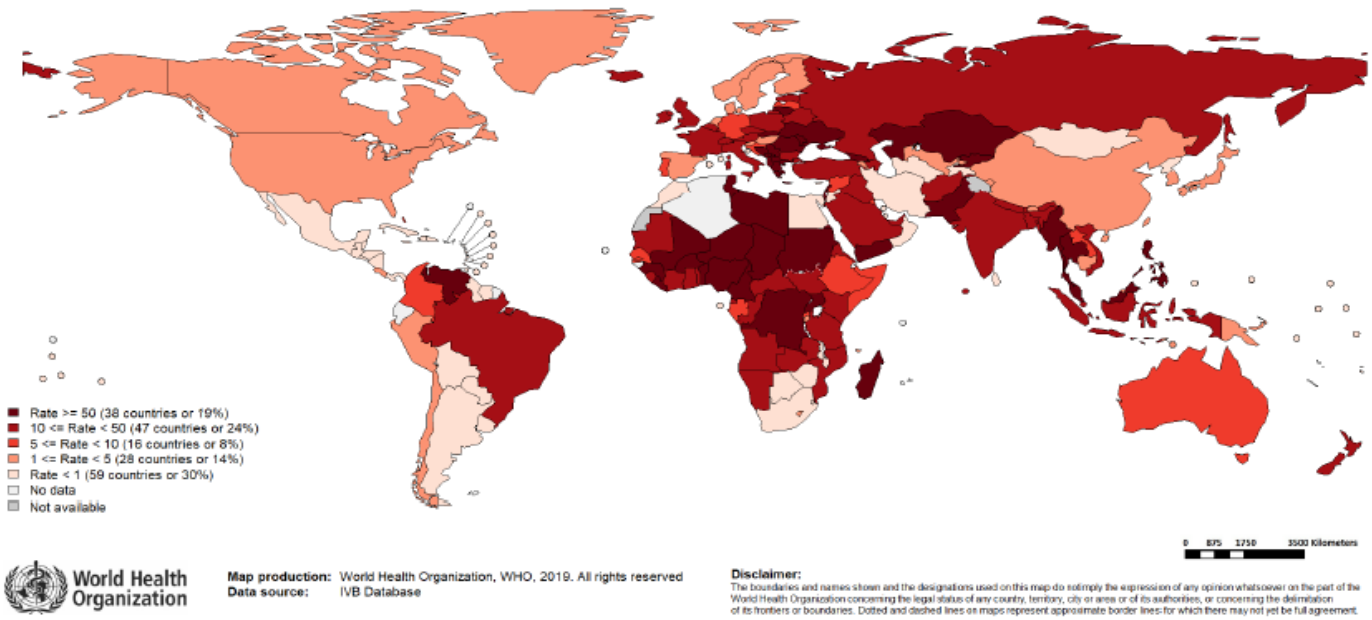
Measles Elimination in the U.S.

- **Elimination: Interruption of year-round transmission**
  - Does not imply zero incidence
- **Vaccine coverage >90% for 2 doses of MMR**
- **Strong public health response to each case**
  - Resource-intensive
- **Epidemiology of measles during elimination characterized by**
  - Importations from endemic areas
  - Limited spread among non-immune persons

Measles Incidence Rate per Million (12M period)

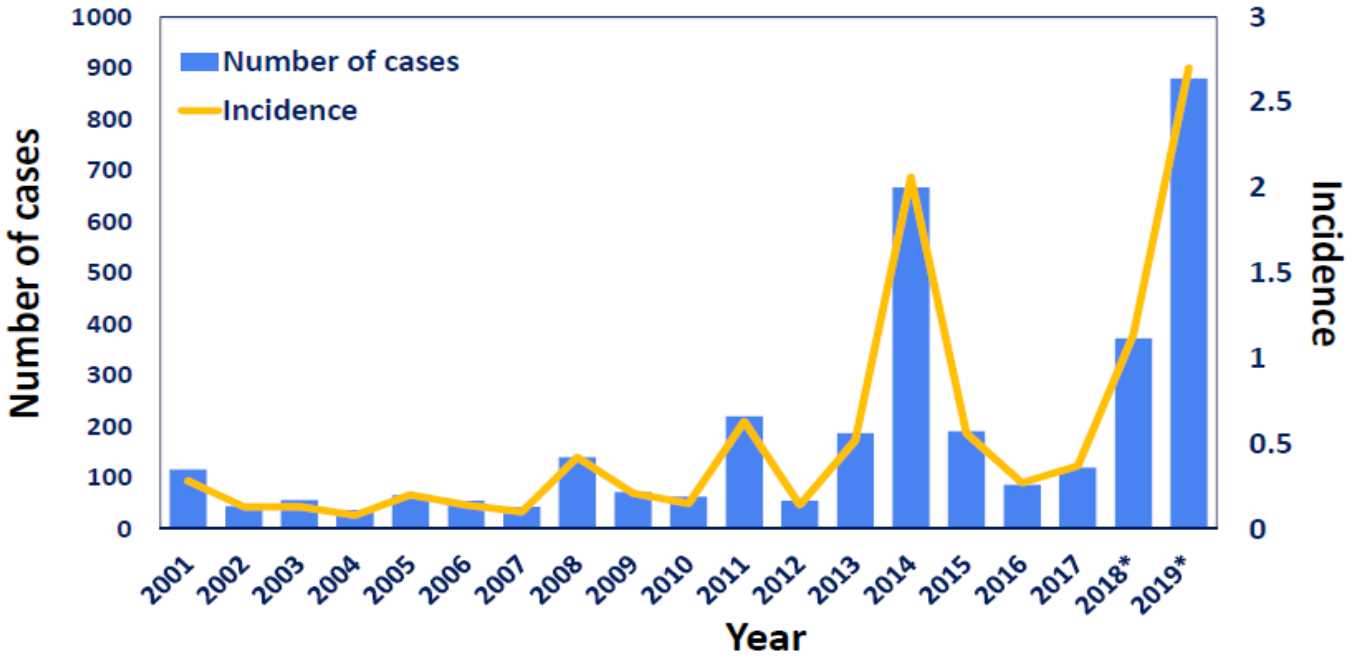
Top 10**		
Country	**Cases**	**Rate**
Madagascar	84804	3406.53
Ukraine	78659	1770.06
India	53170	40.15
Pakistan	22693	117.46
Philippines	16898	163.55
Yemen	13639	494.45
Nigeria	12745	68.53
Brazil	10316	49.68
Thailand	6914	100.4
Kazakhstan	5908	328.45

Other countries with high incidence rates***		
Country	**Cases**	**Rate**
Georgia	4678	1191.72
Liberia	2367	513.02
Israel	3755	458.38
Kyrgyzstan	2534	425.47
The Republic of North Macedonia	885	425.23
Albania	1169	399.47



Based on data received 2019-05 and covering the period between 2018-04 and 2019-03 - Incidence: Number of cases / population* * 100,000 - * World population prospects, 2017 revision - ** Countries with the highest number of cases for the period - *** Countries with the highest incidence rates (excluding those already listed in the table above)

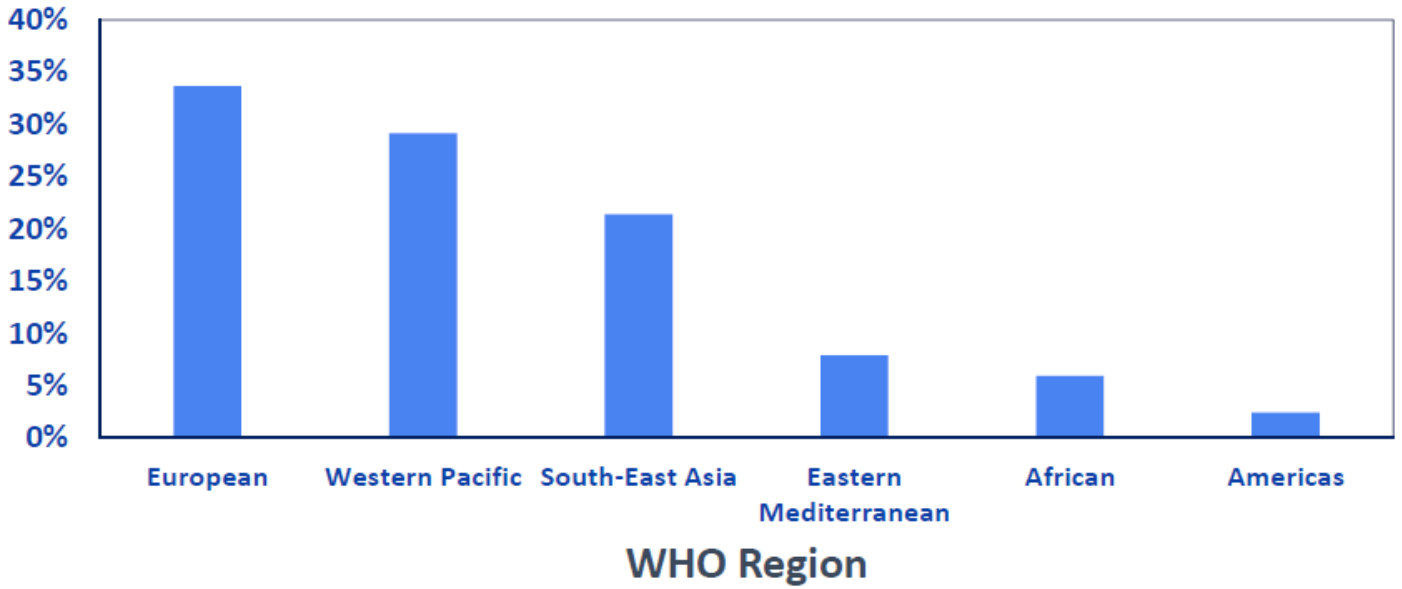
Number and Incidence of Reported Measles Cases – U.S., 2001 –2019* (N=3470)



*Source: National Notifiable Diseases Surveillance System (passive surveillance); 2018 and 2019 data as of May 17, 2019

Measles Importations by WHO Region — U.S., 2001–2019*

- Imported case-patients reported travel to 77 different countries during their exposure periods



*2018 and 2019 data are preliminary as of May 17, 2019

Measles Importations by State— U.S., 2001–2019*

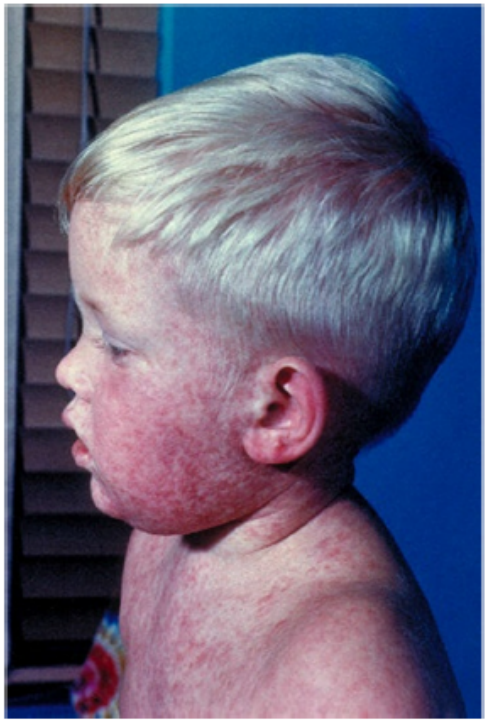
*2018 and 2019 data are preliminary as of May 17, 2019

Summary

- The United States remains in elimination, although ongoing outbreaks in close-knit communities and increased global measles activity puts the U.S. at risk for losing status
- Of the >3400 cases reported from 2001 to May 2019, one-third of cases have occurred in the past 18 months
- U.S. residents traveling abroad account for two-thirds of measles cases directly imported into the U.S.
- Almost 90% of cases reported since 2001 were either unvaccinated or had an unknown vaccination status
  - Unvaccinated infants remain the highest risk group

Measles

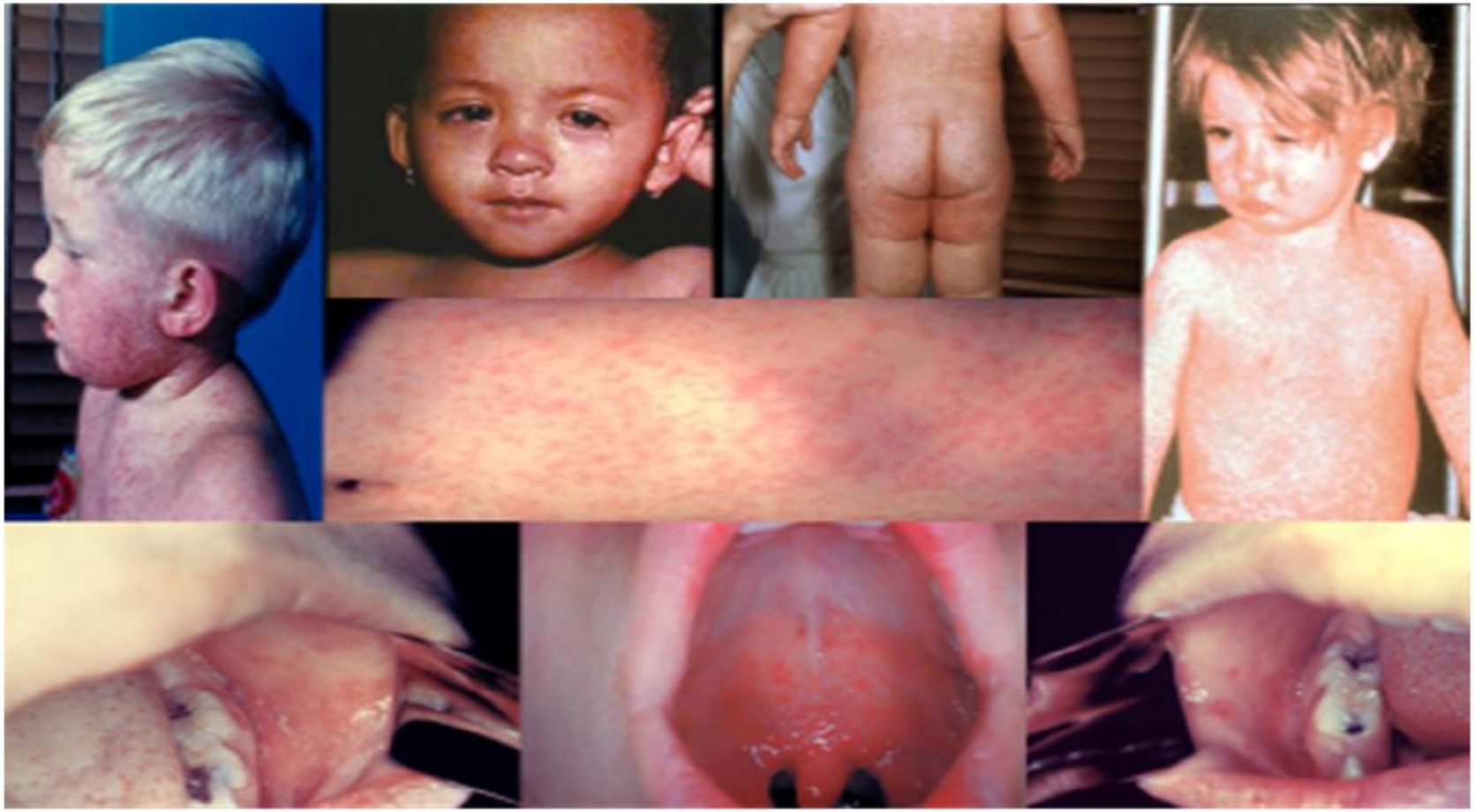
- Acute, febrile rash viral illness
- Transmitted by direct contact with infectious droplets or airborne spread
- Most contagious of the vaccine preventable diseases
  - R_0 = 12-16
  - Secondary attack rate in susceptible household contacts ~90%



Measles - Clinical Features

Rash

- 2-4 days after prodrome, 14 days after exposure
- Maculopapular, becomes confluent
- Begins on face and head
- Persists 5-6 days
- Fades in order of appearance
- Contagious 4 days before until 4 days after rash



Measles Testing

- Have a high index of suspicion for measles if your patient:
  - Is unvaccinated
  - Has traveled internationally, or has been exposed to someone who has traveled internationally, within 21 days
  - Has visited a community where there is an outbreak

Suspect Measles Cases

- Place masked patient in an Airborne Infection Isolation Room (AIIR)
- If AIIR not available, place the masked patient in a private room with the door closed
- **Call your local Health Department or Infection Prevention Team**

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Measles - Diagnosis

- Collect NP or throat swab and urine for identification of measles RNA by RT-PCR
- https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Measles-Testing-InformationVRDL.pdf
- Serum for measles IgM – May be negative in the first 72 hours, or those immunized with 2 doses.
- All cases of suspected measles should be reported immediately to the Health Dept without waiting for the results of diagnostic tests.

Measles Exposures

- Need to be minimized in the healthcare setting
  - Labor intensive
  - Costly
- Challenges
  - Highly contagious
  - Lack of data to clearly define exposure
  - Difficult to define shared air space
  - Airborne survivability up to 2 hours
- HCP have become infected despite adequate immunity

Minimize Potential Measles Exposures

- By phone
- Give clear instructions if patient needs to be seen:
  - Entrance (or outside?)
  - Timing (end of day)
  - Masking
  - See CDPH Measles Investigation Quicksheet for information

Outbreak Control

- Available data suggest that measles vaccine, if given within 72 hours of measles exposure, will provide protection in some cases
- IG is indicated for susceptible household or other close contacts of patients with measles, particularly contacts younger than 1 year of age, pregnant women, and immunocompromised people, for whom risk of complications is highest, or other people for whom measles vaccine is contraindicated
- Immune Globulin (IG) can be given intramuscularly to prevent or modify measles in a susceptible person within 6 days of exposure
- Do not give MMR and IG concurrently

Measles Vaccine

- Children
  - 12-15 months
  - 4-6 years
- Adolescents and Adults without evidence of immunity
  - Most adults need one dose
  - High risk adults need 2 doses, given at least 28 days apart
    - Post high-school students
    - Healthcare Personnel
    - International travelers

Measles Vaccine for Travel

- Infants 6 through 11 months of age should receive 1 dose of MMR vaccine before departure. These infants will still need 2 doses after 12 months.
- Children >12 months of age who have received 1 dose and are traveling to areas where measles is endemic or epidemic should receive their second dose before departure, provided the interval between doses is 28 days or more. This will count as their second dose.
- Adults who have received only one routine dose in the past should receive a 2nd dose.

Measles Vaccine / Immunity Questions

- What are the contraindications to MMR vaccine?
  - History of a severe (anaphylactic) reaction to neomycin (or other vaccine component) or following a previous dose of MMR
  - Pregnancy
  - Severe immunosuppression from disease or therapy

Measles Vaccine / Immunity Questions

- What are the precautions to administration of MMR vaccine?
  - Receipt of an antibody-containing blood product in the previous 11 months (specific intervals are noted in the Red Book)
  - Moderate or severe acute illness with or without fever
  - History of thrombocytopenia

Measles Vaccine / Immunity Questions

- How long should a woman wait after receiving MMR to become pregnant?
  - Package insert recommends 3 month deferral; ACIP recommends 4 weeks.
  - There has never been a case of congenital rubella syndrome linked to MMR receipt.

- Can I give MMR to a breastfeeding mother?
  - Yes.
  - Vaccination poses no risk to the infant being breastfed. Although there is a small chance of rubella virus being transmitted via breastmilk, infection in the infant is asymptomatic.

Measles Vaccine / Immunity Questions

- Can I give MMR to a 15 month old whose mother is pregnant?
  - Yes.
  - MMR vaccine viruses are not transmitted, so there is no risk to the pregnant woman.

Measles Vaccine / Immunity Questions

- Can I give MMR to a child whose sibling is receiving chemotherapy for leukemia?
  - Yes.
  - MMR vaccine viruses are not transmitted, so there is no risk to the immune suppressed child.
  - In fact, since the sibling cannot receive vaccine, it is important to make sure that all household contacts are vaccinated to prevent transmission.
  - This is true for infants too young for routine vaccination and people with medical contraindications to vaccination.

Measles Vaccine / Immunity Questions

- Has the ACIP made any new recommendations for use of MMR vaccine because of the recent measles outbreak?
  - No
  - There is no current recommendation for children 6-11 mos in OC to be vaccinated
  - There is no current recommendation that children 6-11 mos who are to travel to OC from elsewhere in the US be vaccinated (this applies to international travel).

Measles Vaccine / Immunity Questions

- Can I give the second dose of measles vaccine “early” to my patients who are 13 months – 4 years of age?
  - Yes, this would be reasonable while there is a local outbreak
  - This will be valid for school and other requirements
  - We normally wait for this second dose for scheduling convenience reasons – it is not a booster.

Measles Vaccine / Immunity Questions

- How should adolescents / young adultus who are at high risk for measles because of going to college, or international travel without recorded vaccines be managed?
  - Test for immunity, or
  - Give 2 doses of MMR at least 4 weeks apart
  - There is no harm in giving vaccine to someone who is already immune.
  - If immunity testing is equivocal, consider your patient nonimmune

Measles Vaccine / Immunity Questions

- If a patient remembers receiving MMR vaccine but has no written record, or if the parents are sure a child has been vaccinated, is this adequate?
  - No
  - Self-reported doses or a history of vaccination provided by the parent are not considered valid.
  - You can only accept a written, dated record as evidence of MMR vaccination.

Measles Vaccine / Immunity Questions

- What is the recommendation for MMR vaccine for healthcare personnel?
  - All HCP born during or after 1957 should have adequate evidence of immunity to measles, mumps and rubella, defined as:
    - Documentation of 2 doses of measles and mumps vaccine, and at least one dose of rubella vaccine,
    - Laboratory evidence of immunity, or,
    - Laboratory confirmation of disease.
  - ACIP also recommends consideration of evidence for those born before 1957, with confirmation during an outbreak.
  - Concern about those who rec'd vaccine before 1968 who may have rec'd killed vaccine.

Measles Vaccine / Immunity Questions

- What about HCP with 2 documented doses of vaccine, whose serology for 1 or more antigens comes back negative?
  - HCP with 2 documented doses of MMR vaccine are considered immune regardless of subsequent serologic testing. This documentation supersedes the result of serologic testing.
  - HCP who do not have documentation of MMR and whose serologic test is interpreted as “indeterminate” or “equivocal” should be considered not immune and receive 2 doses of MMR vaccine.
  - ACIP does not recommend serologic testing after vaccination.

Measles Vaccine / Immunity Questions

- How long does measles immunity from vaccination last? If a HCP had a positive test for measles immunity > 10 years ago, is it necessary to retest them now?
  - No.
  - Once measles immunity is documented, there is no need for further vaccination or testing.
  - “Once immune, always immune” is true for measles, mumps, rubella and varicella.
  - This holds true regardless of results of subsequent testing.
  - ACIP does not recommend repeat antibody testing once evidence of immunity has been established.

Summary

- Prioritize measles on your differential diagnosis of patients with a febrile rash illness who is unvaccinated, has traveled internationally or been exposed to measles.
- Providers do not need to actively screen their adult patients for measles immunity.
- Providers should ensure that patients who are traveling internationally be vaccinated or have other evidence of immunity.
- Consult with the local healthy department for other advice during outbreaks.