Immunization Update

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Immunization Action Coalition

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Disclosures

- **William Atkinson has no financial relationships with commercial interests to disclose**
- **Any unlabeled/unapproved uses of drugs or products referenced will be disclosed**

Advisory Committee on Immunization Practices (ACIP)

- The recommendations to be discussed are primarily those of the ACIP
  - composed of 15 experts in clinical medicine and public health who are not government employees
  - provides guidance on the use of vaccines and other biologic products to the Department of Health and Human Resources, CDC, and the U.S. Public Health Service

www.cdc.gov/vaccines/acip/

ACIP Recommendations

- Recommendations approved by the Committee are just the first step
- Recommendations do not become official policy until
  - approved by the CDC Director
  - published in Morbidity and Mortality Weekly Report (MMWR)

ACIP Recommendation Categories

- Category A recommendations
  - made for all persons in an age- or risk-factor-based group
  - example: MenACWY vaccine is recommended for all adolescents at 11 or 12 years of age
- Category B recommendation
  - do not apply to everyone, but in the context of a clinician-patient interaction, vaccination may be found to be appropriate for a person
  - example: MenB vaccine series may be administered to adolescents and young adults age 16–23 years

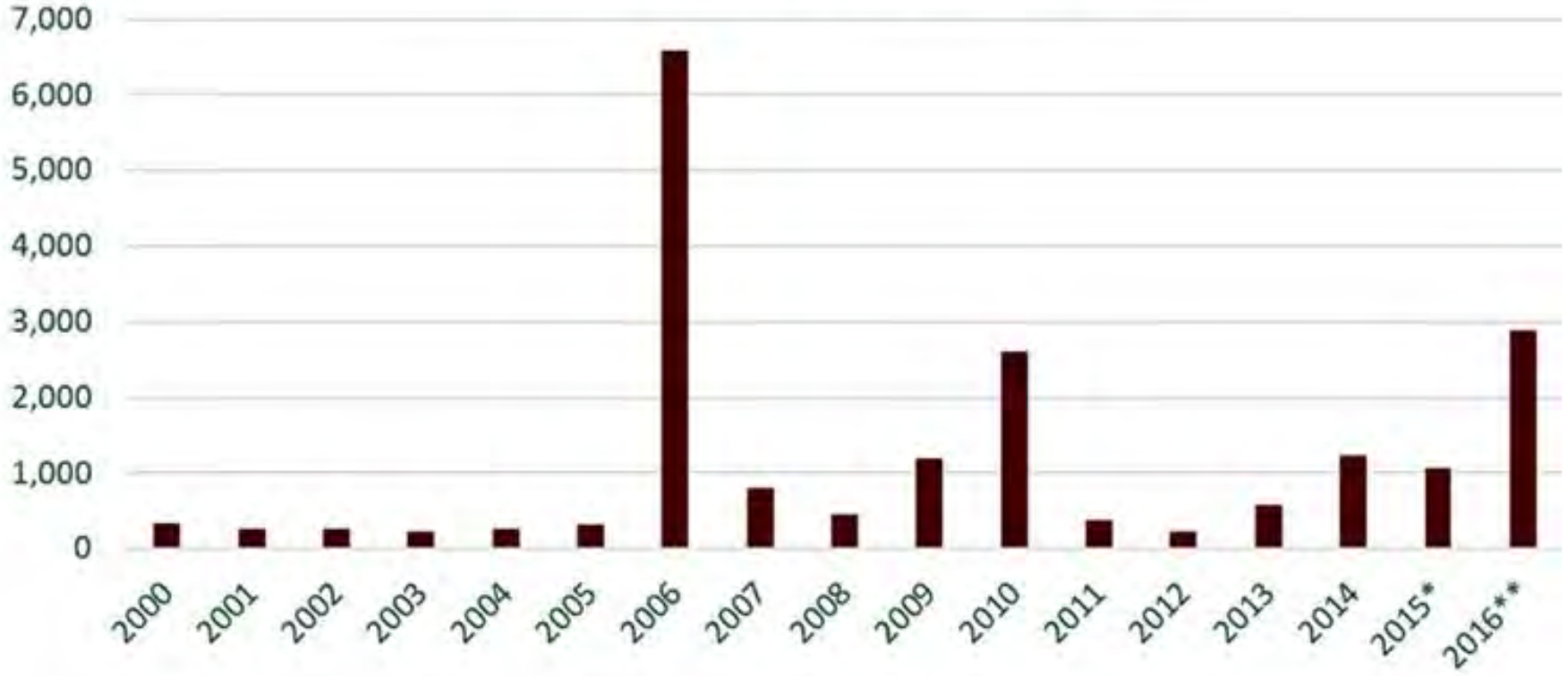
www.cdc.gov/vaccines/acip/recs/GRADE/downloads/handbook.pdf

Vaccination Coverage in the United States - 2015

- Infants and children (0-12 years)
  - 90% or higher except for vaccines given in the second year of life (DTaP4, Hib3/4, PCV4, hepA2)
- Adolescent (13-17 years)
  - ≥85% for Tdap and MCV4, much lower for HPV especially males (22% for 3 doses)
- Adult (18 years and older)
  - far below Healthy People 2020 goals for all vaccines
  - best: 67% for influenza vaccine among persons 65 years and older

www.cdc.gov/vaccines/imz-managers/coverage/imz-coverage.html

Mumps Cases in U.S., by Year



*Cases as of January 2, 2016. Case count is preliminary and subject to change.

**Cases as of November 5, 2016. Case count is preliminary and subject to change.

Source: Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables

Mumps and MMR Vaccine

- Mumps outbreaks can occur any time of year
- A major factor contributing to outbreaks is being in a crowded environment, such as attending the same class, playing on the same sports team, or living in a dormitory with a person who has mumps
- Two doses of MMR are 88% effective at protecting against mumps (range: 66 to 95%)
- One dose is 78% effective (range: 49% to 92%)

www.cdc.gov/mumps/outbreaks.html

What's New for Influenza 2016-2017

- H3N2 strain changed
- New vaccine for children 6-35 months and 65 years and older
- Reduction in emphasis on egg allergy
- Live attenuated influenza vaccine

MMWR 2016;65(RR-5)

Influenza Vaccines by FDA-Approved Age Group, 2016-2017

Age group	Vaccines Approved for This Age Group
0 through 5 months	None
6 months and older	Fluzone IIV4 (not ID or HD), FluLaval IIV4
2 through 49 years	FluMist IIV4
3 years and older	Fluarix IIV4
4 years and older	Fluvirin IIV3, Flucelvax ccIIV4
5 years and older	Afluria IIV3*
18 years and older	Flublok RIV3
18 through 64 years	Fluzone IIV4 intradermal
65 years and older	Fluzone IIV3 high dose, FLUAD IIV3

*Afluria IIV3 is approved by FDA for persons 5 years and older but recommended by ACIP for persons 9 years and older. Afluria is approved for persons 18 through 64 years when given by Stratis jet injector

FluLaval IIV4 (ID Biomedical/GSK)

- Approved in the U.S. since 2006 (18 years and older; 2013 age 3-17 years)
- Approved in November 2016 for children 6 through 35 months
- Dosage is 0.5 mL for all recipients regardless of age
- Available in manufacturer-filled syringes and multi-dose vials

www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm112845.htm

FLUAD IIV3 (Novartis)

- Approved by FDA on November 24, 2015 based on demonstration of noninferiority to licensed trivalent inactivated vaccine
- Approved only for persons 65 years and older
- First U.S. influenza vaccine that contains an adjuvant (MF59)
- Used in Europe since 1997
- Approved in 38 other countries

www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/ucm473989.htm

Choice of Influenza Vaccine

- **Where more than one type of vaccine is appropriate and available, ACIP has no preferential recommendation for use of any influenza vaccine product over another**
  - **quadrivalent vs trivalent**
  - **high-dose/adjuvanted vs standard dose**

***MMWR* 2016;65(RR-5)**

Influenza Vaccine Revaccination

- ACIP recommends only 1 dose of influenza vaccine per season except for certain children younger than 9 years
- IIV4 is not recommended if IIV3 has already been given
- Fluzone High Dose/FLUAD is not recommended if standard IIV has already been given

MMWR 2013;62(RR-7)

Live Attenuated Influenza Vaccine 2016-2017 Season

- ACIP recommends that LAIV not be used in any setting in the U.S. during the 2016-2017 influenza vaccination season
- AAP concurs with the recommendation
- This was done because CDC studies indicated that LAIV was not effective during the last 3 influenza seasons
- Conflicting data from the manufacturer, a European study and a Canadian study

MMWR 2016;65(RR-5)

Live Attenuated Influenza Vaccine 2016-2017 Season

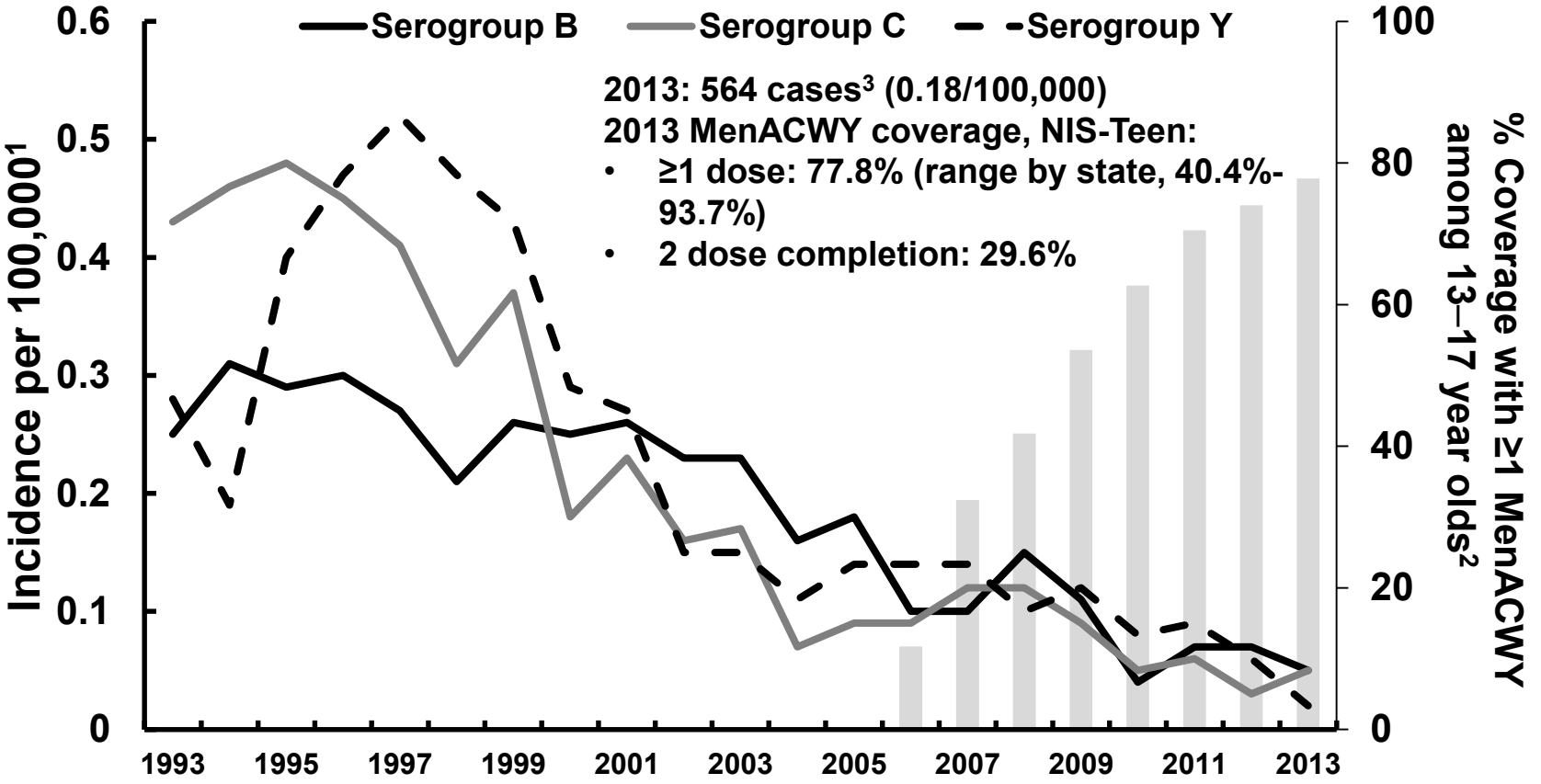
- FDA approved the 2016-2017 formulation of LAIV on July 1, 2016
- It appears that Astra Zeneca will distribute LAIV
  - at least 10 lots of LAIV have been released by FDA
- CDC recommendation is to count as valid doses of LAIV administered during the 2016-2017 season

CDC, personal communication, August 28, 2016

Meningococcal Disease Incidence, United States, 1970-2012

1970-1996 NNDSS data, 1997-2011 ABCs data estimated to U.S. population with 18% correction for under reporting. In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative

Meningococcal Incidence in All Ages by Serogroup and Adolescent MenACWY Vaccine Coverage, 1993–2013

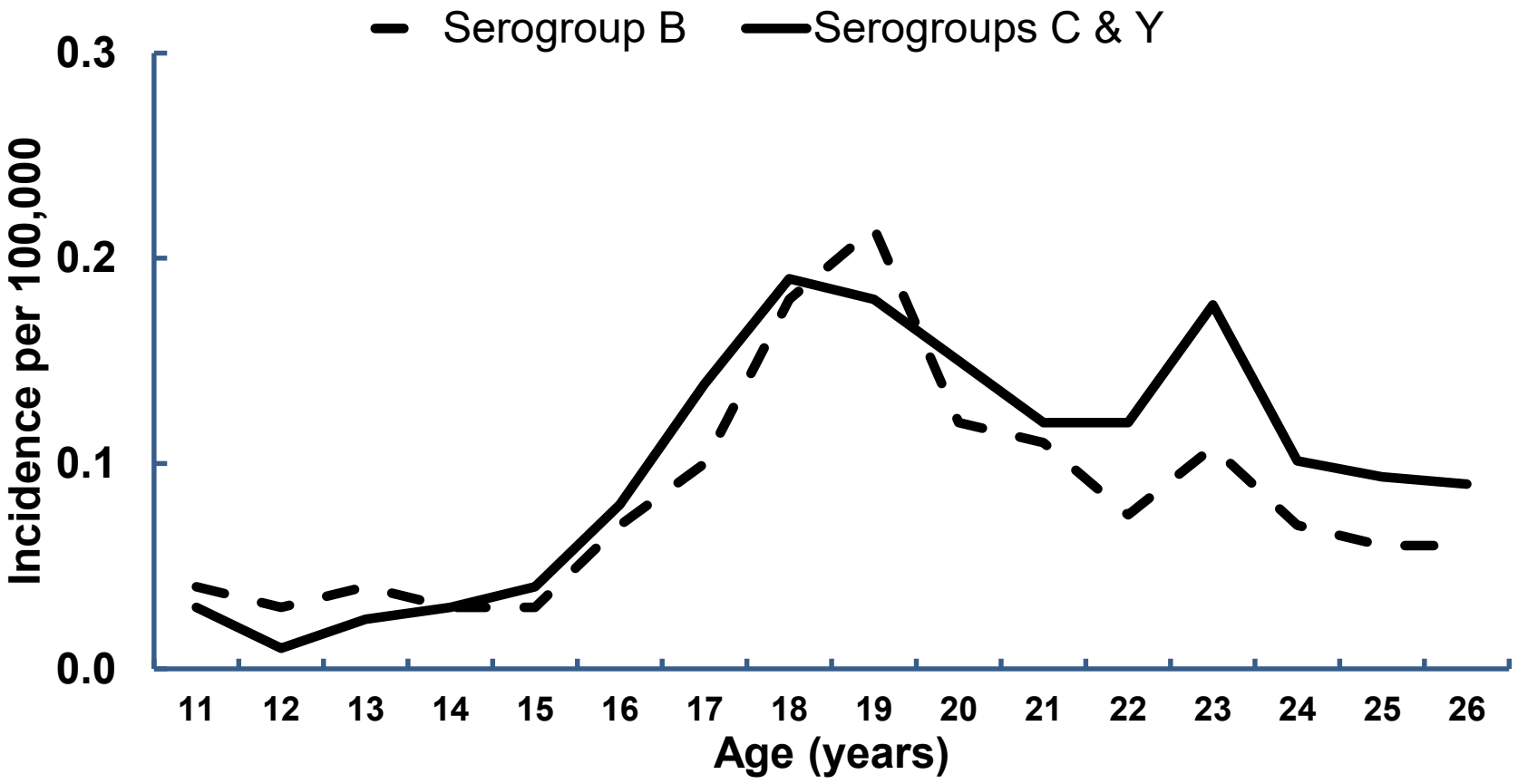


Source: Active Bacterial Core surveillance (ABCs) cases from 1993-2013 estimated to the U.S. population with 18% correction for nonculture confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System (NNDSS) and might not be representative.

[2]National Immunization Survey-Teen; 2006-2013.

[3]NNDSS 2013 final case count

Meningococcal Incidence in Adolescents and Young Adults by Serogroup, 2009–2013



NNDSS data supplemented with additional serogroup data from ABCs and state health departments. Unknown serogroup (19%) and other serogroups (8%) excluded

The Expanding Universe of Meningococcal Vaccine

- Meningococcal polysaccharide vaccine (MPSV4)
  - first licensed in 1974
  - limited indications
- Meningococcal conjugate vaccines (MenACWY)
  - first licensed in 2005
  - contains polysaccharide from serogroups A, C, W, Y
  - recommended routinely for adolescents and high risk groups
- Meningococcal B vaccines (MenB)
  - first licensed in 2014
  - broadly protective against subtypes of B
  - recommended routinely only for high-risk people (asplenia, complement component deficiency, microbiologists)

MenACWY Vaccines

- Approved by the Food and Drug Administration based on serologic non-inferiority compared to meningococcal polysaccharide vaccine
- Menactra
  - approved for persons 9 months through 55 years*
- Menveo
  - approved for persons 2 months through 55 years*

*may be used off-label in persons 56 years and older. *MMWR* 2013;62(RR-2):15

MenACWY Routine Recommendations

Age at first dose	Booster dose
11-12 years	16 years*
13-15 years	16-18 years*
16-18 years	No

- Not routinely recommended for person age 19 years or older who are not at increased risk

*off-label recommendation. *MMWR* 2013;62(RR-2):1-28

Persons at Highest Risk of Meningococcal Disease or Suboptimal Vaccine Response

- Complement deficiency
  - very high antibody titer required to compensate for complement deficiency
- Asplenia
  - evidence of suboptimal response
- HIV infection
- Single dose primary series may not be sufficient to confer protection for persons with these high-risk conditions

MMWR 2013;62(RR-2):18;

MenACWY Recommendations for HIV-infected Persons

- Accumulating evidence indicates that HIV infection increases the risk of invasive meningococcal disease
- ACIP now recommends routine MenACWY vaccination for all HIV-infected persons age 2 months and older
- Number of doses depends on age
  - 2-4 doses for children younger than 2 years
  - Persons 2 years and older should receive 2 doses separated by 8 weeks

MenACWY Recommendations for High Risk Groups

- **Administer 2 doses* of MenACWY at least 8 weeks apart to persons 2 years and older with persistent complement component deficiency, anatomic or functional asplenia, or HIV infection and 1 dose every 5 years* thereafter**

*** off-label recommendations*. *MMWR* 2013;62(RR-2):1-28**

Second Dose MenACWY Coverage is Suboptimal

- First dose coverage at 79% among adolescents 13-17 years of age
- Only 29% for booster dose among 17 year-olds who received a first dose before age 16
- Opportunities to vaccinate are often missed
- Consider every opportunity to vaccinate
  - acute care visits
  - well visits
  - sports and camp physicals
  - routine visits for chronic illness
  - visits for influenza vaccine

MMWR 2015;64(29):784-792

MenACWY Second Dose

Resources to help improve second dose MenACWY coverage available at

www.give2mcv4.org/

A collaborative project between IAC and Sanofi Pasteur

Groups at Increased Risk for Meningococcal B Disease

- High-risk medical conditions:
  - persistent complement component deficiencies
  - functional or anatomic asplenia
- Certain microbiologists
- Populations at risk during an outbreak
- NOT at increased risk: international travelers, first year college students, people with HIV infection

MMWR 2015;64(No. 22):608-12

Meningococcal Serogroup B Vaccines

- rLP2086 (Trumenba, Pfizer)
  - Licensed by FDA on October 29, 2014
  - Approved for 10 through 25 years of age
  - 2 dose (0, 6 months) or 3 dose series (0, 2, 6 months)
  - 2 fHbp components
- 4CMenB (Bexsero, Novartis)
  - Licensed by FDA on January 23, 2015
  - Approved for 10 through 25 years of age
  - 2 dose series (0, 1 months)
  - 4 components

Information from manufacturer's package inserts

ACIP Recommendations for Meningococcal B Vaccine of High Risk Persons

- Certain persons 10 years of age or older* who are at increased risk for meningococcal disease should receive MenB vaccine
  - persistent complement component deficiency
  - anatomic or functional asplenia
  - risk in a serogroup B meningococcal disease outbreak
  - certain microbiologists
- MenB vaccines are included in VFC
- NOT routinely recommended for college students, international travelers, HIV+ persons

Revised Provisional* MenB Vaccine Schedule Recommendations

- For persons at increased risk of meningococcal B disease
  - 2 doses of Bexsero (1 month apart) or
  - 3 doses of Trumenba (0, 2, 6 months)
- For persons not at increased risk of meningococcal B disease
  - 2 doses of Bexsero (1 month apart) or
  - 2 doses of Trumenba (6 months apart)

*unpublished as of November 27, 2016

Meningococcal B Vaccine Limitations

- MenB vaccines are not expected to provide protection against disease caused by all serogroup B strains circulating in the United States
- No data are available on vaccine effectiveness against clinical disease or duration of protection
- The potential impact of MenB vaccines on nasopharyngeal carriage and herd protection is inconclusive

MMWR 2015;64(No. 41):1171-76

ACIP Recommendations for Meningococcal B Vaccine

- Approximately 15 to 29 cases and two to five deaths could be prevented annually with a routine adolescent MenB vaccination program administered at age 11, 16, or 18 years
- A recommendation for college students only is estimated to prevent approximately nine cases and one death annually

MMWR 2015;64(No. 41):1171-76

ACIP Recommendations for Meningococcal B Vaccine

- **A MenB vaccine series *may be administered* to adolescents and young adults aged 16 through 23 years to provide short-term protection against most strains of serogroup B meningococcal disease (Category B recommendation)**
- **The preferred age for MenB vaccination is 16–18 years**
- **Vaccines with a Category B recommendation are included in the VFC program and ACA insurance programs**

***MMWR* 2015;64(No. 41):1171-76**

ACIP Recommendations for Meningococcal B Vaccine

- The two MenB vaccines are NOT interchangeable
- The same vaccine *must* be used for all doses
- Minimum intervals between doses have not been defined – use routine schedule only
- Need for booster dose(s) unknown – not recommended at this time
- MenB vaccines can be given at the same time as other vaccines including MenACWY

MMWR 2015;64(No. 41):1171-76

HPV Infection Is the Most Common Sexually Transmitted Disease in the United States

- Approximately 79 million Americans are currently infected
- 14 million new infections/year in the United States
  - about half of these new infections occur among persons 15-24 years of age
- Almost all sexually active men and women will be infected at some point in their lives
- Immunocompromised persons have higher rates of HPV acquisition and progression to disease

www.cdc.gov/std/hpv/default.htm

Average Annual HPV-Attributable Cancers in the United States, 2008-2012

- 38,793 HPV-associated cancers diagnosed annually
  - 15,793 in men
  - 23,000 in women

Site	Male	Female	Total Cancers
Cervix	0	11,771	11,771
Anus	1,750	3,200	5,010
Vagina	0	802	802
Oropharynx	12,638	3,100	15,738
Vulva	0	3,554	3,554
Penis	1,168	0	1,168

73% attributable to HPV strains included in the 9-valent vaccine

MMWR 2016;65 (No. 26):661-71

Human Papillomavirus Vaccines

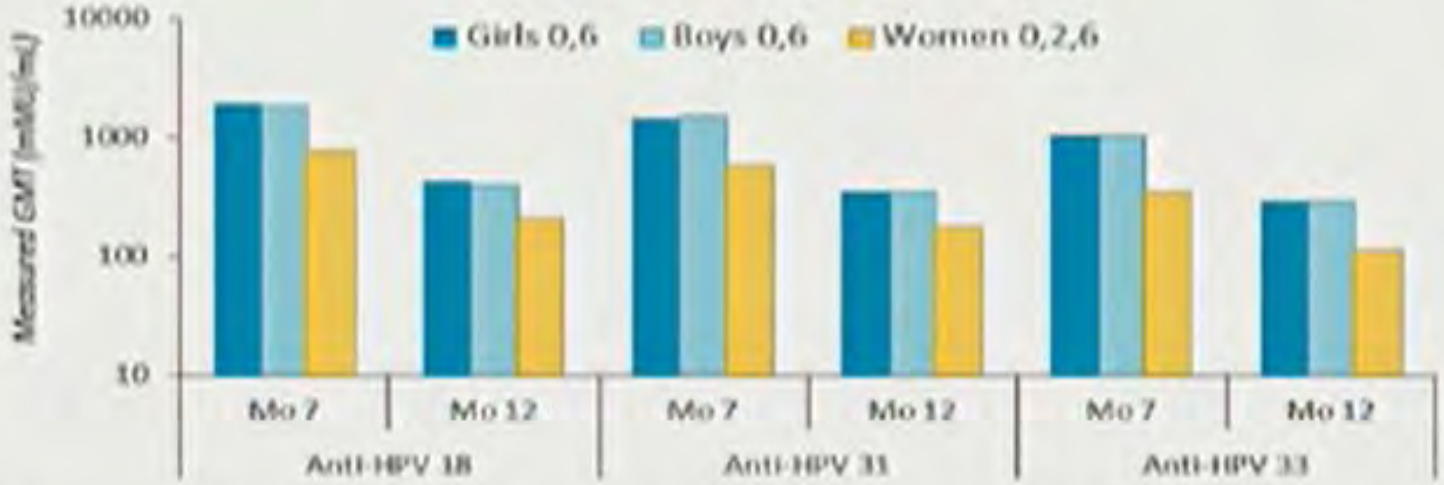
HPV Vaccines	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-valent 9vHPV (Gardasil9)
L1 VLP types	16, 18	6, 11, 16, 18,	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	GSK	Merck	Merck
Contraindications	Hypersensitivity to latex*	Hypersensitivity to yeast	Hypersensitivity to yeast
FDA Indications	Females (9-26 yrs): Cervical precancer and cancer	Females (9-26 yrs): Anal, cervical, vaginal, and vulvar precancer and cancer; genital warts	Females (9-26 yrs): Anal, cervical, vaginal, and vulvar precancer and cancer; genital warts
	Males: Not approved for use in males	Males (9-26 yrs): Anal precancer and cancer; genital warts	Males (9-26 yrs): Anal precancer and cancer; genital warts

***May be present in tip of manufacturer-filled syringes**

In 2017 only 9vHPV vaccine will be available in the United States

9vHPV 2-Dose Immunogenicity Trial

Non-inferior GMTs at 1 and 6 months post-last dose (months 7 and 12) HPV 18, 31, 33



Fold difference (girls/women)	**2.46**	**1.98**	**2.51**	**1.97**	**2.96**	**2.54**
95% CI	*(2.05, 2.96)*	*(1.63, 2.40)*	*(2.10, 3.00)*	*(1.63, 2.38)*	*(2.50, 3.50)*	*(2.13, 3.03)*

Merck, unpublished data

Provisional* ACIP HPV 2-Dose Recommendations

- A 2-dose schedule is recommended for persons beginning the HPV series before 15 years of age
- Persons beginning the series at 15 years or older or who are immunosuppressed should receive a 3-dose schedule
- Doses must be separated by at least 5 months (recommended interval 6-12 months)
- If doses are separated by less than 5 months then 3 doses are recommended
- 2-dose schedule can be completed with any combination of HPV vaccines and is retroactive

*Unpublished as of November 27, 2016

9vHPV ACIP Recommendations

- **ACIP has declined to make any recommendation regarding revaccination with 9vHPV for persons who already completed a series of 2vHPV or 4vHPV**
- **Clinicians are free to revaccinate with 9vHPV but VFC will not cover additional doses and insurance plans may not pay for these doses**

Top 5 Reasons for Not Receiving HPV Vaccine – NIS-Teen, 2013

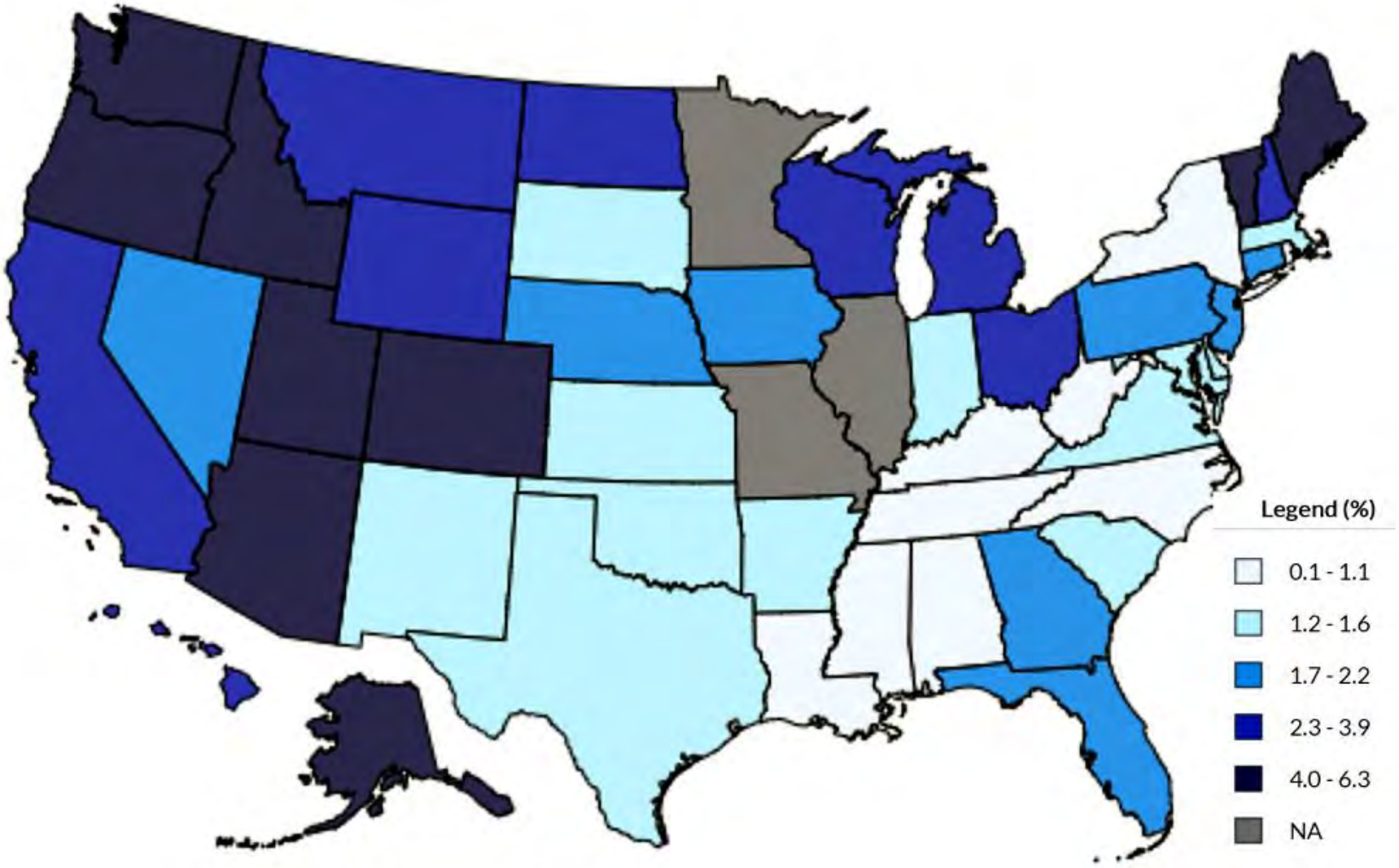
Parents of girls		
Reason	%	(95% CI)
Lack of knowledge	15.5	(13.0–18.5)
Not needed or necessary	14.7	(12.5–17.3)
Safety concern/Side effects	14.2	(11.8–16.8)
Not recommended	13.0	(10.8–15.5)
Not sexually active	11.3	(9.1–13.9)

Parents of boys		
Reason	%	(95% CI)
Not recommended	22.8	(20.6–25.0)
Not needed or necessary	17.9	(15.9–20.1)
Lack of knowledge	15.5	(13.7–17.6)
Not sexually active	7.7	(6.4–9.2)
Safety concern/Side effects	6.9	(5.6–8.5)

Practical Approaches to Improve HPV Vaccination Rates In Your Practice

- **Provide an unequivocal recommendation for the vaccine!**
- **Remind parents that the series is 2 doses 6 months apart if started before age 15 (3 doses if started at 15 years or older)**
- **Check vaccination status of all patients at every visit and vaccinate at every opportunity**
- **Incorporate patient reminder systems such as telephone calls, texts, postcards, or letters**

Kindergarteners with One Or More Exemptions to Vaccination, 2015-2016 School Year



Estimated Vaccination Coverage for Children Attending Kindergarten, 2015-2016

	U.S. (median)	MO
MMR2	94.6%	95.7%
DTaP5	94.2%	95.6%
Var2	94.3%	95.4%

The Causes of Parent/Guardian Immunization Exemptions

- "Lifestyle" issues
- Political issues
- Fear of side effects
  - no vaccine has ever been shown to cause autism, SIDS, or any other chronic condition

Children With Personal Belief Exemption

- 9-fold higher risk of varicella (Colorado, 1998-2008)
- 23-fold higher risk of pertussis (Colorado, 1996-2007)
- Introduce vaccine-preventable diseases (particularly measles) into school settings
- Expose children with medical exemptions to infection

Personal Belief Exemptions

- **Permitting personal belief exemptions and easily granting exemptions are associated with higher and increasing nonmedical U.S. exemption rates**
- **State policies granting personal belief exemptions and states that easily grant exemptions are associated with increased pertussis incidence**

JAMA 2006;296:1757-1763

Reducing Personal Belief Exemptions

- Engage the parent and answer their questions if possible
- Be sure the parent understands that unvaccinated students will be excluded from school in the event of an outbreak
- Provide the parent with information
  - MO DHHS Parent/Guardian Exemption fact sheet
  - IAC “What If” fact sheet (p4017)
- Suggest reliable websites for further information (some are listed on IAC “What If” fact sheet)

Immunization Action Coalition Resources

- **Websites**
  - –www.immunize.org (for HCP)
  - –www.vaccineinformation.org (for the public)
  - –www.izcoalitions.org (for coalitions)
  - –www.izsummitpartners.org (adult immunization)
- **Publications – Needle Tips, Vaccinate Adults, IAC Express**
  - –www.immunize.org/publications/
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