

# Four Great Challenges in Adult Immunization

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# COI Statement

## Robert H. Hopkins, Jr., MD

- No Financial Conflicts re: this talk
  - No Industry consulting/speakers bureaus/advisory work
  - I am employed by UAMS College of Medicine
  - I do consult with ACP, provide Med-Ed re: Immunization
- **Huge** Nonfinancial Conflict
  - **Strong** belief in adult immunization:
    - High-value Care Intervention
    - Low-risk
  - Dismay at the underutilization of this set of tools!!

# Objectives

- Understand the gap between US adult immunization goals and current rates
- Use current ACIP guidelines to vaccinate your adult patients
  - Focus on *Four Great Challenges*
- Implement strategies to improve immunization rates

# Baseline Assessment




- What is your professional role?
  - Student
  - Resident
  - Primary Care Specialist/Generalist
  - Public Health
  - [Non-Primary Care] Specialist/Sub-Specialist
  - Nurse/APN/PA
  - Pharmacist
  - Other

# Adult Immunization Schedule – 2016, By Age

Figure 1. Recommended immunization schedule for adults aged 19 years or older, by vaccine and age group<sup>1</sup>

VACCINE ▼	AGE GROUP ►	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza <sup>2,3</sup>		1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>2,3</sup>		Substitute Tdap for Td once, then Td booster every 10 yrs					
Varicella <sup>2,4</sup>		2 doses					
Human papillomavirus (HPV) Female <sup>2,5</sup>		3 doses					
Human papillomavirus (HPV) Male <sup>2,5</sup>		3 doses					
Zoster <sup>4</sup>						1 dose	
Measles, mumps, rubella (MMR) <sup>2,7</sup>		1 or 2 doses depending on indication					
Pneumococcal 13-valent conjugate (PCV13) <sup>2,8</sup>		1 dose					
Pneumococcal 23-valent polysaccharide (PPSV23) <sup>8</sup>		1 or 2 doses depending on indication					1 dose
Hepatitis A <sup>2,9</sup>		2 or 3 doses depending on vaccine					
Hepatitis B <sup>2,10</sup>		3 doses					
Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4) <sup>2,11</sup>		1 or more doses depending on indication					
Meningococcal B (MenB) <sup>11</sup>		2 or 3 doses depending on vaccine					
<i>Haemophilus influenzae</i> type b (Hib) <sup>2,12</sup>		1 or 3 doses depending on indication					

\*Covered by the Vaccine Injury Compensation Program

-  Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster
-  Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)
-  No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at [www.vaers.hhs.gov](http://www.vaers.hhs.gov) or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at [www.hrsa.gov/vaccinecompensation](http://www.hrsa.gov/vaccinecompensation) or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines) or from the CDC-INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 8:00 a.m. - 8:00 p.m. Eastern Time, Monday - Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), the American College of Obstetricians and Gynecologists (ACOG) and the American College of Nurse-Midwives (ACNM).

# Adult Immunization Schedule – 2016, Medical Indications

Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications<sup>1</sup>

VACCINE ▼	INDICATION ▶	Pregnancy	Immuno-compromising conditions (excluding HIV infection) <sup>4,6,7,8,13</sup>	HIV infection CD4+ count (cells/ $\mu$ L) <sup>4,6,7,8,13</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia and persistent complement component deficiencies <sup>8,11,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel	
				< 200	$\geq$ 200								
Influenza <sup>2,3</sup>													1 dose annually
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>2,3</sup>		1 dose Tdap each pregnancy											Substitute Tdap for Td once, then Td booster every 10 yrs
Varicella <sup>4</sup>			Contraindicated										2 doses
Human papillomavirus (HPV) Female <sup>2,3</sup>													3 doses through age 26 yrs
Human papillomavirus (HPV) Male <sup>2,3</sup>													3 doses through age 21 yrs
Zoster <sup>6</sup>			Contraindicated										1 dose
Measles, mumps, rubella (MMR) <sup>2,7</sup>			Contraindicated										1 or 2 doses depending on indication
Pneumococcal 13-valent conjugate (PCV13) <sup>2,8</sup>													1 dose
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>													1, 2, or 3 doses depending on indication
Hepatitis A <sup>2,9</sup>													2 or 3 doses depending on vaccine
Hepatitis B <sup>2,9</sup>													3 doses
Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4) <sup>2,11</sup>													1 or more doses depending on indication
Meningococcal B (MenB) <sup>11</sup>													2 or 3 doses depending on vaccine
<i>Haemophilus influenzae</i> type b (Hib) <sup>2,12</sup>													3 doses post-HSCT recipients only 1 dose

\*Covered by the Vaccine Injury Compensation Program

Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster
  Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)
  No recommendation
  Contraindicated



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

These schedules indicate the recommended age groups and medical indications for which administration of currently licensed vaccines is commonly recommended for adults aged  $\geq$ 19 years, as of February 2016. For all vaccines being recommended on the Adult Immunization Schedule: a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Licensed combination vaccines may be used whenever any components of the combination are indicated and when the vaccine's other components are not contraindicated. For detailed recommendations on all vaccines, including those used primarily for travelers or that are issued during the year, consult the manufacturers' package inserts and the complete statements from the Advisory Committee on Immunization Practices ([www.cdc.gov/vaccines/hcp/acip-recs/index.html](http://www.cdc.gov/vaccines/hcp/acip-recs/index.html)). Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

# Why '4 Great Challenges'?

- ◆ Current ACIP Adult schedule is complex
- ◆ Vaccine ~% Adults for whom Vax. indicated
  - Influenza 100%
  - Tdap 100%
  - PneumococcalS 60+% [100% in 65+ age]
  - Zoster 40% [100% in 65+ age]
  - HBV 60%

- 
- ◆ Less prevalent adult indications:  
HPV, HAV, MMR, VAR, Men<sub>4</sub>, MenB, HiB

# Adult Vaccination Rates = Inadequate

Vaccine [Population]			
<b>Influenza</b>	Early 2013-14	Early 2014-15	HP 2020
Influenza [Early 2014– 2015 Season] –Adults	39.0%	39.7%	90%
[All] 18 – 49 years	31.4%	30.6%	60%
[All] 50 – 64 years	39.1%	43.7%	60%
≥ 65 years	61.8%	61.3%	90%
HCW [19 – 64 years]	62.9%	Not asked	90%
<b>PPS23 &amp; PCV13</b>	Rate 2013	Rate 2014	HP 2020
High risk 19 – 49 years	20.0%	21.2%	60%
≥ 65 years	59.9%	59.7%	90%
<b>Tetanus [19 – 49 years, received &lt; 10 years]</b>	64.2%	62.9%	90%
<b>Tetanus/Pertussis [19+, received &lt; 8 yrs]</b>	14.3%	17.2%**	90%
<b>Shingles [Zoster] age 60+</b>	20.1%	24.2%**	60%
<b>Hepatitis B Vaccine [High risk 19 – 49 years]</b>	35.3%	32.6%**	60%
<b>HPV Vaccine [women 19 – 26 years]</b>	34.5%	36.9%	90%

<http://www.cdc.gov/flu/fluview/nifs-estimates-nov2014.htm#place>  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6305a4.htm>



# Poor Adult Vaccination Rates

- **Vaccine preventable diseases kill** more Americans annually than
  - traffic accidents
  - breast cancer
  - HIV/AIDS
- 2.1% of eligible adults (18-64) received **Tdap** in the past 2 years
- <2% of persons >60 years have had the **Zoster** vaccine
- 36.1% of all adults are vaccinated annually against **Influenza**
  - 69% of >65 have received the vaccine
  - 58% of Medicare beneficiaries [all ages]
- 66.9% of eligible patients 65+ received 1 **Pneumococcal** vaccine
- Major **racial and ethnic disparities** for adult vaccination
  - Despite closure of these gaps in child immunization in last decade...

*<http://healthyamericans.org/assets/files/TFAH2010AdultImmznzBrief13.pdf>*

# Disparities

- Despite closure of childhood racial/ethnic gaps
- Significant gaps remain for adults
  - Influenza, Pneumococcal, Tdap, HBV, HPV, Zoster,...
  - Gaps by racial/ethnic origin
  - Gaps by presence/lack of health insurance
  - Gaps between public/private insured

# Why Review This Data?

- WE must be strong advocates for adult immunization!
  - Individual benefits
  - Community benefits
- WE need to lead our teams/colleagues to protect patients
- ALL of us are needed to make these improvements!!
  - Patients and their families
  - Primary Care and Non-Primary Care Specialists
  - Nurses, other patient care team members
  - Pharmacists
  - Public health

# Challenge 1:

## Reaching HP2020 Flu Goal

- Current rates 40-70% [at best]
- Goal >90 % vaccinated

# Case 1

32 year-old Internist in practice in Yourtown. He has a history of egg allergy, manifest as hives if he eats eggs...It is the middle of the annual push to vaccinate the medical staff and the CEO has mandated 100% adherence for employees... Which of the following vaccines is most appropriate to use in immunizing JM?

- a. tIIV [Trivalent Influenza Vaccine]
- b. LAIV [Live-attenuated Influenza Vaccine]
- c. qIIV [Quadrivalent Influenza Vaccine]
- d. rIIV [Recombinant Influenza Vaccine]
- e. hdIIV [High-Dose Influenza Vaccine]
- f. NONE: He has egg allergy and needs an excused exception letter and to wear a mask in order to practice during flu season
- g. Multiple correct options

# Influenza= AAAA

## All Adults [*And kids 6 mo+*] Annually!!!

- **1 dose for adults**
- Vaccines: IIV = TIV, QIV, hdlIV, sqlIV, 'egg-free', adjuvanted. LAIV = LQIV.
- **US 'Season': Vaccine avail. >> 'disease passed' (Aug/Sept-April)**
- Predominant strain types (Dz and Vax) since 1977:
  - A H<sub>1</sub>N<sub>1</sub>, A H<sub>3</sub>N<sub>2</sub>, B
- **2015-16** Vaccine strains:
  - A/California/7/2009 (H<sub>1</sub>N<sub>1</sub>)-like virus
  - **A/Switzerland/9715293/2013 (H<sub>3</sub>N<sub>2</sub>)-like virus**
  - **B/Phuket/3073/2013-like (Yamagata lineage) virus**
  - B/Brisbane/60/2008-like (Victoria lineage) virus (*QUAD Vaccines only*)

IIV = Inactivated Influenza vaccine; QIV = Quadrivalent influenza vaccine; hdlIV = High-dose influenza vaccine; sqlIV = Subcutaneous influenza vaccine; LAIV = Live inactivated influenza vaccine (Quadrivalent).  
<http://www.cdc.gov/vaccines/recs/acip/downloads/mtg-slides-feb09/04-1-flu.pdf>.

# Influenza 'Nuts and Bolts'<sup>1</sup>

- 30-50K deaths and 200K Hosp Annually
  - Highest M&M in adults 65+ years
- Vaccine efficacy varies by patient, timing...
  - Early 2015 season: ~60%
- Egg allergy: NO contraindication.
  - Anaphalaxis EXCEEDINGLY rare [~1 in 4 million doses]
  - Risk/benefit of disease vs. vaccine → favors vaccine...
    - Hives-only reactions are 'lowest risk' for routine vaccination
    - Vaccinate with traditional vax: observe in office ~ 30 minutes
  - New vaccines with no egg content: FluBlock, Flucelvax

<http://www.cdc.gov/vaccines/pubs/vis/downloads/vis-flu.pdf>

<http://www.premierinc.com/all/safety/safety-share/12-05-downloads/03-shea-hcw-flu-position-paper.pdf> .

DiazGranados, et.al. NEJM 371(7), August 14, 2014.

<http://www.uptodate.com/contents/influenza-vaccination-in-individuals-with-egg-allergy>

# US Influenza Vaccines 2015-16

Trade name	Manufacturer	Presentation	Mercury thimerosal ( $\mu\text{g}$ Hg/0.5mL)	Ovalbumin content ( $\mu\text{g}/0.5\text{mL}$ )	Age indications	Latex	Route
Fluarix Quad	GSK	0.5 mL single-dose syringe	—	$\leq 0.05$	$\geq 3$ yrs	No	IM
FluLaval Quad	ID Biomedical Corp. Quebec (distrib GSK)	5.0 mL multi-dose vial	$< 25$	$\leq 0.3$	$\geq 3$ yrs	No	IM
Fluzone Quad	Sanofi Pasteur	0.25 mL single-dose syringe	—	§	6–35 mos	No	IM
		0.5 mL single-dose syringe	—	§	$\geq 36$ mos	No	IM
		0.5 mL single-dose vial	—	§	$\geq 36$ mos	No	IM
		5.0 mL multi-dose vial	25	§	$\geq 6$ mos	No	IM
Fluzone ID Quad	Sanofi Pasteur	0.1 mL single dose micro injection system	—	§	18-64 years	No	ID
Afluria	Bio-CSL	0.5 mL single-dose syringe	—	$< 1$	$\geq 9$ yrs	No	IM
		5.0 mL multi-dose vial	24.5	$< 1$	$\geq 9$ yrs needle, 18-64 yrs Jet Injector	No	IM
Fluvirin	Novartis	0.5 mL single-dose syringe	$\leq 1$	$\leq 1$	$\geq 4$ yrs	Yes	IM
		5.0 mL multi-dose vial	25	$\leq 1$	$\geq 4$ yrs	No	IM
Fluzone	Sanofi Pasteur	5.0 mL multi-dose vial	25	§	$\geq 6$ mos	No	IM
Flucelvax	Novartis	0.5 mL single-dose syringe	—	**	$\geq 18$ yrs	Yes	IM
Fluzone High Dose	Sanofi Pasteur	5.0 mL multi-dose vial	—	§	$\geq 65$ yrs	No	IM
FluBlok	Protein Sciences	0.5 mL single-dose vial	—	0	$\geq 18$ yrs.	No	IM
FluMist Quad	Medimmune	0.2 ml single-dose prefilled Nasal sprayer	—	0.24 (per 0.2 ml)	2-49 yrs.	No	IN

Key:  TRivalent  
 QUADivalent  
 Recomb/NO EGG

Adapted from <http://www.cdc.gov/flu/pdf/protect/vaccine/influenza-vaccines-table-2015-16.pdf>



# Influenza-Associated Hospitalization Rates

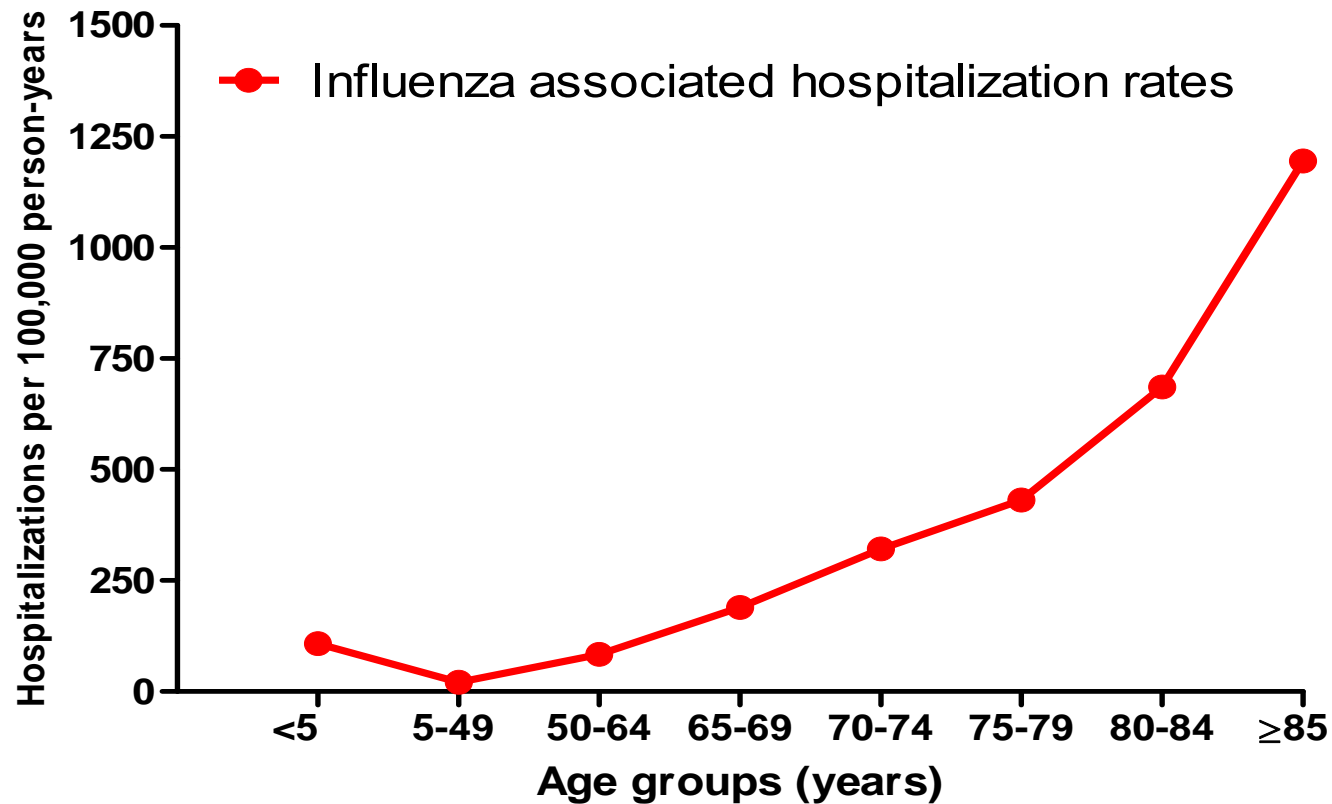
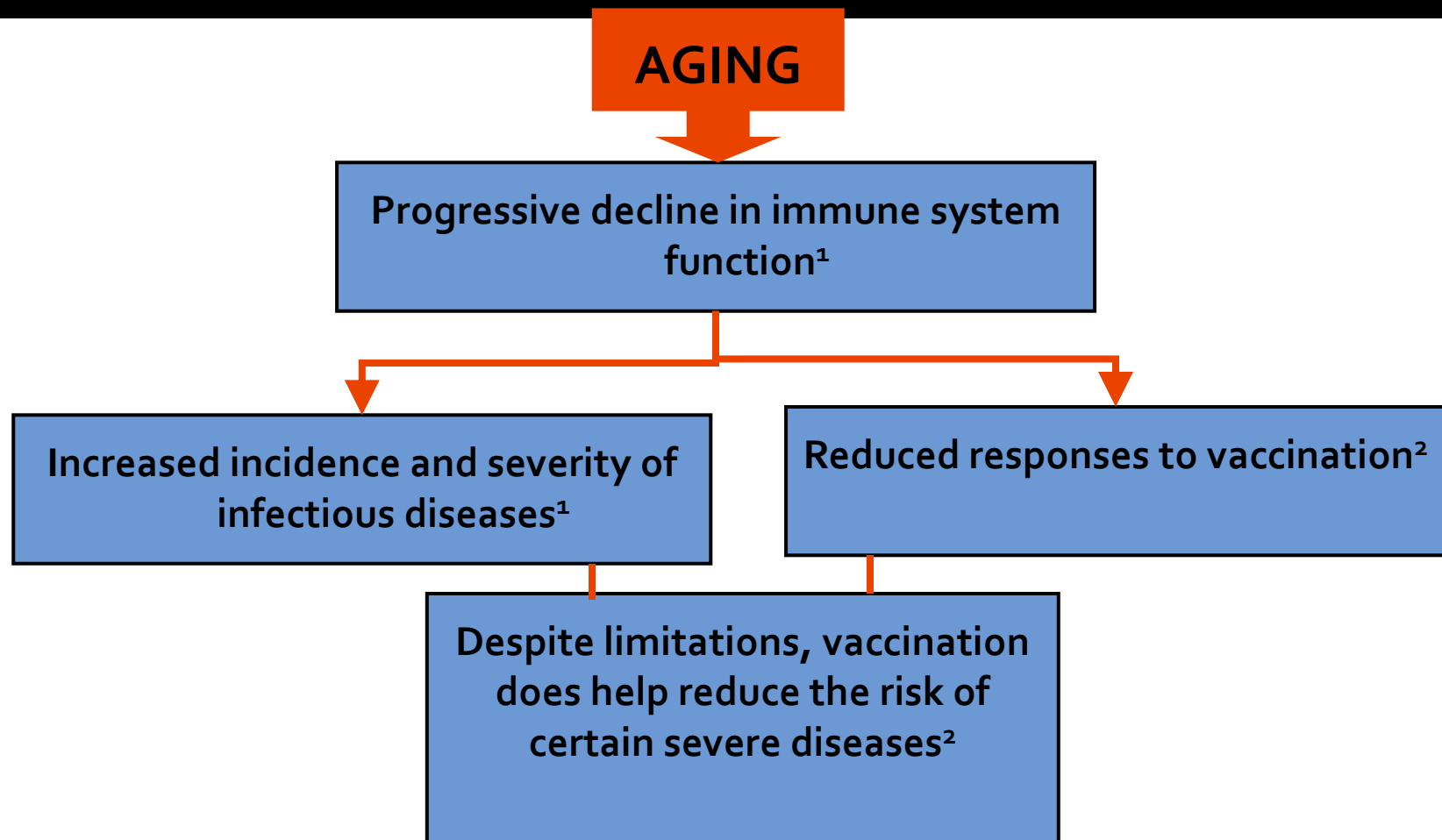


Figure 1. Estimated average seasonal influenza associated hospitalization rates by age groups. (modified from Thompson et al. JAMA 2004)

# Aging, Immunity, and Vaccination



1. Kumar R, Burns EA. *Expert Rev Vaccines*. 2008;7:467–479. 2. High K. *Clin Geriatr Med*. 2007;23:669–685.

ORIGINAL ARTICLE

# Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults

Carlos A. DiazGranados, M.D., Andrew J. Dunning, Ph.D., Murray Kimmel, D.O., Daniel Kirby, B.Sc., John Treanor, M.D., Avi Collins, B.Sc.N., Richard Pollak, D.P.M., Janet Christoff, R.N., John Earl, M.D., Victoria Landolfi, M.Sc., M.B.A., Earl Martin, D.O., Sanjay Gurunathan, M.D., Richard Nathan, D.O., David P. Greenberg, M.D., Nadia G. Torniepoth, M.D., Michael D. Decker, M.D., M.P.H., and H. Keipp Talbot, M.D., M.P.H.

## ABSTRACT

### BACKGROUND

As compared with a standard-dose vaccine, a high-dose, trivalent, inactivated influenza vaccine (IIV3-HD) improves antibody responses to influenza among adults 65 years of age or older. This study evaluated whether IIV3-HD also improves protec-

# Safety of All Influenza Vaccines

- Local reactions: soreness at vaccination site= Common
  - Mild, rarely interferes with usual activities
- Placebo-controlled trials:
  - NO association with higher rates for systemic symptoms
  - Fever, malaise, myalgia, headache
- CANNOT get influenza from inactivated vaccine (IIV)
  - What about those who get achy, fever- to point of 'prostration'?
- Rare events:
  - **Immediate hypersensitivity:** 1 per 500,000
  - **Guillain-Barré Syndrome (GBS):**
    - In general population incidence 10-20/million/yr. [~ Background]
    - Except (possibly) associated with 1976 'Swine Flu' vaccine, no compelling evidence of association with influenza vaccine

# Influenza

- No CLEAR indication to choose 1 IIV over another
  - Exception1: HD vs. IIV in adults 65+ years
  - Exception2: Severe [Anaphylactic] Egg Allergy- egg free vax
- Vaccine effectiveness is multifactorial
  - Match with 'disease' strains
  - Vaccine availability and timing
  - Patient 'substrate':
    - 'Healthy young < 65' @ ~60-80% v. 'Sick older > 65' @ 30-40%
- Ongoing vaccine research
  - Adjuvants
  - Newer production methods
  - Higher Ag content
  - New delivery devices
  - Holy Grail: Vaccine covering many strains, durable immunity over years..
- 'New Flu's'
  - Surveillance and candidate vaccine development: H5N1, H7N3, H9 ...

<http://www.cdc.gov/flu/professionals/antivirals/index.htm> <http://www.cdc.gov/flu/professionals/diagnosis/>

# Influenza:

## How can we reach our goals?

- Immunizers
  - Consistent STRONG recommendations
  - Vaccinate at every opportunity
  - Team work [Office and 'Neighborhood']
- Public Health
  - Engage communities
  - Reinforce value
  - Improve IIS functionality
- Scientists/Industry
  - Assure vaccine supply [safety]
  - Development of Polyvalent vaccine...

# Challenge 2: Implementation of Complex Schedules

- Pneumococcal
  - PCV<sub>13</sub>
  - PPSV<sub>23</sub>
- HBV
  - Many indications
- HPV
  - Different rec's for women, men
- Meningococcal
  - Quad [MCV<sub>4</sub> and MPSV<sub>4</sub>]
  - MenB

## Case 2

27 woman who is in the office for follow-up of her longstanding diabetes. She delivered her first child last June. She received her childhood immunizations on time [and you have this primary data in your EMR], Tdap during pregnancy and a flu vaccination from her employer in September.

What immunization[s] would you recommend for her today?

- a. PPSV23 [Pneumococcal Polysaccharide]
- b. PCV13 [Pneumococcal Conjugate]
- c. Tdap [Tetanus, Diphtheria, Pertussis]
- d. HPV9 [Human Papillomavirus]
- e. HBV [Hepatitis B]
- f. a and e
- g. b and d
- h. b and e



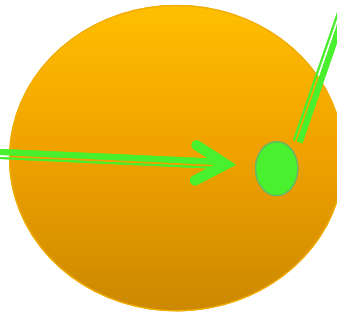
# Pneumococcal: PCV13, PPSV23

## PNEUMOCOCCAL DISEASE:

- Sinusitis
- Otitis media
- Pneumonia
- IPD
- Cases USA
  - 4,000,000 cases/yr
  - 445,000 hosp. admits/yr
  - 22,000 deaths/yr

## INVASIVE PNEUMOCOCCAL DISEASE (IPD):

- Bacteremia
- Meningitis
- Sepsis
- Cases USA
  - 12.9 cases/100K
  - ~10% case fatality rate
  - ^^ in Seniors, CMC
  - >2000 deaths/yr in 65+



# Pneumococcal Disease and Vaccination

- PPSV23 = 'adult standard' vaccine = capsular polysaccharide
  - 23 types -> cause of 88% of bacteremic PNC disease
  - PPS23 has 60-70% efficacy vs. invasive disease (IPD)
  - Immunity lasts at least 5 yr following 1 dose
  - Local reactions – only common AE
  - **BOOSTER: not routine**
- PCV13 = 'pediatric standard' vaccine = conjugated to protein
  - 13 types -> ~50% IPD in immune compromised adults
  - 1 large study of efficacy in seniors
  - Smaller studies in subgroups of younger IC adults
- No studies of combined PCV/PPS strategy recommended by ACIP

# PPSV<sub>23</sub> Vaccine Effectiveness

- 7 Meta-Analyses of RCT (Most recent Cochrane 1/2013)
  - Conclusions inconsistent re: cause specific outcomes
  - Agreement: REDUCTION in IPD; NO reduction in ALL CAUSE mortality, pneumonia
- 3 Meta-Analyses of OBS studies
  - Consistent results: vaccine is effective for prevention of IPD
- Recent RCT Results
  - Invasive PNC Dz: Odds ratio (consistent) 0.26 (CI 0.25-0.46)
  - Pneumonia: Odds ratio (signif. heterogeneity) 0.71 (CI 0.52-0.97)
  - Mortality: Odds ratio 0.87 (CI 0.69-1.10)
- Summary
  - Data = *PPS prevents IPD, not compelling for Pneumonia, Mortality*

Fine, et al. *ArchivesIM*. 1994(154):2666. Hutchinson, et al. *CanJFP*. 1999(45):2381. Watson, et al. *Vaccine*. 2002(20):2166. Conaty, et al. *Vaccine*. 2004(22):3214. Dear, et al. *Cochrane DB Syst Rev*. 2004, Issue 3. Moberley, et al. *Cochrane DB Syst Rev*. 2008, Issue 1. Moberly, et al. *Cochrane DB Syst Rev*. 2013, Issue 1.

# PCV<sub>13</sub> Adult Vaccine Effectiveness

## CAPiTA

- PC RCT PCV<sub>13</sub> unimmunized 65+ aged adults, Netherlands
  - PCV<sub>7</sub> in Dutch infants since 6/2006 -> PCV<sub>10</sub> in March 2011
- 84,000+ participants PCV<sub>13</sub> vs Placebo
  - Enrolled 9/2008-1/2010, follow-up ended 8/2013
  - Primary: 1<sup>st</sup> bacteremic CAP with vaccine-type PNC
  - Secondary: 1<sup>st</sup> non-bacteremic CAP, Other IPD
- Serologic and Urinary Ag used to identify PNC infection
- Met Primary and secondary endpoints
  - Reduced PNC infection
  - Reduced IPD
- Considered by ACIP Pneumococcal group in summer 2014
  - One element in development of combined PPSv<sub>23</sub>/PCV<sub>13</sub> adult strategy
- DID NOT address sequential PCV<sub>13</sub>/PPSV<sub>23</sub> immunization

# Adult Pneumococcal Immunization

## HIGHEST Risk

PCV<sub>13</sub> + PPSV<sub>23</sub>

Immune compromise [IC], 'Anatomic Risk',  
Adults 65+ [NEW 9/2014]

NO

## INCREASED Risk

PPSV<sub>23</sub> ONLY

Smokers, Chronic Medical Conditions- Not  
Immunocompromised

NO

## AVERAGE Risk

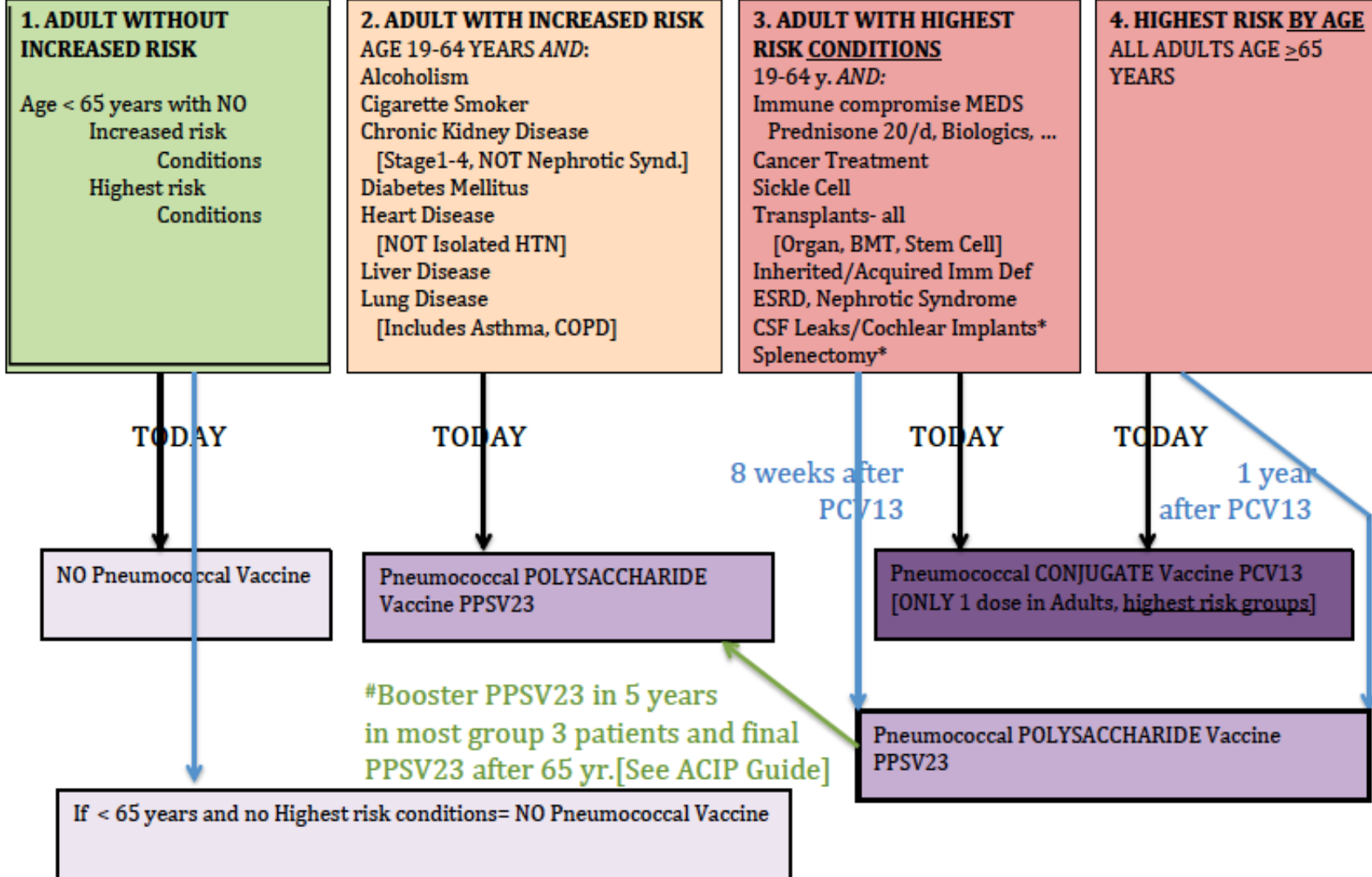
NO PNEUMOCOCCAL VACCINE

Young [< 65], NO Chronic Medical Conditions

# Pneumococcal: It is complex!!

- Adult Pneumococcal Recommendations are complex
  - 2 Vaccines: 13 and 23 Serotypes
  - 3 Intervals: 8 wk, 12 months [1 year], 5 yr...
  - 3 Risk Strata: AVERAGE, INCREASED, HIGH
  - FDA and ACIP NOT in exact agreement
- Evidence for PCV13 and PPSV23 is individual
  - No trial data published on combined strategy
  - Both vaccines reduce IPD
- CDC: “Vaccination rates unacceptably low...”

## ADULT PNEUMOCOCCAL VACCINES: RISK GROUPS and RECOMMENDATIONS



**Footnotes:**

\*PCV13/PPSV23 -and other appropriate immunizations- should be given 2+ weeks PRIOR to elective Splenectomy, Cochlear Implant(s).  
 #Highest risk patients with medical indications -excluding cochlear implant, CSF leak- should receive PPSV23 booster 5 years after initial dose and those who received 1-2 doses of PPSV23 before 65 should receive their final dose after age 65 and 5+ years after last dose.  
 IF PPSV23 is given prior to PCV13, the PCV13 should not administered until 1 year after the PPSV23 dose. **RHH, MD 7/22/2015**

## Case 3

Mr. H is a 53 year old man with HTN and CAD who was hospitalized last week with altered mental status. He was ultimately diagnosed with uncontrolled DM2 with hyperglycemia and UTI. He was given influenza and PPSV23 vaccines prior to DC and is here today [1 week later] for followup. Which of the following vaccines is indicated today?

- a. IIV [Influenza vaccine]
- b. PCV13 [Pneumococcal conjugate vaccine]
- c. Tdap [Tetanus, diphtheria, pertussis adult]
- d. HepA [Hepatitis A]
- e. HepB [Hepatitis B]
- f. Zoster [Shingles]



# Hepatitis B Vaccination

- Universal recommendation for children
- 3 dose series => lifelong immunity in most
  - Testing after immunization only recommended routinely in HCW
  - Nonresponders
    - Uncommon
    - Repeat series once
  - Primary immunity is T-cell mediated, not all HBsAb+
- Adult vaccination= Risk-based
  - 60-80% of adult population, but highly underused

# Sequela of HBV Infection

- Acute liver failure
- Chronic liver disease
  - Persistent
  - Active
- Acute on Chronic Liver failure
  - Persons with chronic liver disease
    - NASH/NAFLD
    - HCV
    - [Others]
- Hepatocellular CA

# Hepatitis B and Diabetes

- October 2011: ACIP recommends Hepatitis B vaccine in unimmunized diabetic patients
  - Aged 19-59 years
  - Age 60+ is at **discretion** of physician [Cat A, type 2 evidence]
    - My implementation: Shared living/glucometer  
Injectable insulin  
Any other HBV risk...
- Why??
  - Patients with DM2 have 2.1 fold increased risk for acute HBV compared with non-DM
  - NASH more common in diabetics and this and other chronic liver disease increases HBV-associated morbidity/mortality
  - NHANES: Seroprevalence for HBV [Anti-HBVc IgG] is 60% higher in DM than non-DM

<http://www.cdc.gov/mmwr/pdf/wk/mm6050.pdf>

# What other adults should be vaccinated against Hepatitis B?

- Behavioral and social:
  - >1 sex partner in 6 months
  - Household contacts and sex partners of HBsAg + people
  - MSM
  - Inmates in long-term correctional facilities
- Occupational:
  - Health care worker
  - Public safety workers
  - Staff working with developmentally disabled
- Medical:
  - IVDU
  - People seeking STD evaluation or treatment
  - Hemodialysis patients and ESRD patients awaiting dialysis
  - Persons with chronic liver disease
- Travel:
  - Personal risk depends on destination and/or activity
- All adults who want to be protected from hepatitis B (HBV)

# Hepatitis B Vaccines, Schedules

- 2 vaccines for HBV alone
- Combination HAV/HBV vaccine
  - More limited HAV recommendations in adults
- High-dose HBV vaccine for Hemodialysis
- Schedules
  - Standard: 0, 1 m., 6 m
  - Several alternative schedules
  - No need to start over if completion is delayed

# Hepatitis B

- **Formulations/Route: IM**

- 3 and 4 dose schedules over at least 4 month interval
- STD: time 0, 1 and 6 months later [alt1: 0, 2, 4 months; alt2: 0, 1 4 mo; Alt 3: 0, 1, 2, 12 mo (Engerix only)]
- If series is delayed, no need to restart. Complete series from prior dose(s)
- High dose vaccine, specific schedule for dialysis patients

- **Systems**

- Hepatitis B vaccine is covered by all insurance payers with proper documentation
- Link administration to diagnosis code for which immunization is indicated
- High-Dose [40 mcg] indicated for ESRD

<http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hepb.html>

## Case 4

22 man presents to the office today at the request of his girlfriend for evaluation of a positive STD test. He has no symptoms and has no medical history. He has not had any vaccinations since he left the Navy after his 5 year initial enlistment ended.

What vaccines would you recommend for him today?

- a. Influenza
- b. Hepatitis B
- c. HPV9
- d. PPSV23
- e. Tdap

# HPV Facts

- >150 types of HPV identified to date
  - HPV-16, HPV-18 most common oncogenic types [14 high risk types]
  - HPV-6, HPV-11 associated w genital warts, respiratory papillomatosis
  - 30+ HPV types infect the human genital tract
- >50% [...near all SA] men, women have 1+ HPV infx/lifetime
  - Many spontaneously clear; but not all...
- Malignancies associated w/ persistent HPV infection:
  - 99% of cervical cancers and cervical dysplasia
  - 13% to 74% of malignancies in the oral cavity
  - 50% of penile and vaginal cancers
  - 90% to 95% of anal cancers
- 25,000 HPV-associated cancers in United States annually

Emerging data on  
respiratory tract SCCA,  
others

Markowitz LE, et al. *MMWR*. 2007;56(RR02):1-24.

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm>. Accessed April 10,

2012



# HPV

- 3 current vaccines available for use in women
  - HPV<sub>2</sub>, HPV<sub>4</sub>, HPV<sub>9</sub>
  - Only HPV<sub>4</sub>, HPV<sub>9</sub> recommended in men
- Misguided public perception problem
  - This is a CANCER PREVENTION VACCINE
    - *[NO SEX TALK... Remember the lessons of 1998 and HBV!!!]*
  - This vaccine is safe and effective!
- Different age recs for Male/Female makes implementation more difficult

# HPV by the Numbers..

- US Population: 319 million [7/2/2014 Census.gov]
- Current HPV infections: 79 million
- New HPV infections/year: 14 million in 15-60 yr. olds
  - *Half of these are in 15-24 year-olds...*
- New Cervical CA/year: 11,000
- Cervical CA deaths/year: 4,400
- June 2006-March 2014: 67,000,000 doses HPV<sub>4</sub> dist.
  - 25,000 VAERS reports:
    - 92.4% non-serious: dizzy, faint, HA, nausea most common
    - 7.6% serious: HA, N/V, fever most common
    - 96 deaths reported 47 confirmed: all investigated, no vaccine link

# HPV: [Must respond to:

# 'I have good kids--- they would never!..']

- WE need to reformulate the debate about HPV vaccine...
- We have not learned from our past mistakes:
  - Mis-steps similar to those when universal HBV vaccine first recommended for adolescents in the 1990's...
  - Mandate resistance *esp.* for this 'moral issue' vaccine
  - 'STD prevention'– *How dare you suggest!!!*
- **Do not link HPV vaccine, 'SEX' in initial conversation**
- HPV vaccine is a **CANCER PREVENTION VACCINE!**
  - Cervical cancer
  - Oropharyngeal cancers
  - Respiratory papillomatosis
  - Genital warts and pre-cancers

# HPV

- Effective for virus strains in vaccine
  - patient not previously exposed to...
- 3 Dose series [0, 1-2, 6+ months]
- Female 9-26
- Male 9-21 [+ 21-26 @ risk]
- Strong recommendation
  - Emphasize personal experience
  - Emphasize value [safety, efficacy, risk]
- Does not eliminate need for Pap screening!

# HPV: [Must respond to:

**'I have good kids--- they would never!..']**

- Value: Reduction of cancer in young people
  - *I have given this to my 2 sons, 4 nieces, 2 nephews!!*
  - *I will give this to my daughter when she is old enough!!*
- HPV 2, 4, 9: 3 vaccines, 1 standard series 0, 2m, 6m
  - Do not need to start over if series completion delayed
  - **Does not protect against strains patient previously exposed to...**
- HPV 2, 4, 9: women 9-26
- HPV 4, 9: men 9-21
- Studies show long-lasting benefit [to 8 yr. and beyond].
- **DOES NOT CHANGE CERVICAL CA SCREENING REC'S!!!**

# Meningococcal Vaccination: Adult

- Highly-Contagious gram-negative bacterium
  - Sero-groups causing human disease: A, B, C, Y, W<sub>135</sub>
  - US Rates at historic low... but outbreaks and sporadic disease still occur!
- Quadrivalent Vaccines: Types A, C, Y, W<sub>135</sub>
  - Conjugate: 3 vaccine products [MCV<sub>4</sub>], IM 2 doses, booster 5 yr
    - Prefer for persons <56 years and/or likely to need revaccination
  - Polysaccharide [MPSV<sub>4</sub>], SQ admin 1 dose
    - Prefer for persons 56+ years and likely to need only 1 dose
- Type B vaccines: FDA Approved (accel.) 2014, ACIP Recommended 2015
  - Multiple types in serogroup B – difficult vax. devel challenge
  - Vaccines affect Factor H binding protein
  - MenB-FHbp (Trumenba- Wyeth) FDA 2 doses [4/2016] ACIP\* 3 doses
  - MenB-4C (Bexsero- Novartis) FDA/ACIP 2 doses

# Meningococcal

- Mening A, C, Y, W135 Vaccination Recommended in:
  - All adolescents [11-12 years, 16-18 years]
  - College freshmen who will live in a dormitory and military recruits
  - Asplenia (anatomic or functional)
  - Persistent complement component deficiencies
  - Travelers to 'at-risk areas': Sub-Saharan Africa, December-June
  - Microbiologists (possible occupational meningococcal contact)
  - Outbreak situations
  - HIV: **NOT** an indication (NEW 2014-> Low absolute risk)
- Men B Recommended [at MD Discretion] in:
  - Young adults 16-23 to provide short term protection against MenB serotypes [preferred age 16-18]
  - During outbreaks serogroup B Neisserial disease
  - Asplenia (anatomic or functional)
  - Persistent complement component deficiencies
  - Microbiologists (possible occupational meningococcal contact)

# Challenge 3: Vaccination of Seniors in 2016

- Tdap
- Zoster
- Pneumococcal
  - Highest risk due to Age



## Case 5

Patient 5 is a 66 year old woman with hypertension only. She is preparing to travel to central America on a medical mission. In addition to travel-specific vaccine recommendations, what other vaccines do you recommend she receive during her office visit today (April 27)?

- a. IIV [Influenza]
- b. PPSV23 [Pneumococcal polysaccharide]
- c. PCV13 [Pneumococcal conjugate]
- d. Hep B [Hepatitis B]
- e. Zoster [Shingles]
- f. a and b
- g. a and c
- h. c and d
- i. c and e

# Tdap, Td: Tetanus and Pertussis

- Tetanus is not common but can be devastating
- Pertussis outbreaks are common
  - Communities
  - Hospital units and Residential Care facilities
  - Significant morbidity for all affected
  - Contagious in close contact
  - Highest mortality risk in infants
    - who cannot be vaccinated until 2 months...
  - '100 days Cough'
    - Complications common, most frequent= Pneumonia

# Tdap, Td: Tetanus and Pertussis

- Primary series of Tetanus containing vaccine
  - 3 doses over 6+ months
  - Provides immunity to ~all for 10+ years
  - Many do not get recommended [q10] boosters
- **Tdap should replace 1 dose Td for all adults**
  - Interval following last Td is not important
  - Regardless of underlying condition, age!!
  - Repeated dosing is being studied in adults
- And Tdap at 26-37 weeks gestation
  - Every pregnancy
  - [find reference for recent study on safety of this]

# Td >> Tdap

- All patients should have primary Tetanus, diphtheria series
  - Yields protective Ab ~ all for 10 years<sup>+</sup>
  - Many adults > 60 y. never received primary T, d series
  - Over 50% adults do not have protective T, d Ab's
  - Booster Td every 10 years [Many adults do not receive boosters]
    - Most boosters given are 'episodic trauma-related'
- System Challenge:
  - ACA Covered benefit for all privately-insured patients
  - M'Care, MCD: PHARMACY [not medical] Benefit
    - In absence of trauma/wound...
- Td/Tdap Contraindications
  - Severe allergy to vaccine comp. or Arthus Reaction following T vax.
  - [Tdap] Encephalopathy < 7 days after pertussis containing vaccine
  - [Tdap] Unstable neurologic disease, Moderate-severe acute illness

<http://www.cdc.gov/vaccines/vpd-vac/combo-vaccines/DTaP-Td-DT/Tdap.htm>

# Td >> Tdap

- **Tdap Recommendation: All Adults**
  - Single dose to replace one dose Td [Booster or primary]
  - Current recommendation: subsequent Td q10yr
  - May give any time following last Td
  - Don't forget seniors!
- Special emphasis: adults with close infant contact:
  - HEALTHCARE
  - Parents
  - Child Care, etc.
- **Tdap intrapartum: every pregnancy [since 2013]**
  - Regardless of interval/prior Tdap [Best @ 27-35 weeks]
  - Focus: Protect infants [Highest M&M] thru passive immunity
- Problem: Pertussis immunity not longlasting [Dz or Vax]

# Zoster: Shingles

- Almost all adults born before 1980 had chicken pox
  - If you have had varicella, you are at risk of having Zoster...
  - Reactivation=> Shingles
  - Estimated 1million cases/year in US
- Most who have varicella have antibody [IgG] for life
  - Ab only indicate that you have had disease or vaccine...
- Zoster occurs when CMI [*not Ab*] declines
- Lifetime risk is 1 in 3 for an episode of Zoster
  - Increases with age: if live to 85, risk ~ 50%
  - Post Herpetic Neuralgia occurs in as many as 1/3 pt
    - higher in: > 70 years, Immune compromised

# Zoster

- Most who have varicella have measureable Ab for life
  - Zoster occurs when CMI surveillance declines [theoretical]
  - Reactivation or Varicella exposure re-stimulates CMI [Cycle repeats]
- Lifetime risk of Zoster ~33% [99.5% adults serology + prior Varicella]
  - At 85- lifetime risk ~ 50%
  - PHN= most common AE
    - Up to 1/3 pt with Zoster
    - More common
      - > 70 years with Zoster
      - Immunocompromised
  - Vaccination stimulates CMI

# Zoster: Shingles

- Vaccinate healthy adults 60 years and older
  - ACIP: **Not immune compromised**
- FDA approved from age 50
  - Differs from ACIP recommendation
- Regardless of prior Zoster
  - Opinion: wait ~1 year
- ACR recommends vaccination prior to immune suppression
  - Preliminary study shows no risk in pt. on Biologics
- No need to test/vaccinate vs. Varicella first



# Zoster: Shingles

- Contraindications
  - Pregnancy
  - Anaphylactic sensitivity
    - Neomycin, Gelatin
  - No need to defer for 'at risk contacts'
    - Transmission risk very low
- Frozen live-virus vaccine:
  - Give with 60 minutes of reconstitution
  - 0.65 ml SQ Deltoid
- Duration of protection: At least 4 years
- No booster

# Seniors= Highest risk for Invasive Pneumococcal Dz

- Those with medical conditions
  - Intermediate risks: Non IS Chronic Conditions
    - PPSV<sub>23</sub> prior to age 65
    - NOW: PCV<sub>13</sub> ONCE [at least one year after PPSV<sub>23</sub>]
    - PPSV<sub>23</sub> ONCE [at least 1 year after PCV and 5 years after last PPSV<sub>23</sub>]
  - Highest risk: Chronic IS Conditions
    - PCV<sub>13</sub> [only if not received prior to age 65]
    - PPSV<sub>23</sub> ONCE [at least 1 year after PCV and 5 years after last PPSV<sub>23</sub>]
- No medical conditions:
  - PCV<sub>13</sub> ONCE, now
  - PPSV<sub>23</sub> ONCE [at least 1 year after PCV]

# Challenge 4: Overcoming vaccine resistance

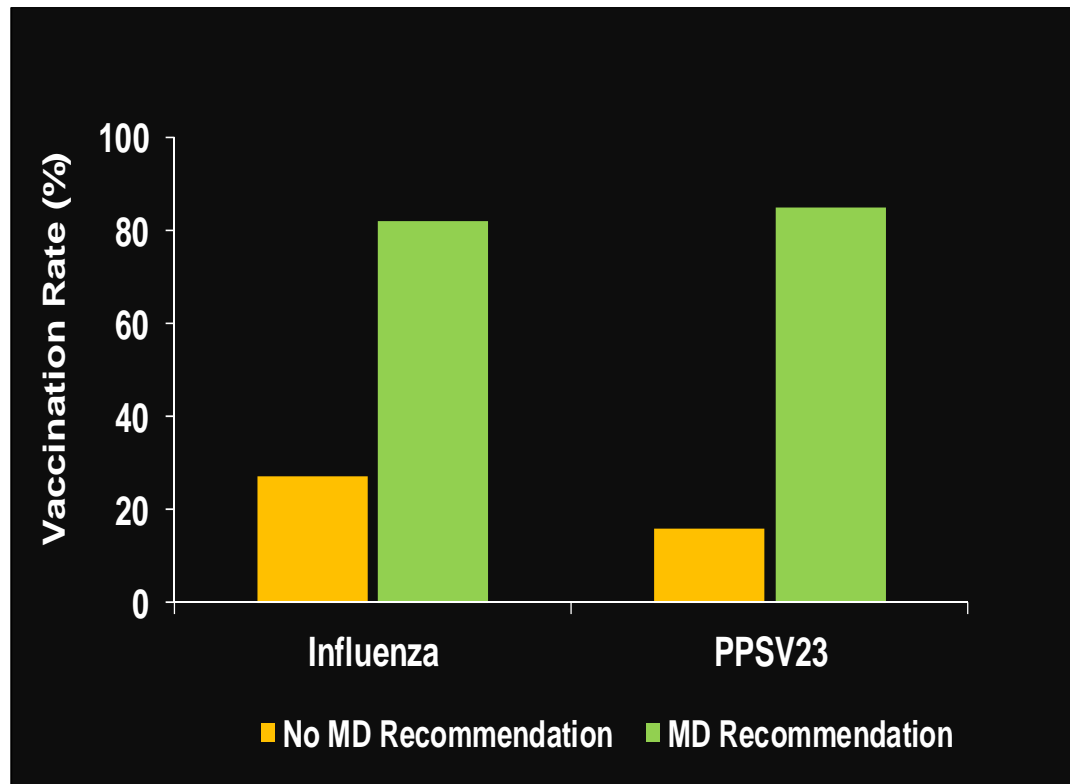
# Make Strong Vaccine Recommendations

- Your recommendation is key
  - 88% of consumers said they were likely to get vaccinated if recommended by their doctor\*
- Make education materials available
  - Wall posters, Vaccine Information Sheets [VIS]
  - Sources:
    - [www.immunize.org/catg.d/p4030.pdf](http://www.immunize.org/catg.d/p4030.pdf)
    - [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines)
- Encourage dialogue, answer questions
- Personalize the vaccine experience
  - Would you take the vaccine yourself or give it to your parents? If so, let the patient know. Do not take No for an answer!

\*National Foundation for Infectious Diseases. Call To Action: Adult Vaccination Saves Lives. Bethesda, MD, 2012. <http://www.adultvaccination.org/resources/cta-adult.pdf>. Accessed March 4, 2015.

# Provider Recommendation Can Overcome Negative Attitude Among Patients

Vaccination Rates Among High-Risk Patients With Negative Attitudes



# Systems Issues

- Racial and Ethnic Disparities
  - Major factor in inadequate rates
- Standards: Assess->Recommend->Administer-> Document
- Insurance/Coverage
  - All ACIP recommendations covered in Private plans
    - BUT reimbursement can be a challenge
  - MCD, MCARE
    - Pneumococcal and Flu covered
    - Tdap [except injury], Zoster: Drug benefits only
  - Careful planning to make imm. Not a loss/profitable
- Immunization is a TEAM SPORT!!
  - Office team
  - Immunization Neighborhood

# Systems Issues: Responding to Anti-VAX and Imm-Nihilists

- RISK REDUCTION
  - High risk patients may not understand this
- VALUE to INDIVIDUAL
  - Cost of illness in work loss/effectiveness
  - Cost of treatment of illness
- VALUE to FAMILY/COMMUNITY
  - Not there -or not at best- to care for family
  - e.g. Flu, Tdap= 'Grandparent Vaccines...'
- LOW COST
  - ACA-Mandated first dollar coverage
- SAFETY of vaccines

# Team Vaccination

- In office
  - Delegate
  - Standing orders
- If you do not vaccinate in office
  - Refer!!
  - Best practice: Written, request feedback!



# Systems: VIS Access

[www.mass.gov/dph/iis](http://www.mass.gov/dph/iis)

Introducing the  
Massachusetts Immunization Information System

# MIIS

## Information for Providers



The routine immunization schedule for children is getting more and more complex. Now there's a new tool from the Massachusetts Department of Public Health (DPH) to help you meet these challenges – an immunization registry called the Massachusetts Immunization Information System (MIIS). The MIIS is a secure, confidential, and easy-to-use system designed to support a complete set of immunization-related functions.

### What can the MIIS do for you?

- Provide quick access to patient immunization records at point of care.
- Make immunization histories for children new to your practice readily available.
- Validate patient vaccine history and forecasts due dates for future vaccinations.
- Identify unimmunized and under-immunized children.
- Prevent duplicate immunization.
- Print forms for school and camp.
- Create reminder and recall materials for your patients with due or overdue immunizations.

- Integrate immunization delivery and disease control.
- Provide infrastructure for communication and tracking for vaccines, medications, and other countermeasures needed during natural disasters, bio-terrorism events, flu pandemics and other emergencies.

### Immunization Forecasting

The MIIS features an Immunization Forecast Module (IFM) to validate vaccine history and forecast the due dates of future immunizations based on:

- Current age
- Historical vaccinations
- Special circumstances such as allergies or immunities

The IFM is based on a complex set of rules and clinical guidelines – and is constantly updated to reflect the latest recommendations.

### What are some of the other benefits of the MIIS?

- Share data between practices, schools and other delivery sites.
- Help to evaluate immunization usage and coverage for your practice.



For more information about the MIIS, please visit:  
[www.contactMIIS.info](http://www.contactMIIS.info)  
or contact the MIIS Help Desk at:  
(617) 983-4335  
[MIIShelpdesk@state.ma.us](mailto:MIIShelpdesk@state.ma.us)



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### The MIIS for Practices with Paper-Based Health Records

Your practice will be able to log into the MIIS web-based interface from your office computer to routinely enter and access immunization information for your patients. To access the secure login to the MIIS, you simply need a computer with internet access.

### The MIIS for Practices with Electronic Health Records (EHR)

Many EHR systems can exchange data directly with the MIIS – so you will not need to enter immunization information into two different systems.

### How does data exchange with the MIIS work?

- MIIS can accept data feeds in real-time or periodically, depending on your EHR system.
- Data will be available for immediate use as soon as it's received by the MIIS from your EHR system.
- MIIS uses HL7 (version 2.5.1), a standard for exchanging health-

related information between medical applications that is currently used by many EHR systems.

- Your EHR software provider or IT department can help assess your specific EHR system capabilities.
- If your EHR system is not capable of transmitting immunization data to the MIIS, you will need to enter your patients' immunizations directly into the MIIS.
- Regardless of your data exchange capabilities, you can utilize the Immunization Forecast Module (IFM) and reporting features within the MIIS for immunization tracking, reminder-recall notification, and form printing.

### New – Online Vaccine Ordering in 2013!

The MIIS will roll out a comprehensive Vaccine Management module in 2013 that will include online provider enrollment and vaccine ordering. Providers that currently order vaccine from MDPII should **register now at [www.contactMIIS.info](http://www.contactMIIS.info)** to ensure timely access to this new module.

### HL7 Data Exchange... what is HL7?

- HL7 (Health Level Seven) is a national standard for exchanging health-related information between medical applications.
- MIIS will exchange data in the following format: HL7 version 2.5.1. Many EHR systems currently use this data format.
- Your EHR software provider or IT department can talk to you about your specific EHR system capabilities.

### "Meaningful Use"

- The 2009 federal stimulus bill (also known as ARRA) outlined incentives to increase adoption and utilization of EHRs in a meaningful way.
- Incentive payments are available for Medicare and Medicaid eligible providers and hospitals that purchase, implement, and meaningfully use federally certified EHR systems. Please see [www.cms.gov/EHRIncentivePrograms](http://www.cms.gov/EHRIncentivePrograms) for more information.
- Certified EHRs must meet a predetermined set of objectives and be able to report on a set of quality measures.
- Data exchange with the MIIS will satisfy the Public Health Objective for meaningful use.
- For more information or to find out if you qualify for incentives, contact the Massachusetts e-Health Institute (MeHI), the Regional Extension Center for the Commonwealth, at [info@maehi.org](mailto:info@maehi.org) or (617) 371-3999. You may also visit [www.maehi.org](http://www.maehi.org).

# USA, ACA and Adult Immunization

- VFC: federal program allowed access to childhood imm for low income children= **GOOD**
- ACA: private plans must provide first \$ coverage for ACIP recommended immunizations= **GOOD!**
- CMS: Medicare and Medicaid rules for AI are not the same as private plans= **NOT SO GOOD!**
  - Vaccines for specific indications: covered if correctly coded
  - Medicare part B: Influenza, PPSV<sub>23</sub>, PCV<sub>13</sub>, Tdap/Td\*
  - Medicare part D: Zoster, Tdap/Td\*
  - Medicaid: rules vary by state but most use M'care rules...

\*Td/Tdap only covered under part B if admin for injury

# Other Adult Vaccines: Less common- still important

- HAV
  - Travel, Liver disease
- Rabies
  - Exposure
- Travel Vaccines
  - Typhoid, Yellow fever, Japanese Encephalitis
  - Strongly endorse: <http://wwwnc.cdc.gov/travel/destinations/list>

# Questions and Resources

- ACP:
  - <http://immunization.acponline.org/>
- Immunization Action Coalition:
  - <http://www.immunize.org/>
- CDC Immunization:
  - <http://www.cdc.gov/vaccines/>