Melissa Martinez, MD, FAAFP

The Rationale Behind Vaccine Recommendations

60th Annual NMAFP
Family Medicine Seminar
July 27, 2017

Discloser

The AAFP Vaccine Science Fellowship

Funded by a grant from Merck & Co Inc.

The AAFP had full control over the content of the fellowship and selection of fellows.


Off Label
Sub unit/Adjuvant Shingles Vaccine

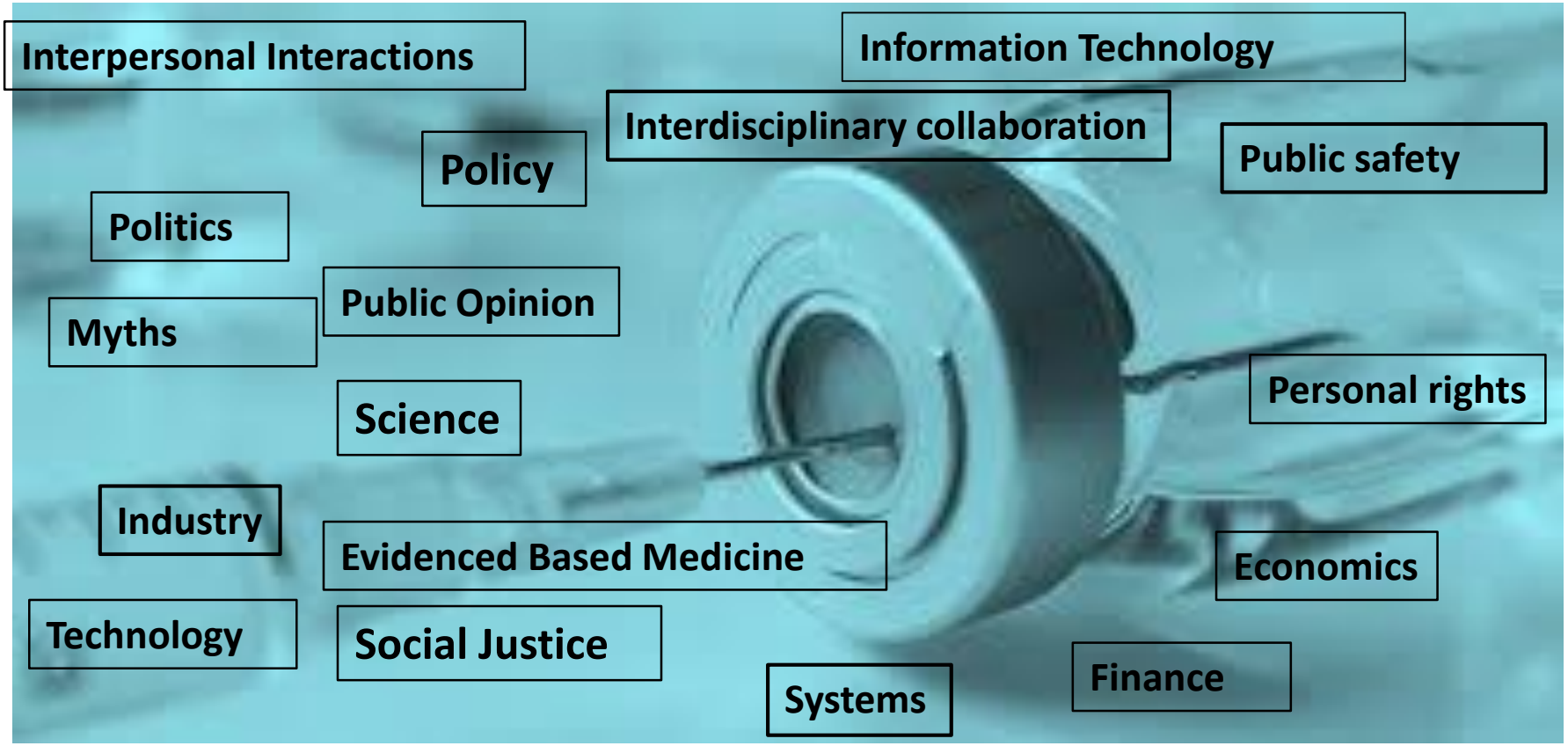
Melissa Martinez MD FAAFP
Vaccine Geek

- SHOTS app content expert
- National Vaccine Advisory Committee

  US Department of Health and Human Services
- Liaison Mumps Work Group of the Advisory Council on Immunizations Practices (ACIP,CDC)
- Fellowship: Vaccine Science

Co Chair New Mexico Immunization Practice Advisory Committee

UNMH Adult Immunization Task Force


Interpersonal Interactions
Information Technology
Interdisciplinary collaboration
Policy
Public safety
Politics
Public Opinion
Myths
Personal rights
Science
Industry
Evidenced Based Medicine
Economics
Technology
Social Justice
Systems
Finance


… we ought to be debating the science.

Objectives

- Describe the rational for two pneumococcal vaccines
- Compare influenza vaccines
- Explain current recommendations for HPV 9
- Talk to patients/parents about the safety of vaccines
- Contrast the current and new shingles vaccine

AN ACT

RELATING TO HEALTH; MAKING THE OFFERING OF INFLUENZA AND PNEUMOCOCCAL IMMUNIZATIONS TO SENIOR CITIZENS MANDATORY UPON RELEASE FROM A HOSPITAL.

BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF NEW MEXICO:

SECTION 1. A new section of the Public Health Act is enacted to read:

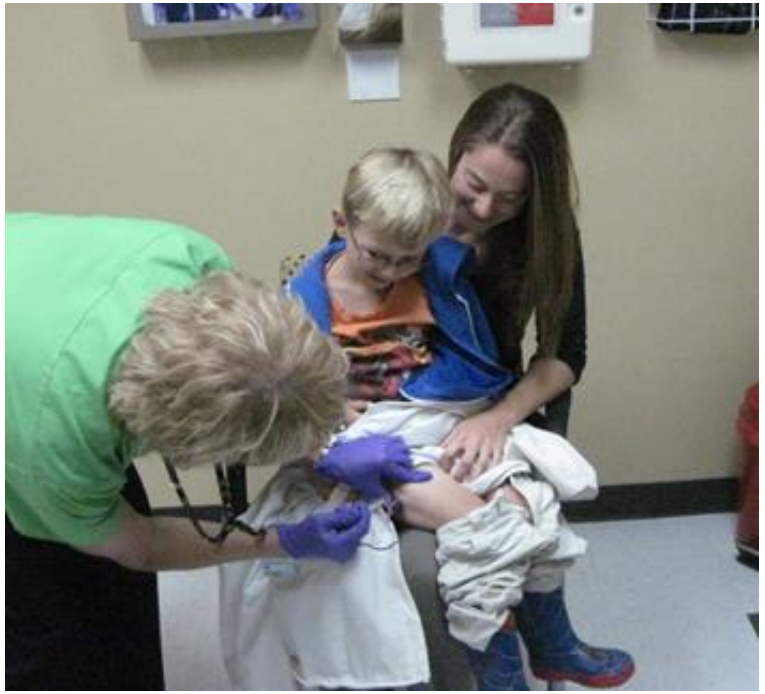
"HOSPITALS--REQUIREMENT TO OFFER INFLUENZA AND PNEUMOCOCCAL IMMUNIZATIONS.--Each year between October 1 and March 1 and in accordance with the latest recommendations of the advisory committee on immunization practices of the federal centers for disease control and prevention, each hospital licensed by the department of health shall offer, prior to discharge, immunizations against the influenza virus and pneumococcal disease to all inpatients sixty-five years of age and older unless contraindicated for a patient and contingent upon the availability of the vaccine."

PNEUMOCOCCAL IMMUNIZATIONS.--Each year Between Oct 1 and March 1
March 1 and in accordance with the latest recommendations of
the advisory committee on immunization practices of the
federal centers for disease control and prevention, each
hospital licensed by the department of health shall offer,
prior to discharge, Immunizations against influenza and pneumococcal
and pneumococcal disease to offered to all **inpatients** 65 or older
age and older unless contraindicated for a patient and
contingent upon the availability of the vaccine."

Implementation

Influenza

- All patients 6 months and up



Trivalent (The standard flu shot)

- Efficacy (RRR)= 60% (95% CI 53% to 66%)
- NNV (number needed to vaccinate) = **71** (95% CI 64 to 80)

- When vaccine matches the circulating strain the efficacy = 62% (95% CI 52%to 69%)
- NNV is **58** (95%CI 52 to 69)

Cochrane 2014

High Dose

Small advantage for the high dose

	Flu	No Flu	Total
High dose	228	15763	15,991
Standard dose	301	15697	15,998

ARR=CER-EER 301/15998-228/15991=0.018-0.014=0.004 NNT =1/AAR =250

We need to give 250 adults over 65 the high dose in place of the standard dose to prevent one case of flu in a season

RRR=EER/CER=0.014/0.018=0.73 or 73% or a 27% reduction

N Engl J Med 2014; 371:635-645

Quadrivalent flu shots have two A strains and 2 B strains

Influenza A

Influenza B

How important is the extra B strain? Depends on the year:

Some years Influenza B is common

About 30% of all cases of flu

If the B strain in the vaccine does not cover the circulating B strain then getting the extra B is important

Some years Influenza B is not as common

About 0-5%

In year where there is not much influenza B circulating the extra B protection is not important

ACIP

- **Advisory Council on Immunizations Practices**
- No Preference

Pneumococcal Vaccines

Pneumovax® PPSV23

Polysaccharide

1980s

23 Valent

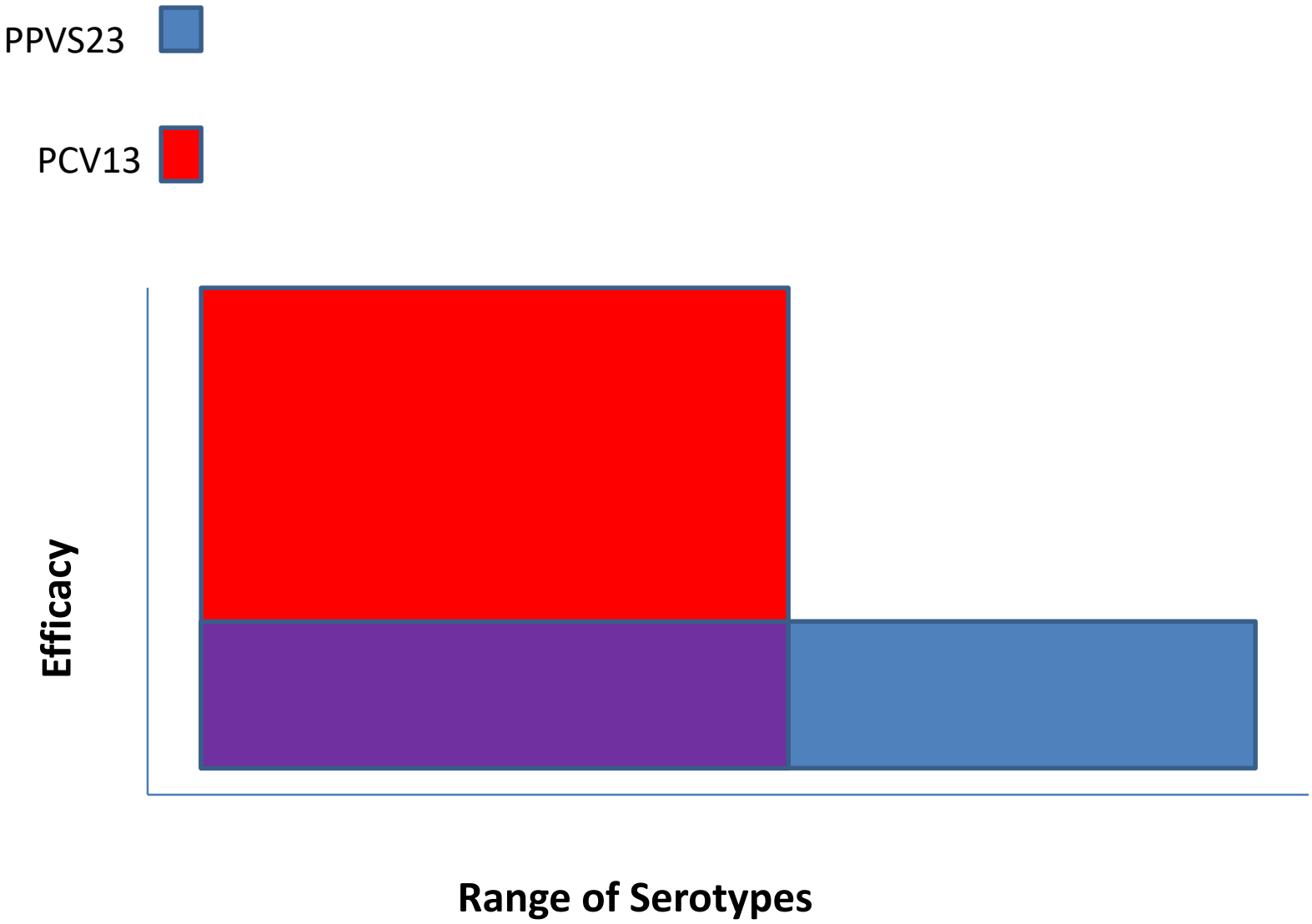
Prevnar® PCV13

Conjugated protein to Polysaccharide

PCV7 -1998

PCV13 2009

13 types


PPVS23
PCV13
Efficacy
Range of Serotypes

PCV13

CAPiTA Trial

84,496 age 65+ in Netherlands

Placebo=42,250

PCV13=42,240

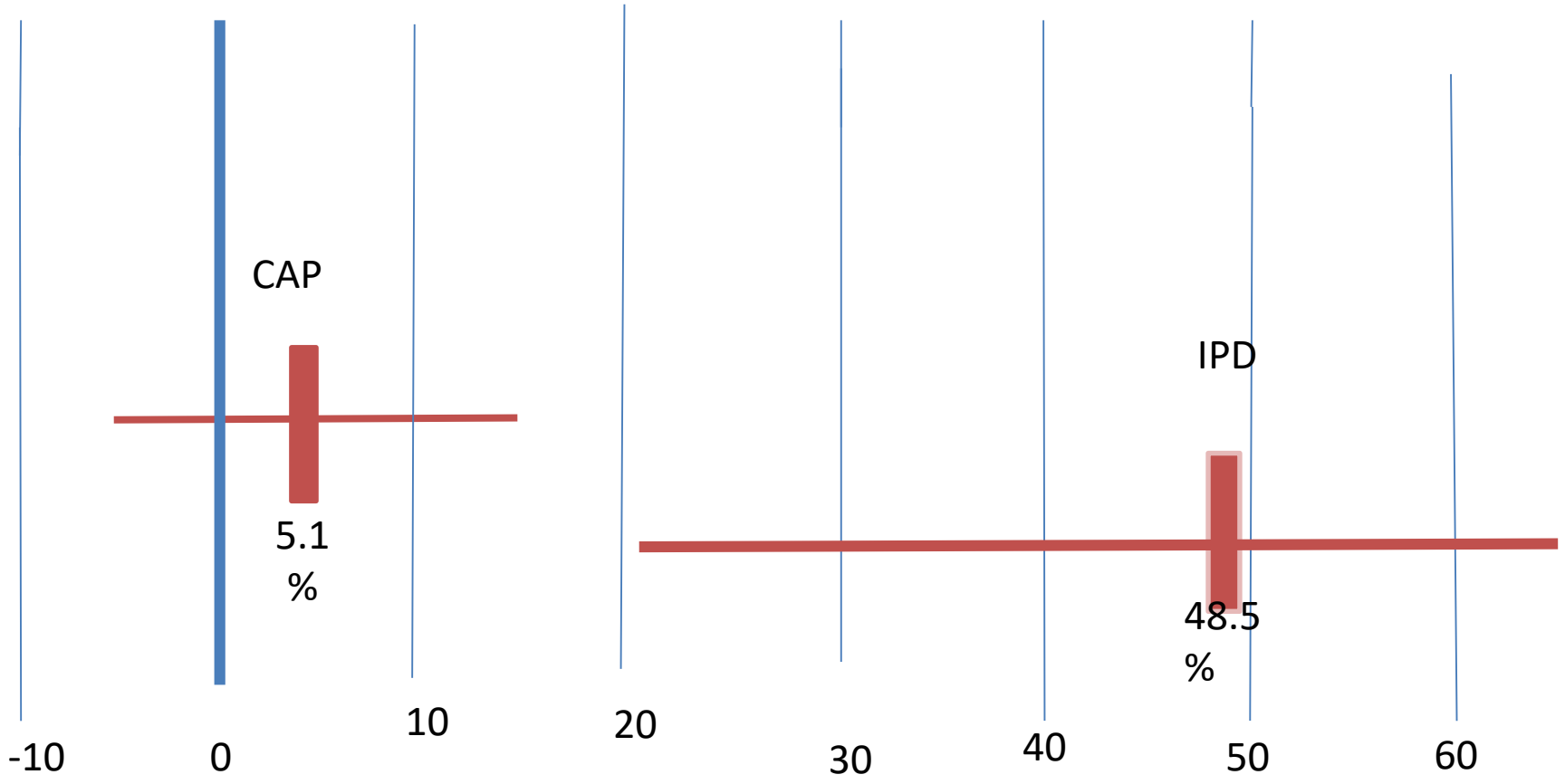
Mean follow up 3.97 years

Bonten NEJM 2015

Prevnar® (PCV13)
CAPiTA Trial

Dx	Efficacy	95%CI	p	ARR	NNT
CAP	5.1%	-5.1,14.2	0.32		
IPD	48.5%	20.9,67.0	.006	.0007	1,428

Bonten NEJM 2015


CAP
5.1
%
IPD
48.5
%
-10
0
10
20
30
40
50
60

PPSV23
Meta-analysis

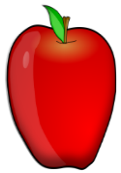
Selection Criteria

- Subjects age 50+
- Outcomes CAP or IPD

Kraicer-Melamed Vaccine
2016

PPSV23
Meta-analysis

Dx	Efficacy	95%CI	p	ARR	NNT
CAP cohort	17%	-26,45			
CAP Case Co	7	-10,21			
IPD cohort	50%	21,69			
IPD Case Co	54%	32,69			



CAP

IPD

5.1%

17%

48.5%

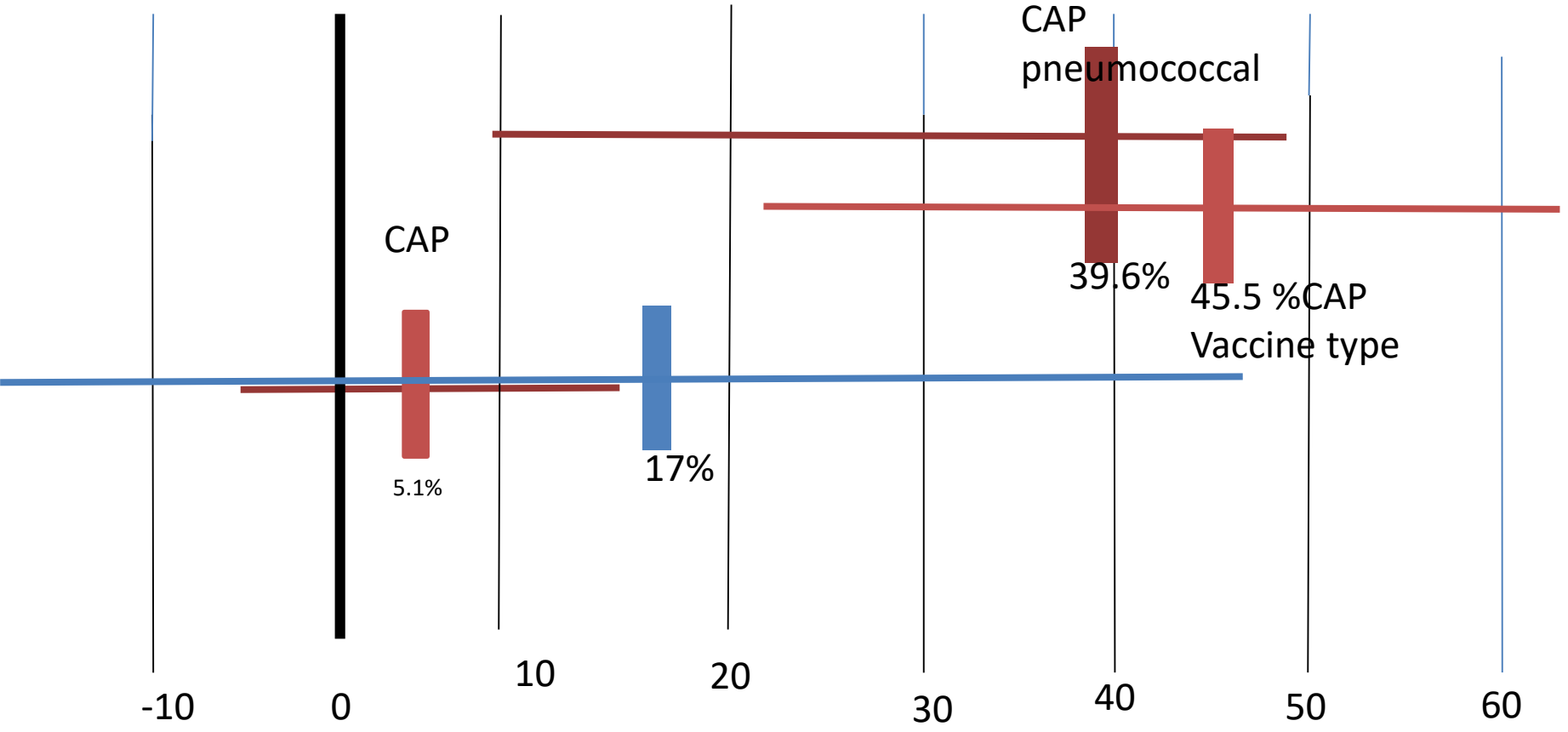
50%

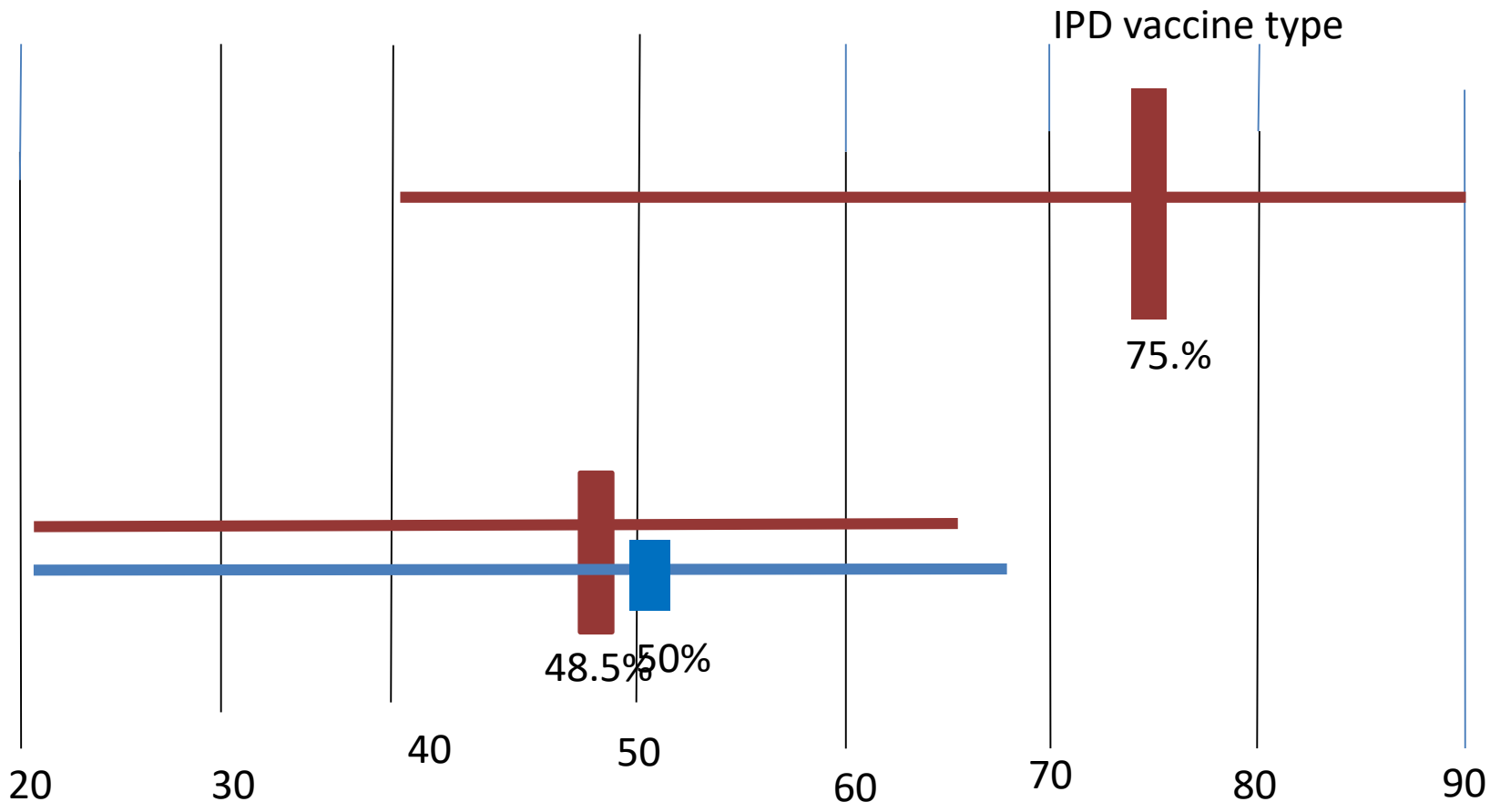
-10 0 10 20 30 40 50 60

PCV13
CAPiTA Trial

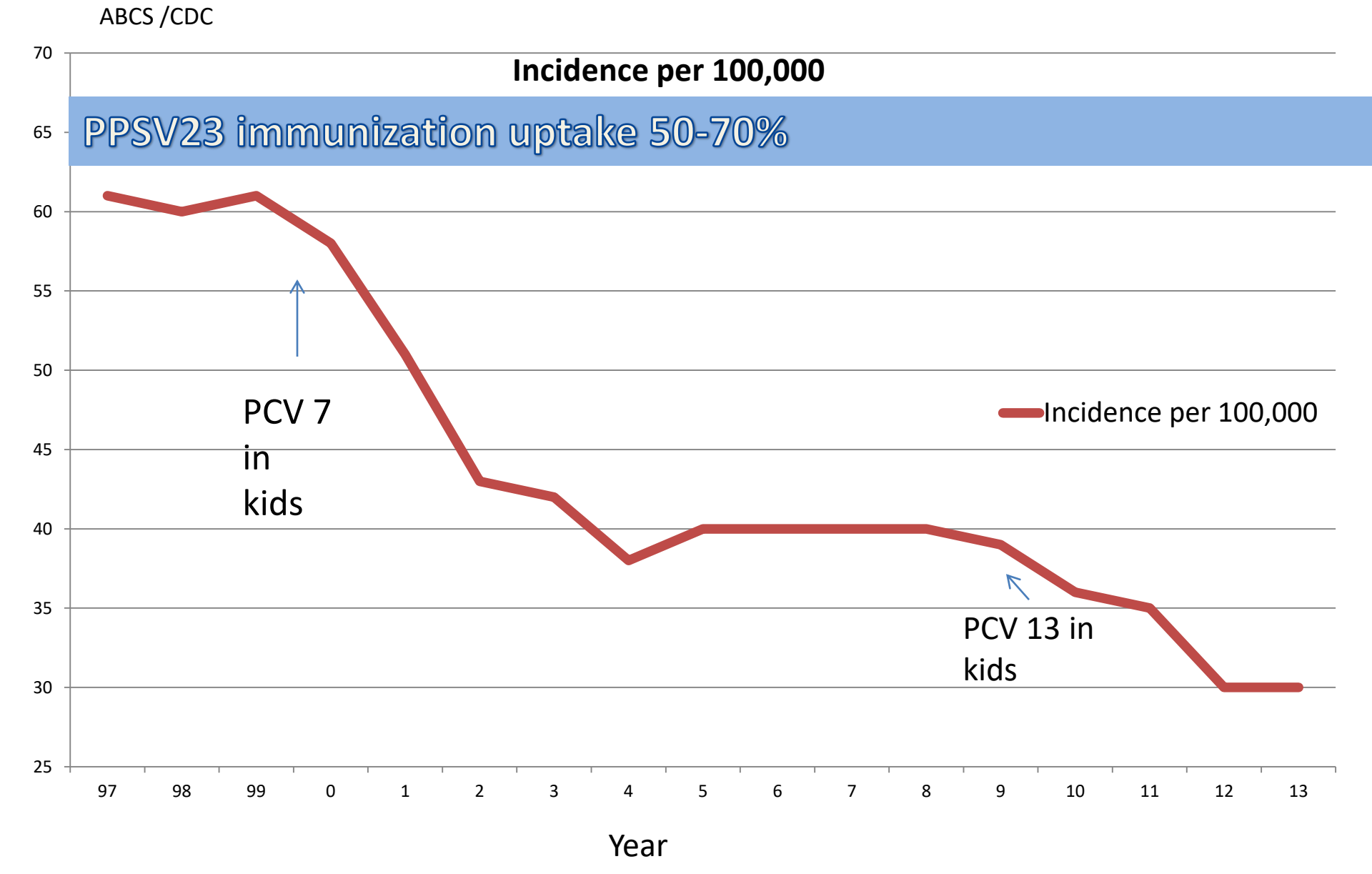
Dx	Efficacy	95%CI	p	AAR	NNT
CAP	5.1%	-5.1,14.2	0.32		
CAP Pneumococcal	39.6%	9.8-46.7	.008	.0009	1111
CAP Vaccine type	45.6%	21-65	<0.001		
IPD	48.5%	20.9, 67.0	.006	.001	1000
IPD Vaccine type	75%	41.4-90.8	<0.001		

Bonten NEJM 2015


CAP
pneumococcal
CAP
39.6%
45.5 %CAP
Vaccine type
5.1%
17%
-10
0
10
20
30
40
50
60


IPD vaccine type
75.%
48.5%
50%
20
30
40
50
60
70
80
90

Pneumococcal Incidence for 65+



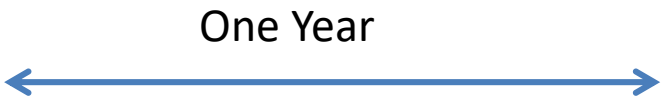
Theory: PCV13 deceases asymptomatic carriage rates

5-10% of adults without children colonized

20-60% of school age kids colonized

CDC pink book 2015

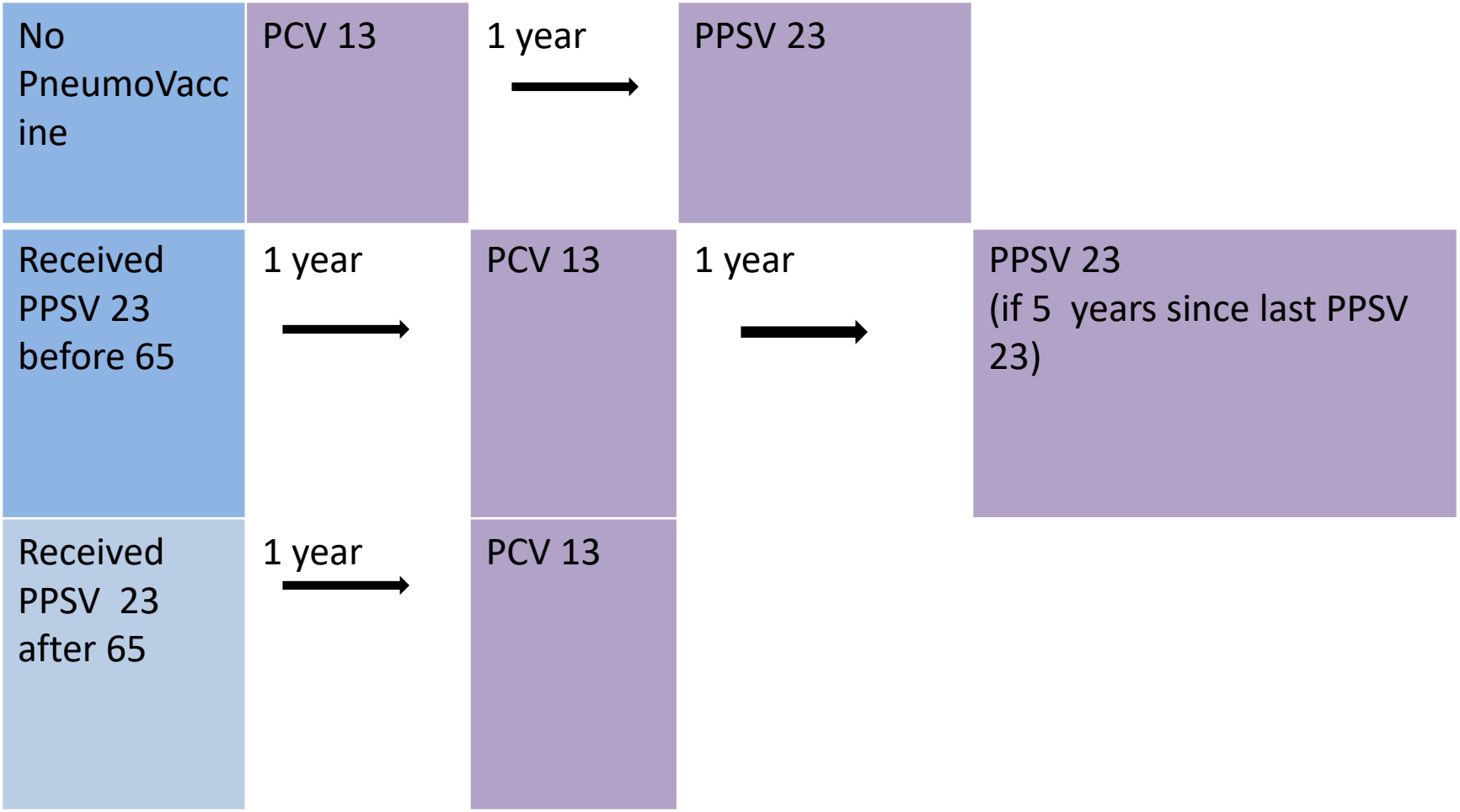
Age 65 and up

PCV13 

PPSV23

If possible PCV13 first

≥65


No PneumoVaccine
PCV 13
1 year
PPSV 23
Received PPSV 23 before 65
1 year
PCV 13
1 year
PPSV 23 (if 5 years since last PPSV 23)
Received PPSV 23 after 65
1 year
PCV 13

Under 65

No chronic conditions

Immuno-compromised

Increased Risk

Blood Brain Barrier disruption

<65 and No Chronic Conditions

No pneumococcal vaccines

<65 and at increased risk PPSV23 only

- Chronic heart disease
- Chronic lung disease (Asthma)
- Diabetes mellitus
- Alcoholism
- Chronic liver disease
- Cigarette smoking

PPSV23 only

Immuno-compromised

- Hemoglobinopathies
- Asplenia
- Chronic Renal Failure
- Nephrotic Syndrome
- Generalize Malignancy
- Leukemia
- Lymphoma
- Hodgkins
- HIV/Immunocompromised
- Immunosuppression
- Solid Organ Transplant
- Multiple Myeloma

PCV13 first
PPSV23 **8 weeks** later

Or

If PPSV23 first, PCV13 in **one year**

Repeat PPSV23 in 5 years

Blood Brain Barrier Disruption

- Cochlear Implant
- CSF Leak

PCV13 first
PPSV23 **8 weeks** later

Pneumococcal Vaccine Timing For Adults

DO NOT administer PCV13 and PPSV23 at the same visit.

Age 65 Years or Older

- If PCV13 was given before age 65 years, no additional PCV13 is needed.

No history of pneumococcal vaccine → **PCV 13** (Prevnar 13®) → **1 year** (8 weeks for groups B & C as defined below) → **PPSV 23** (Pneumovax® 23)

Received PPSV23 before age 65 → **1 year** → **PCV 13** → **1 year** (8 weeks for groups B & C as defined below) **and 5 years** after prior dose of PPSV23 → **PPSV 23**

Received PPSV23 at age 65 or older → **1 year** → **PCV 13**

Age 19-64 Years With Underlying Condition(s)

- Prior doses count toward doses recommended below and do not need to be repeated.
- If PPSV23 given previously – wait one year before giving PCV13
  – for group B, wait at least five years before giving a second dose of PPSV23
- No more than two doses of PPSV23 recommended before 65th birthday and one dose thereafter.

A. Smoker, Long-term facility resident, or Chronic conditions: → **PPSV 23**

- heart disease (excluding hypertension)
- lung disease (including asthma)
- liver disease (including cirrhosis)
- diabetes
- alcoholism

B. Immunocompromised (including HIV infection), **Chronic renal failure, Nephrotic syndrome, or Asplenia** → **PCV 13** → **8 weeks** → **PPSV 23** → **5 years** → **PPSV 23**

C. CSF leaks or Cochlear implants → **PCV 13** → **8 weeks** → **PPSV 23**

IPAC Immunization Practices Advisory Council | New Mexico Immunization Coalition | Quality Improvement Organizations – Sharing Knowledge. Improving Health Care. Centers for Medicare & Medicaid Services | HealthInsight

A JOINT MEMORIAL

REQUESTING ALL STATE PRIVATE AND PUBLIC HIGH SCHOOLS, COLLEGES AND UNIVERSITIES TO PROVIDE INFORMATION TO ALL STUDENTS AND PARENTS ABOUT MENINGOCOCCAL DISEASE, EXPLAINING THE DIFFERENT DISEASE SEROGROUPS, SYMPTOMS, RISKS, VACCINES AND TREATMENTS.

Meningococcal B

Mortality 10 to 15%

Morbidity 19% of survivors

- loss of limb(s)
- deafness
- brain damage
- seizures
- spasticity/ paralysis

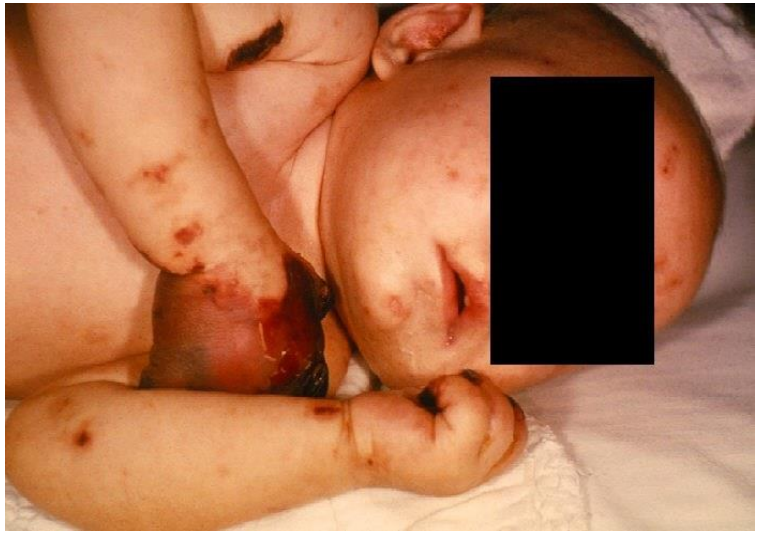


Photo from CDC

Meningococcal B Vaccines

$4,100,000

Cost per QALY

ACIP June 2014, ACIP 2015

QALY

- Haemophilus B vaccine in kids cost saving
- Shingle vaccine at age 60 $80,000 per QALY
- PCV at age 65 $62,065 per QALY
- UK £50,000 per QALY

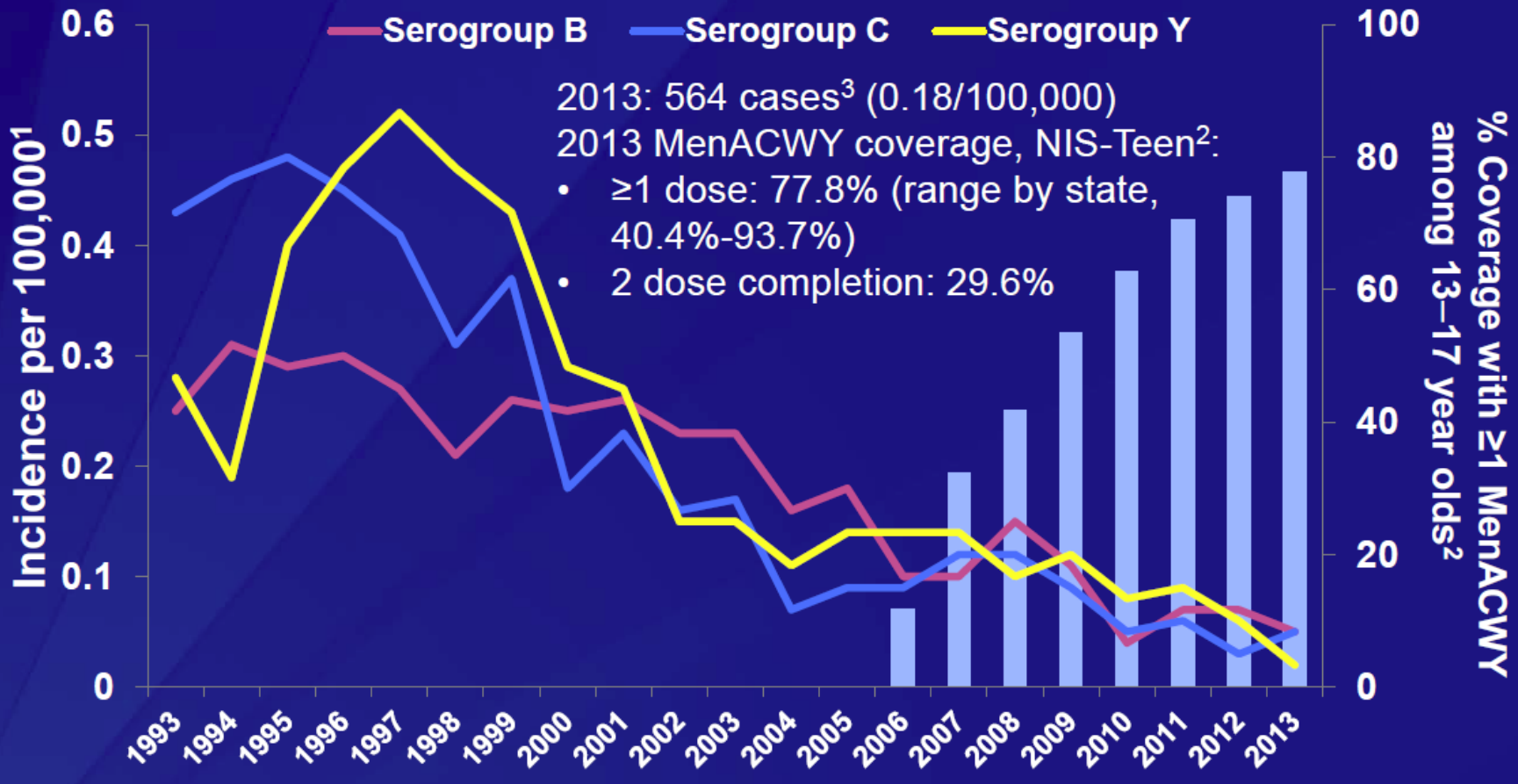
Meningococcal B Vaccines

$4,100,000

Cost per QALY

ACIP June 2014, ACIP 2015

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



[1]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 Vaccines

- Meningococcal Polysaccharide Vaccine
- Meningococcal Conjugate Vaccine
- Meningococcal B Vaccines

Meningococcal Polysaccharide Vaccine

Menommune®

licensed ≥56

1 year or less

Meningococcal Conjugate Vaccine

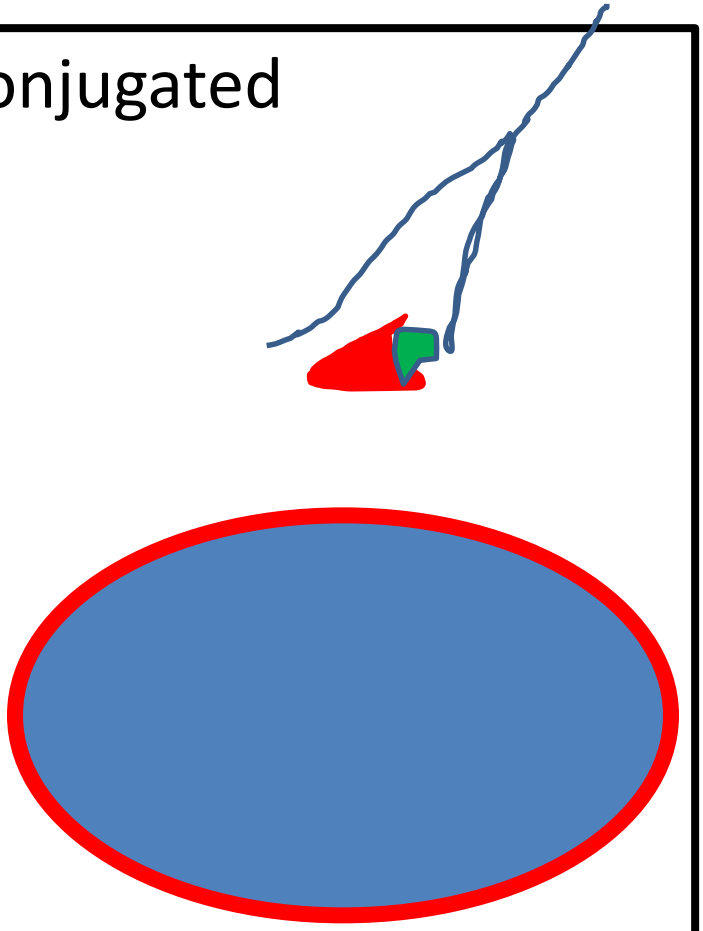
ACWY strains

Recommendation for Age 11-18 + booster age 16

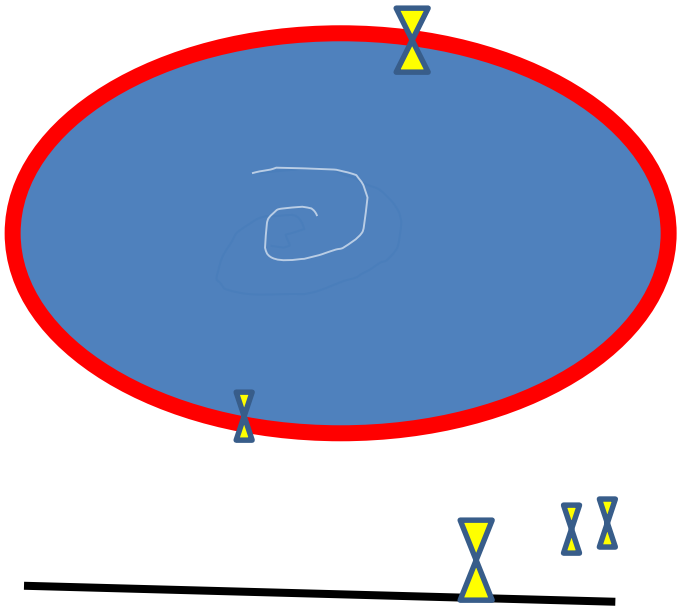
High risk > 2 months

Men ACWY versus Men B

- Conjugated



- Meningococcal B



Meningococcal B Vaccine:

MenB-FHbp (Trumenba®, Pfizer) Bivalent

3-dose series

115.75 X3 = $ 347.25

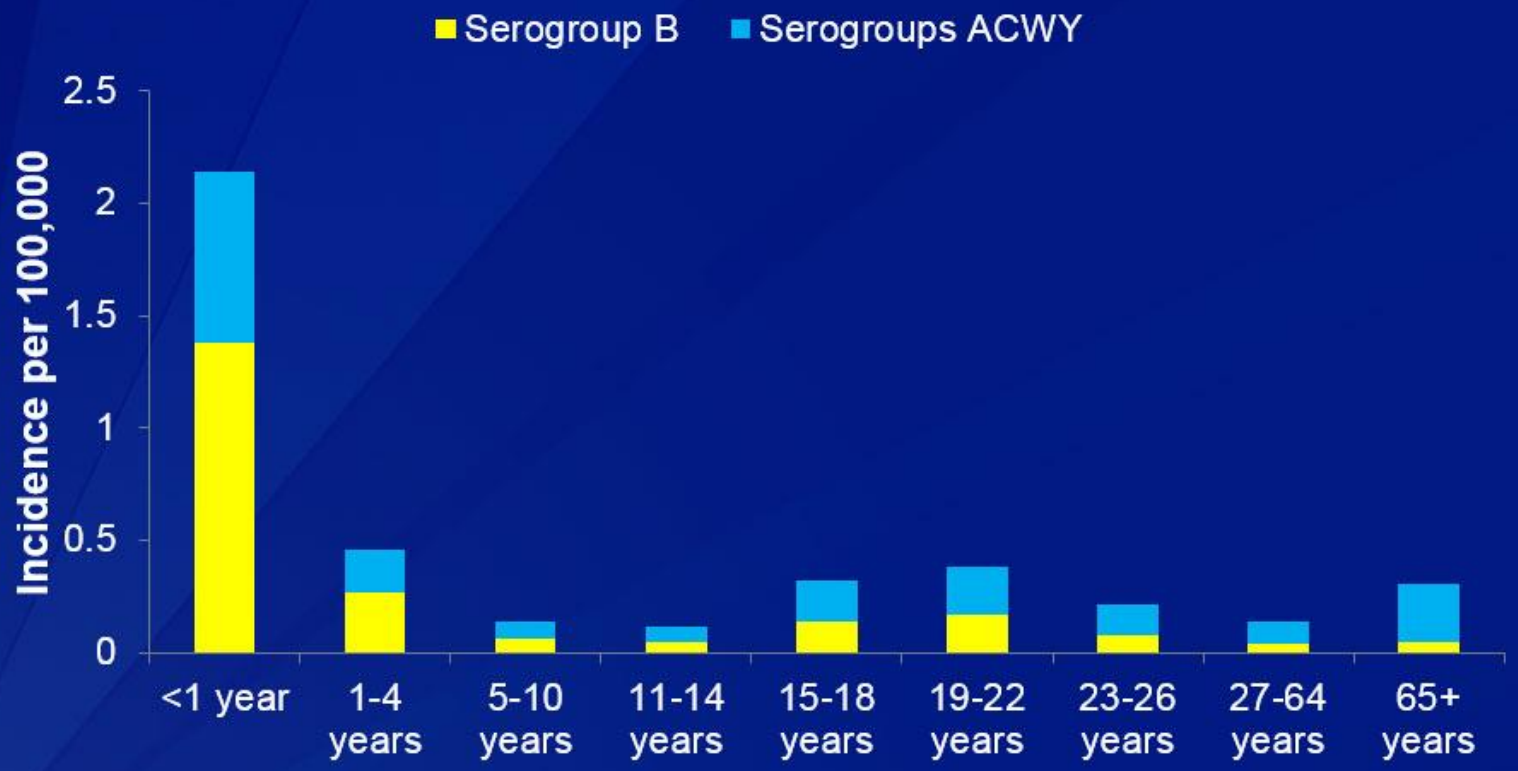
MenB-4C (Bexsero ®, Novartis) 4 Valent

2-dose series

$160 X2= $ 320

MacNiel ACIP June 2015 CDC Adult Vaccine Price List 2015

Meningococcal Incidence by Serogroup and Age-Group, United States, 2005-2013



SOURCE: CDC. National Notifiable Diseases Surveillance System with additional serogroup data from Active Bacterial Core surveillance and state health departments.

Unknown serogroup (25%) and other serogroups (8%) excluded

Men B vaccine series aged ≥10 years at increased risk (Category A)

- Complement component deficiencies
- Anatomic or functional asplenia (including sickle cell disease)
- Microbiologists exposed to *N. meningitidis*
- During Outbreaks

ACIP Category B

A serogroup B meningococcal vaccine series may be administered to adolescents and young adults 16-23 years of age to provide short term protection against most strains of group B meningococcal disease.

Burden of Disease

CDC Estimated Annual Meningococcal B Cases in 11-24 year olds

Cases	Deaths	Sequelea
54-67	5-10	5-13

MacNiel ACIP June 2015

Vaccine Efficacy

Immunogenicity Studies

Serum bactericidal activity using human complement (hSBA)

MenB-4C 63-94%

MenB FHbp 83.9%

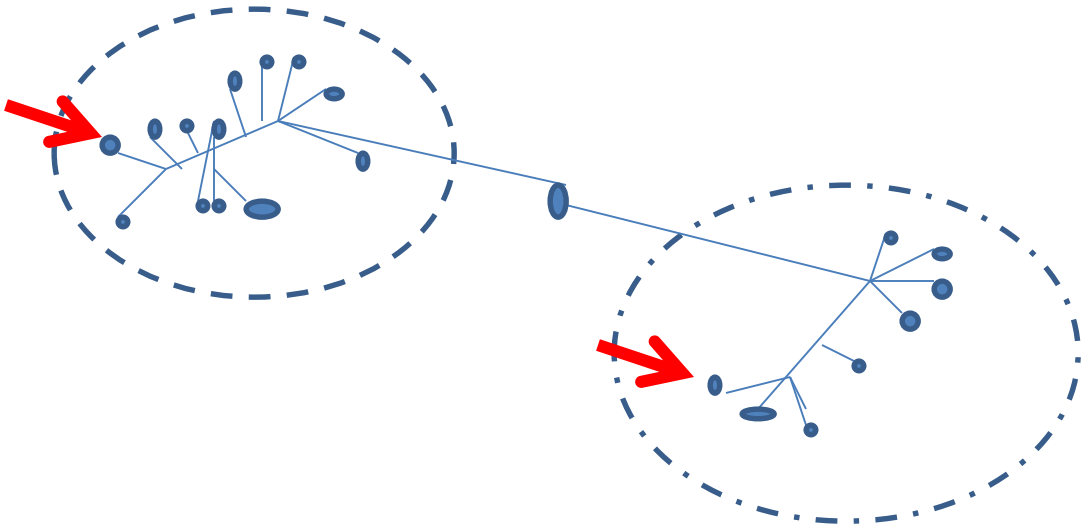
MacNiel ACIP June 2015

Waning Immunity

- MenB-4C: 66% 11 months after 2nd dose
- MenB-FHbp : 40-60% 6 months after 3rd dose,

MacNiel ACIP June 2015

Strain Coverage



Men B safety

Factor H binding protein

Animals:

- Antibodies cross react with Human Factor H
- Are antibodies to human factor H generated in humans?

Rate of autoimmune disease not higher than expected

Theoretically, onset of autoimmune-disease-related symptoms could be delayed

MacNiel ACIP June 2015, MMWR 2015

Men B vaccine Safety

MenB-4C

rhabdomyolysis, anaphylaxis, fever

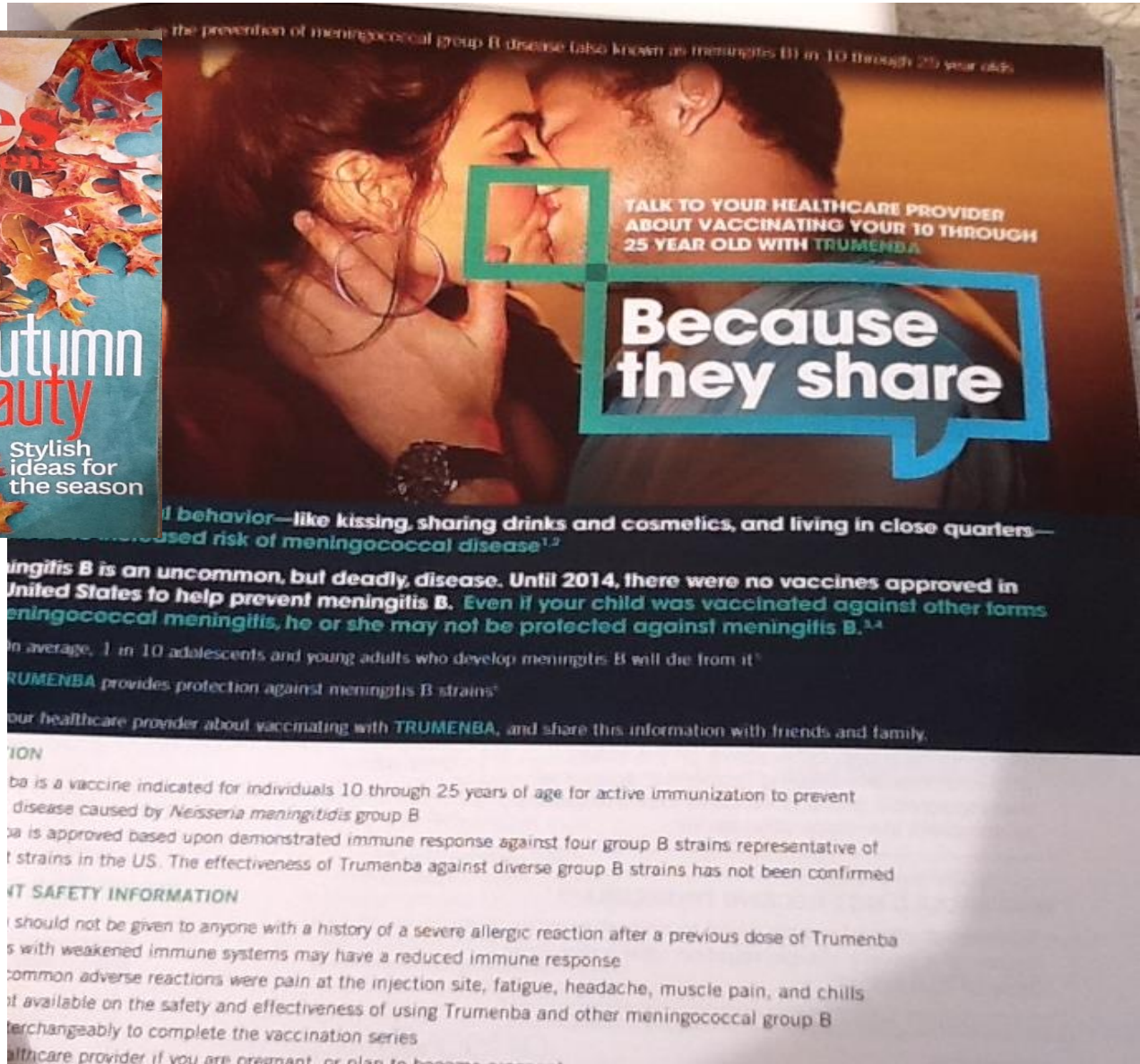
Men B-FHbp

Pyrexia, vomiting, vertigo, chills, headache, anaphylaxis, neutropenia

MacNiel ACIP June 2015

Marketing


Better Homes and Gardens
OCTOBER 2015
BHG.COM
WARM AUTUMN COLORS FOR YOUR WALLS p.66
BACKYARD FOR ALL SEASONS p.100
BRING INNOVATION HOME! WAYS TO LIVE SMARTER p.61
autumn beauty
Stylish ideas for the season


TALK TO YOUR HEALTHCARE PROVIDER ABOUT VACCINATING YOUR 10 THROUGH 25 YEAR OLD WITH TRUMENBA
Because they share
behavior—like kissing, sharing drinks and cosmetics, and living in close quarters—
risk of meningococcal disease[1,2]
ingitis B is an uncommon, but deadly, disease. Until 2014, there were no vaccines approved in United States to help prevent meningitis B. Even if your child was vaccinated against other forms eningococcal meningitis, he or she may not be protected against meningitis B.[3,4]
n average, 1 in 10 adolescents and young adults who develop meningitis B will die from it[5]
RUMENBA provides protection against meningitis B strains[6]
our healthcare provider about vaccinating with TRUMENBA, and share this information with friends and family.
ION
ba is a vaccine indicated for individuals 10 through 25 years of age for active immunization to prevent disease caused by Neisseria meningitidis group B
a is approved based upon demonstrated immune response against four group B strains representative of strains in the US. The effectiveness of Trumenba against diverse group B strains has not been confirmed
NT SAFETY INFORMATION
should not be given to anyone with a history of a severe allergic reaction after a previous dose of Trumenba
s with weakened immune systems may have a reduced immune response
common adverse reactions were pain at the injection site, fatigue, headache, muscle pain, and chills
t available on the safety and effectiveness of using Trumenba and other meningococcal group B
terchangeably to complete the vaccination series
althcare provider if you are pregnant, or plan to

Patient Education

Pros

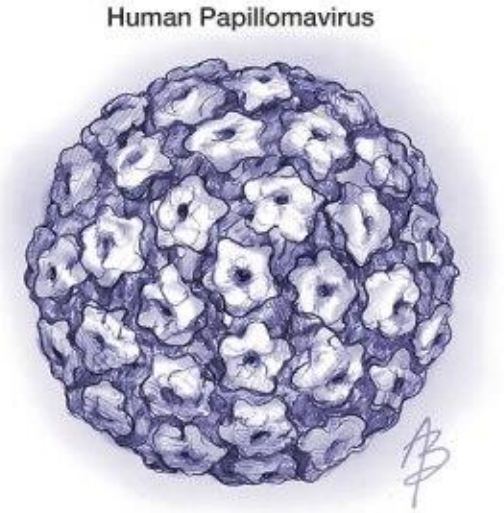
- If you got Men B you would likely die or be disabled
- The disease rate could go up
- The CDC will monitor the safety
- Insurance covers the vaccine
- It is the only vaccine we have against this type of meningitis

Cons

- The disease is very rare and seems to be getting rarer
- There may be side effects from the vaccine
- The vaccine is expensive
- We do not know how well the vaccine works in protecting people-it does not cover all strains and is not 100% effective
- It looses its effectiveness over time

Up dates

Should HPV9 Replace HPV4?



Human Papillomavirus

- 40+ Types in Humans
- 12 considered carcinogenic

  16, 18 plus 10 more
- HPV 6 or 11 cause 90% of anogenital warts (condylomata)

Erickson, Am J Obst & Gyn 2013

ACIP

- Routine HPV vaccination at age 11 or 12 years.
- Can start at age 9 years.
- Recommended for females aged 13-26 and males 13-21 years who have not been vaccinated previously or who have not completed the 3-dose series.

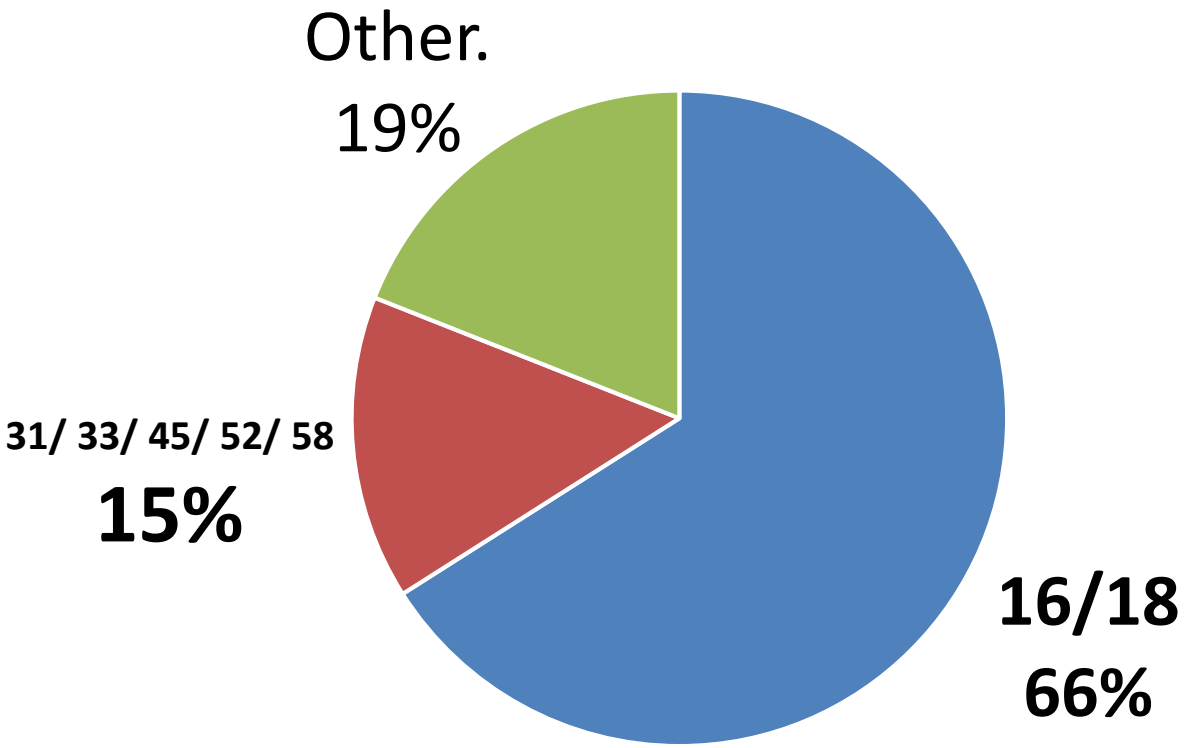
MMWR / March 27, 2015 / Vol. 64 /
No. 11

Vaccine	Coverage	Cost per dose
HPV 2 *Cervarix®*	16/18	$128.75
HPV 4 *Gardasil 4®*	6/11 /16/18	$160.70
HPV 9 *Gardasil 9®*	6/11/16/18 31/33/ 45/ 52/58	$177.70

Erickson, Am J Obst & Gyn 2013
CDC Vaccine price list

HPV Types

Cervical Cancer



Erickson, Am J Obst & Gyn
2013

HPV Attributable Cancers in US

Caner	HPV 16/18 %	HPV 31/33/ 45/ 52/58
vaginal	55	18
vulvar	49	14
penile	48	9
anal male	79	4
anal female	80	11
oral male	63	4
oral female	51	9

Saraiya JNCI 2015

Repeat HPV 9 after HPV4 series ?

- $117,400–$156,000 per QALY
  - –Not cost effective
  - –Only benefit to females
  - –No safety concerns
  - –Only serologic evidence for benefit

- “effort toward raising the HPV9 rates in those who have not completed the series instead of giving additional doses”

MMWR March 2015

Series Started with HPV 4 or HPV2

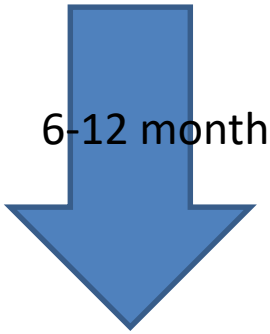
- Continue with HPV9
- No additional doses

MMWR March 2015

How many doses of HPV?

9-15 years
Immunocompetent

Dose 1



Dose 2

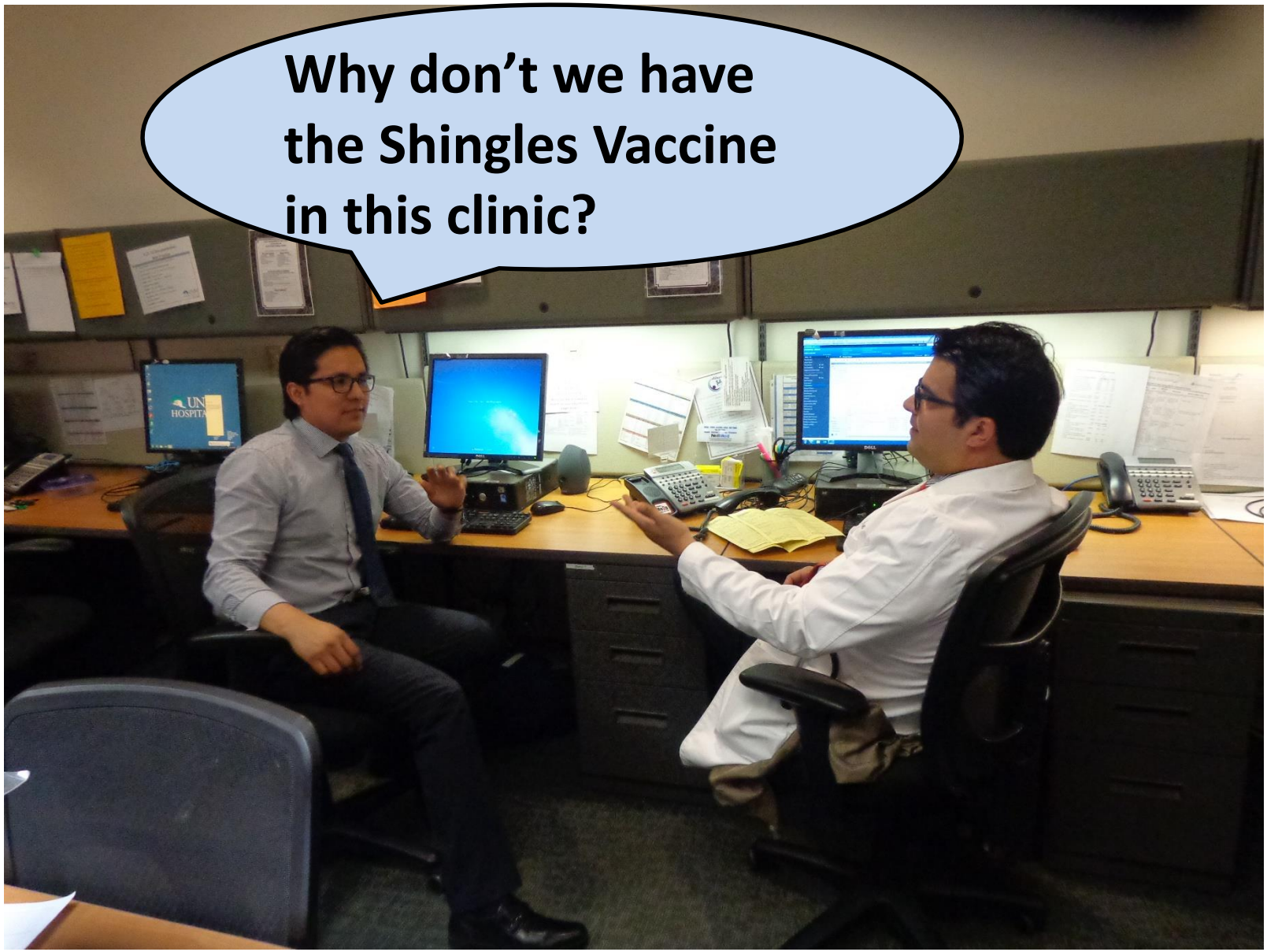
15 years or more
Immunocompromised

Dose 1

Dose 2

Dose 3

What if Molly was pregnant?


Why don’t we have the Shingles Vaccine in this clinic?

Shingles (Zostavax®)

- Covered as pharmacy benefit not as a medical benefit
- Cost $212

- FDA age 50 ACIP age 60

New Shingles Vaccine

HZV (Zostavax®)

- Herpes Zoster

Efficacy 51.3%

4 years duration

- Post Herpetic Neuralgia

Efficacy 66.5%

HSV Sub unit/adjuvant

- Herpes Zoster

Efficacy 89.9% (over 70)

3.7 years and going

- Post Herpetic Neuralgia

Efficacy 89%

N Engl J Med. 2015;372:2087-96

N Engl J Med. 2016;375:1019-32.

N Engl J Med 2005; 352: 2271-84.

HZV sub unit

- More reactions:

Vaccine 79.0% Placebo 29.5%

- 2 Doses
- Questions
  - Price
  - Previous HZV
  - Long term duration and safety

N Engl J Med. 2016;375:1019-32.

Summary

- Flu and Pneumo for hospitalized over 65
- Men B Vaccines-Still a lot of unknowns/very expensive
- Pneumococcal –use two vaccines in select adults
- High dose flu-a little better immunity in over 65 but standard dose okay
- New: 2 dose HPV under 15
- New zoster vaccine….

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