Red Book Update 2014

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Financial Disclosure

Michael T. Brady, M.D.

In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in this presentation.

Routine Immunizations: Paraguay & United States

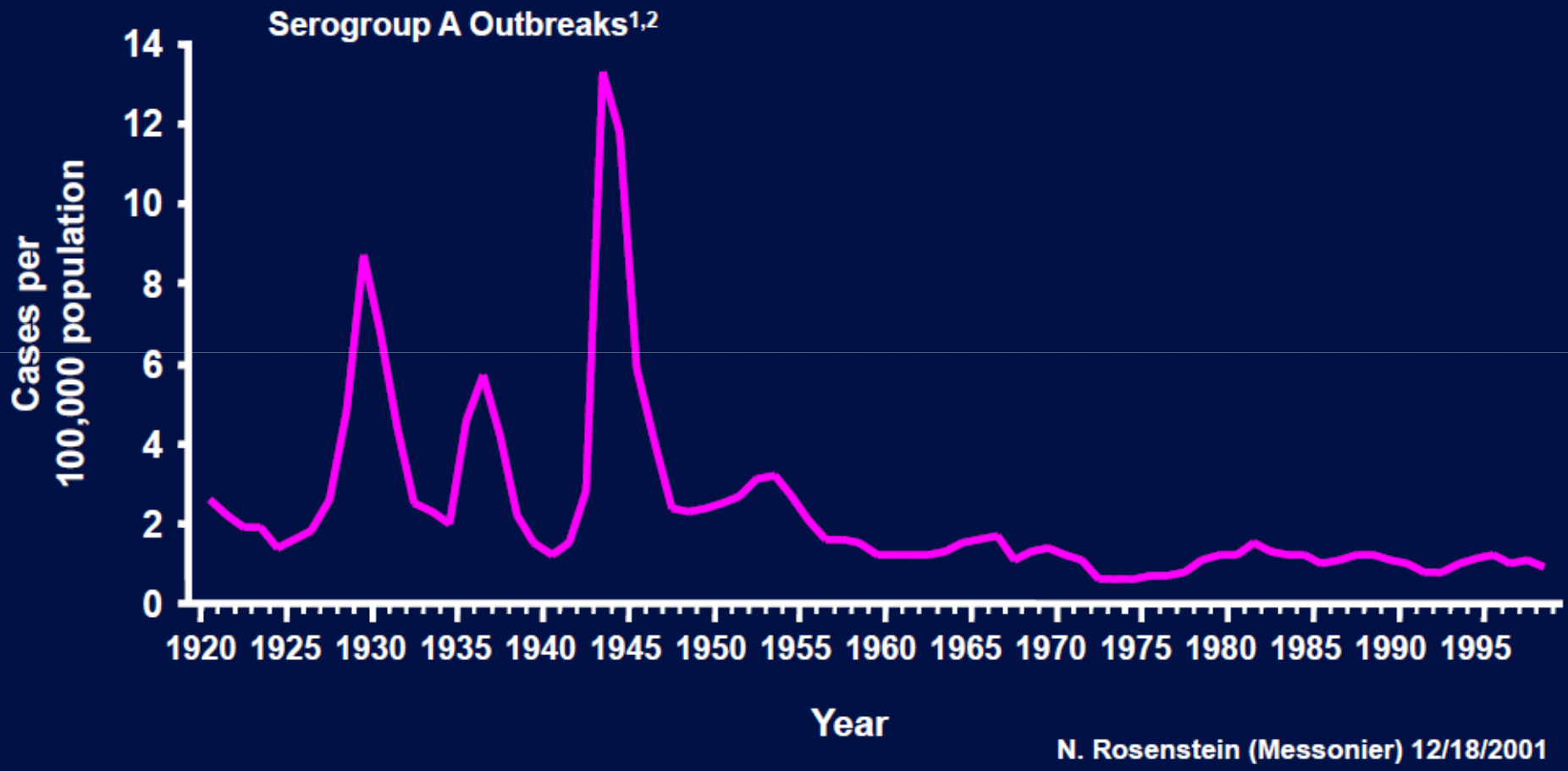
Vaccine	Paraguay	US
BCG	Yes	No
Hepatitis VB	Yes (NB and risk groups)	Yes (NB)
Diphtheria	Yes	Yes
Tetatius	Yes	Yes
Pertussis	Yes	Yes (acellular)
Hib	Yes	Yes
Rotavirus	Yes (Rotarix)	Yes (Rotarix & Rotateq)
Polio	Yes (OPV)	Yes (IPV)
Pneumococcus-conjugate	Yes	Yes
Measles	Yes	Yes
Mumps	Yes	Yes
Rubella	Yes	Yes

Routine Immunizations: Paraguay & United States (cont'd)

Hepatitis A	No	Yes
Varicella	No	Yes
Yellow Fever	Yes: Border areas	No
HPV	No	Yes
Meningococcal (A,C,W;Y)	No	Yes: Adolescents & Risk Groups
Tdap	No	Yes
Influenza	Yes: 6-35 m; pregnant women; risk groups	Yes->6 months; pregnant women
Typhoid Fever	No	No
*2012 PAHO data		

Meningococcal Vaccines

Meningococcal Disease – By Year, United States, 1920-1998

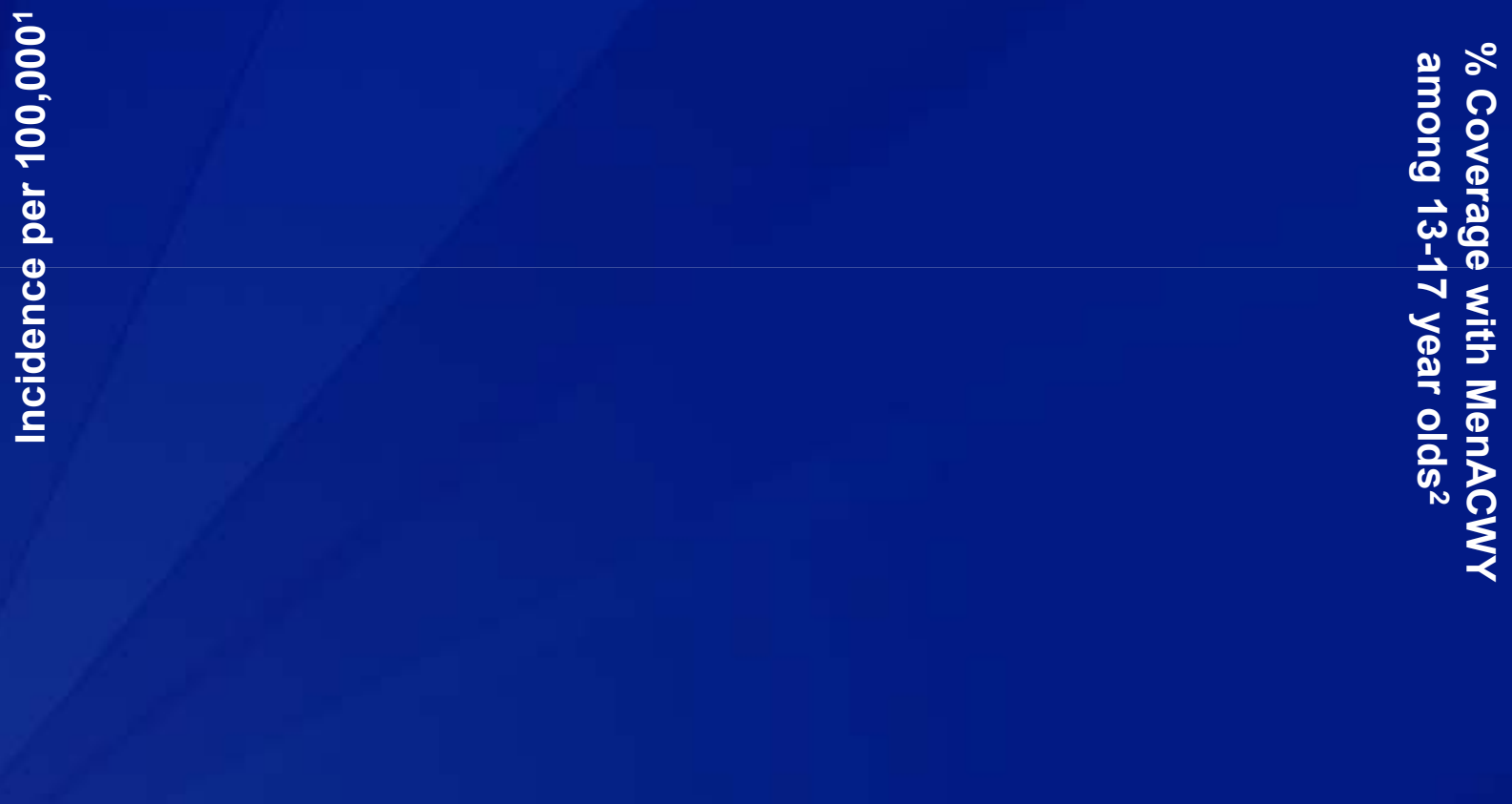


N. Rosenstein (Messonier) 12/18/2001

CDC
Centers for Disease Control and Prevention

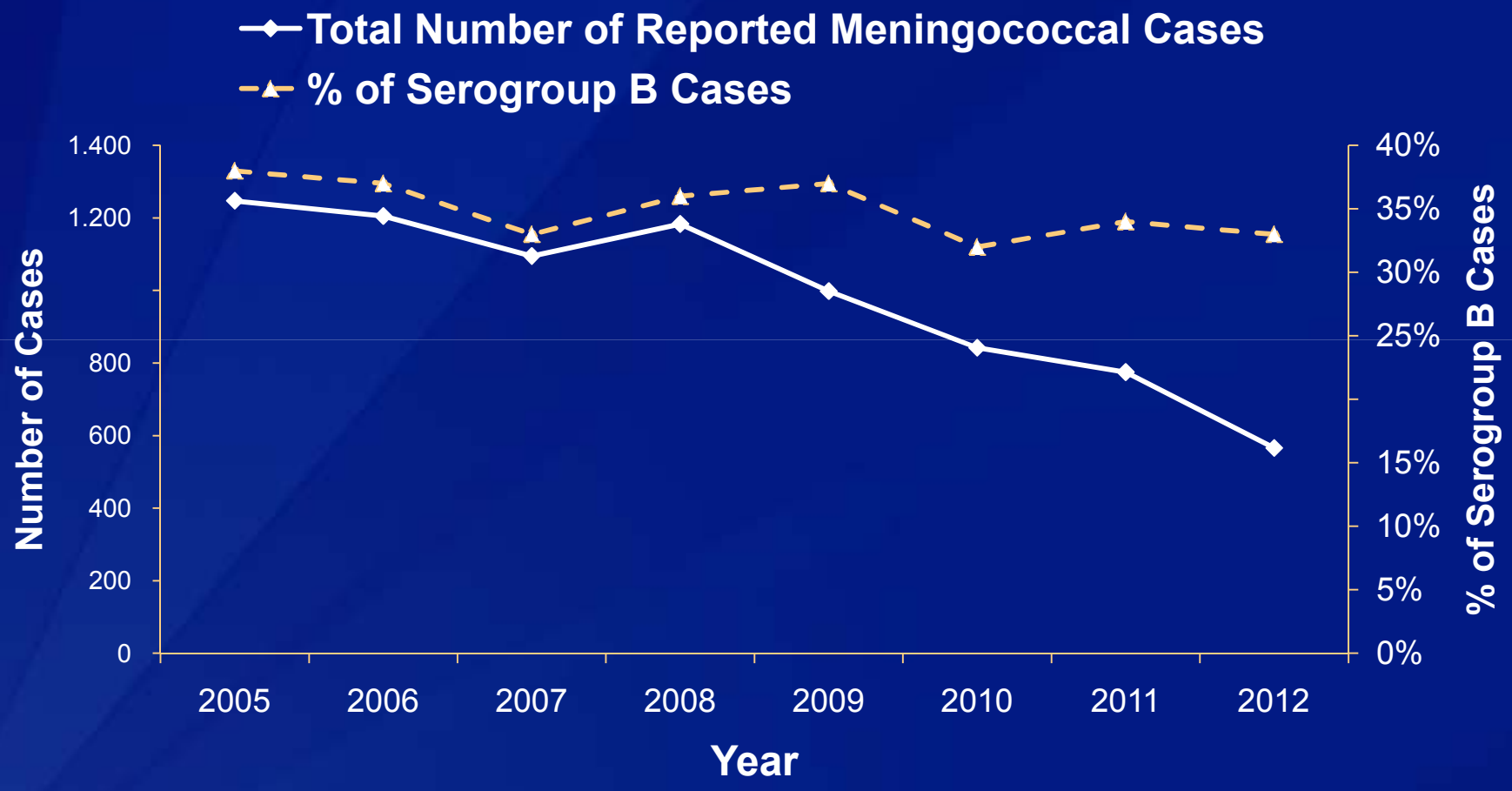
1. Branham S. Serological relationships among meningococci, Bacteriol Rev 1953
2. Hedrich A. Recent trends in meningococcal disease, Public Health Reports 1952

Incidence by Serogroup and Vaccine Coverage, United States, 1993-2012



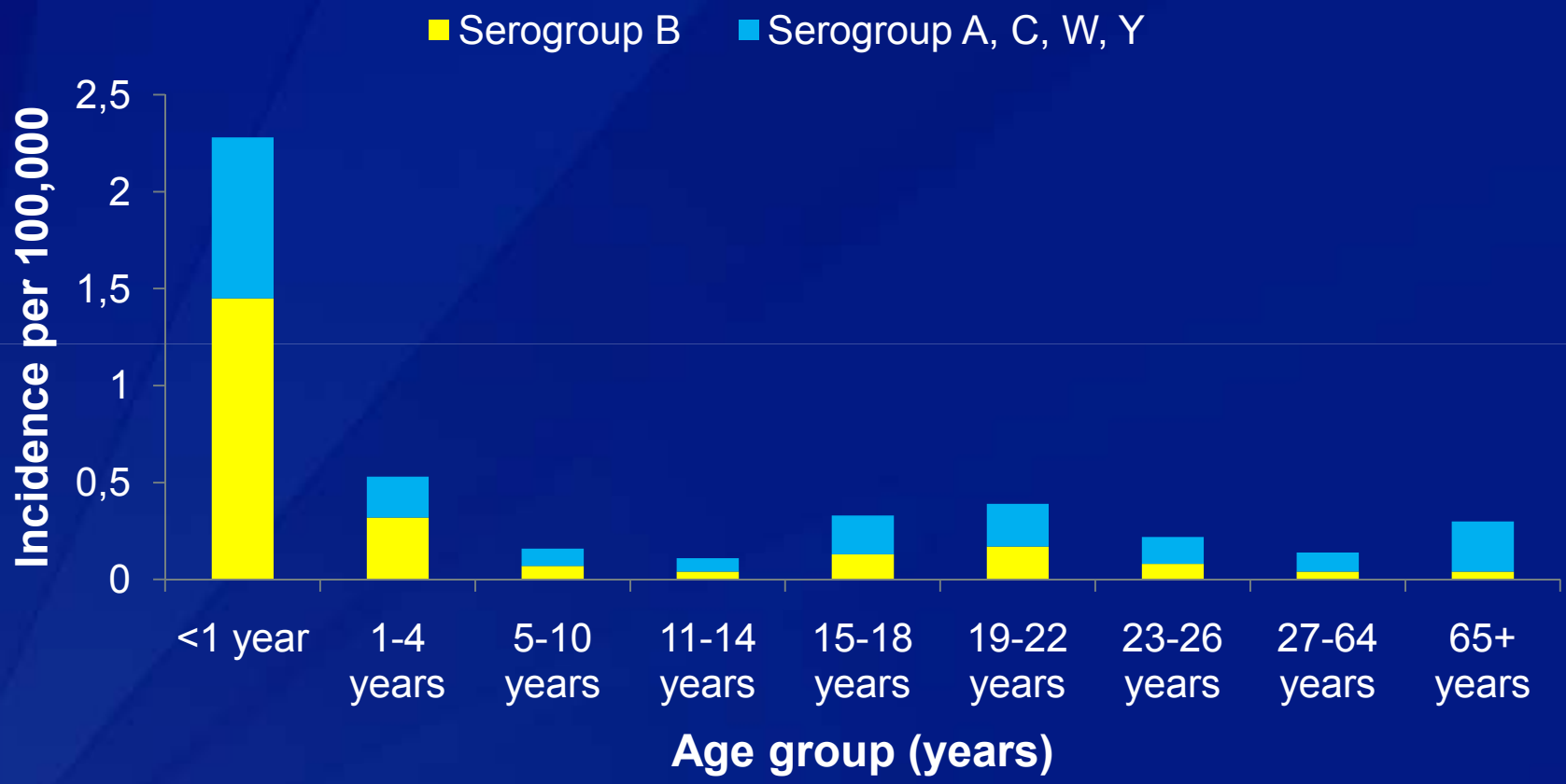
[1]Source: ABCs cases from 1993-2012 estimated to the U.S. population with 18% correction for under reporting
[2]National Immunization Survey – Teen; 2006-2012

Serogroup B Meningococcal Disease – United States 2005-2012



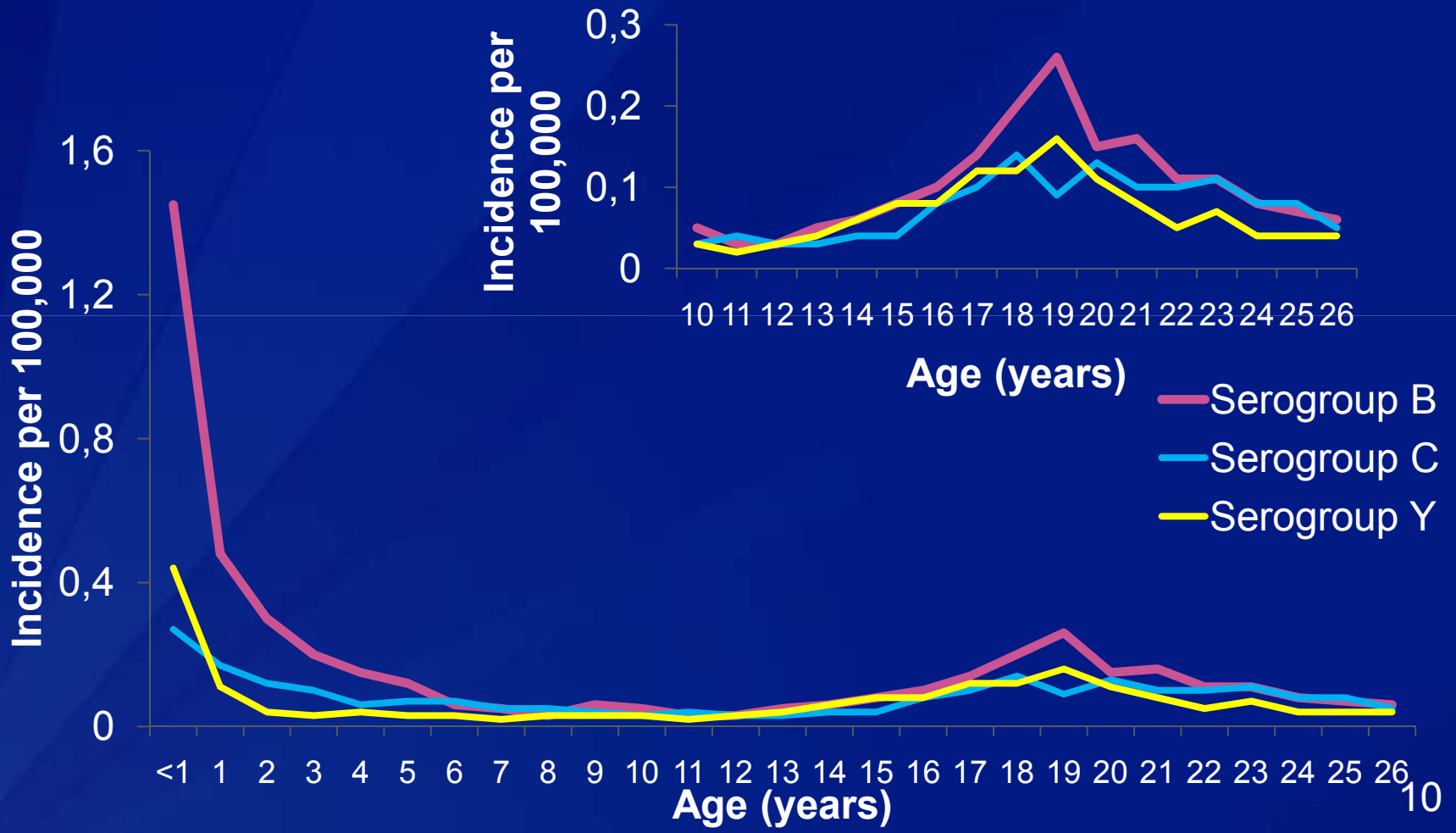
Source: National Notifiable Diseases Surveillance System (NNDSS)
Additional serogroup data provided by state and local health departments; % of serogroup B cases out of cases with known serogroup

Incidence by Serogroup* and Age-Group, United States, 2005-2012



*NNDSS data with additional serogroup data from ABCs and state health departments. Unknown serogroup excluded (23%)

Incidence of Meningococcal Disease by Age and Serogroup, United States, 2005-2012



Case-Fatality Ratio by Serogroup and Age-Group, United States, 1997-2011

Serogroup	<5 years	5-10 years	11-19 years	20 years	Total
B	4%	22%	15%	23%	13%
C	13%	9%	12%	16%	13%
Y	0%	13%	13%	12%	10%
W	<1%	0%	0%	10%	7%
Total	5%	12%	15%	15%	12%

ABCs cases from 1997-2011 estimated to the US population

Meningococal Disease in Paraguay

- **0.1 cases per 100,000 population**

  (similar rates in Boliva, Peru & Mexico; 2.0 per 100,000 population in Brazil)
- **Serogroups:**
  - **C-44%**
  - **B-29%**
  - **W-20%**
  - **Y-5%**
- **Rates highest in infants ≤ 9 mos of age**

Safadi M J Pediatr Infee Dis Soc-online April 25, 2014

Meningococcal Vaccines for Infants and Toddlers

- **MCV4-D (Menactra–Sanofi)**
  - **2 dose series at 9 & 12-15 mo**

    (FDA approved April 2011)
  - **Co-administration with pneumococcal conjugate vaccine → decreased antibody responses to some pneumococcal serotypes**
- **HibMenCY-TT (GSK)**
  - **3 dose priming (2,4,6m) + 12-15 mo booster**

    (FDA approved June 2012)
- **MCV4-CRM (Menveo –Novartis)**
  - **3 dose priming (2,4,6m) + 12-15 month booster**

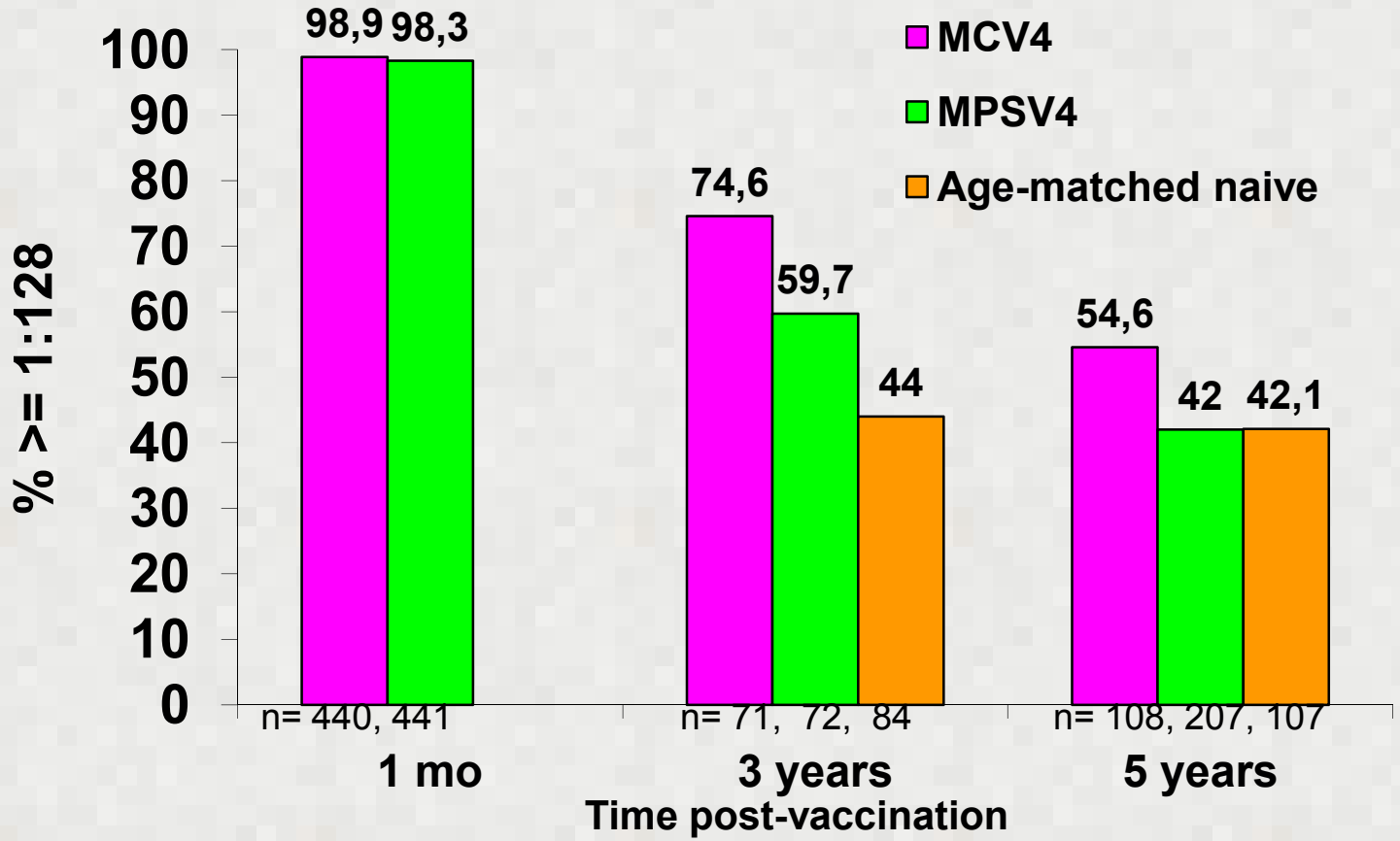
    (FDA approved June 2013)

Average Annual Cases of Meningococcal Diseases in Children <5 years, 2001-2010

Age	Serogroup B	Serogroup C	Serogroup Y	Serogroup C + Y
				(Incidence)
0-2 months	38	4	9	13 (1.3)
3-5 months	30	2	12	14 (1.4)
6-8 months	22	4	9	13 (1.3)
9-11 months	15	6	3	9 (0.9)
1 year	27	9	2	11 (0.3)
2 years	20	8	4	12 (0.3)
3 years	9	4	2	6 (0.2)
4 years	5	4	3	7 (0.2)
Total	166	41	44	85 (0.40)
58 of 251 (23%) of cases prevented				

ABCs cases from 2001-2010 and estimated to the U.S. population (2010 data provisional)

SBA-BR seroresponse ≥1:128 post-vaccination, serogroup C in Adolescents



*Data courtesy of sanofi pasteur, 3 year follow-up of MTA02 (11-18 year-olds), 5 year follow-up of 603-02 (2-10 year-olds)

Breakthrough Cases in Adolescents

- 14 breakthrough cases identified during 2005-2008 (used for VE analysis)
- 7 additional cases identified so far in 2009 and 2010
  - In process of confirming cases and vaccination histories
  - 2 CO, 1 OR, 1 MN, 2 WI, and 1 IN
- Illness in breakthrough cases was not attenuated but similar morbidity/mortality as seen in those who never received vaccine

MMWR 2011;60:72-76

Adolescent Meningococcal Vaccine: Concerns with Current Recommendations

- Antibodies wane prior to peak incidence of disease
- Breakthrough cases are as severe as in those who never received vaccine
- Anamnestic response occurs but is not rapid enough to prevent invasive disease (7-10 days)

Children at Increased Rick for Meningococcal Disease

- **Persistent complement component deficiencies (C3, C5-C9, Properdin, Factor D and Factor H)**
- **Functional or anatomic asplenia**
- **Travel to or reside in an area with hyperendemic or epidemic meningococcal disease**
- **Residence in a community with a meningococcal outbreak**

Recommended Meningococcal Vaccines by Age Group

Age group	MenACWY-D (Menactra)	MenACWY-CRM (Menveo)	HibMenCY-TT (MenHibrix)
2 months – 10 years	• Not routinely recommended in this age group • Recommended for persons at increased risk starting at age 9 months • For children with asplenia this vaccine should be postponed until pneumococcal vaccine series is complete	• Not routinely recommended in this age group • Recommended for persons at increased risk	• Not routinely recommended in this age group • Recommended for persons at increased risk up to age 18 months • Not appropriate if protection for serogroups A or W-135 is warranted.

Recommended Meningococcal Vaccines by Age Group

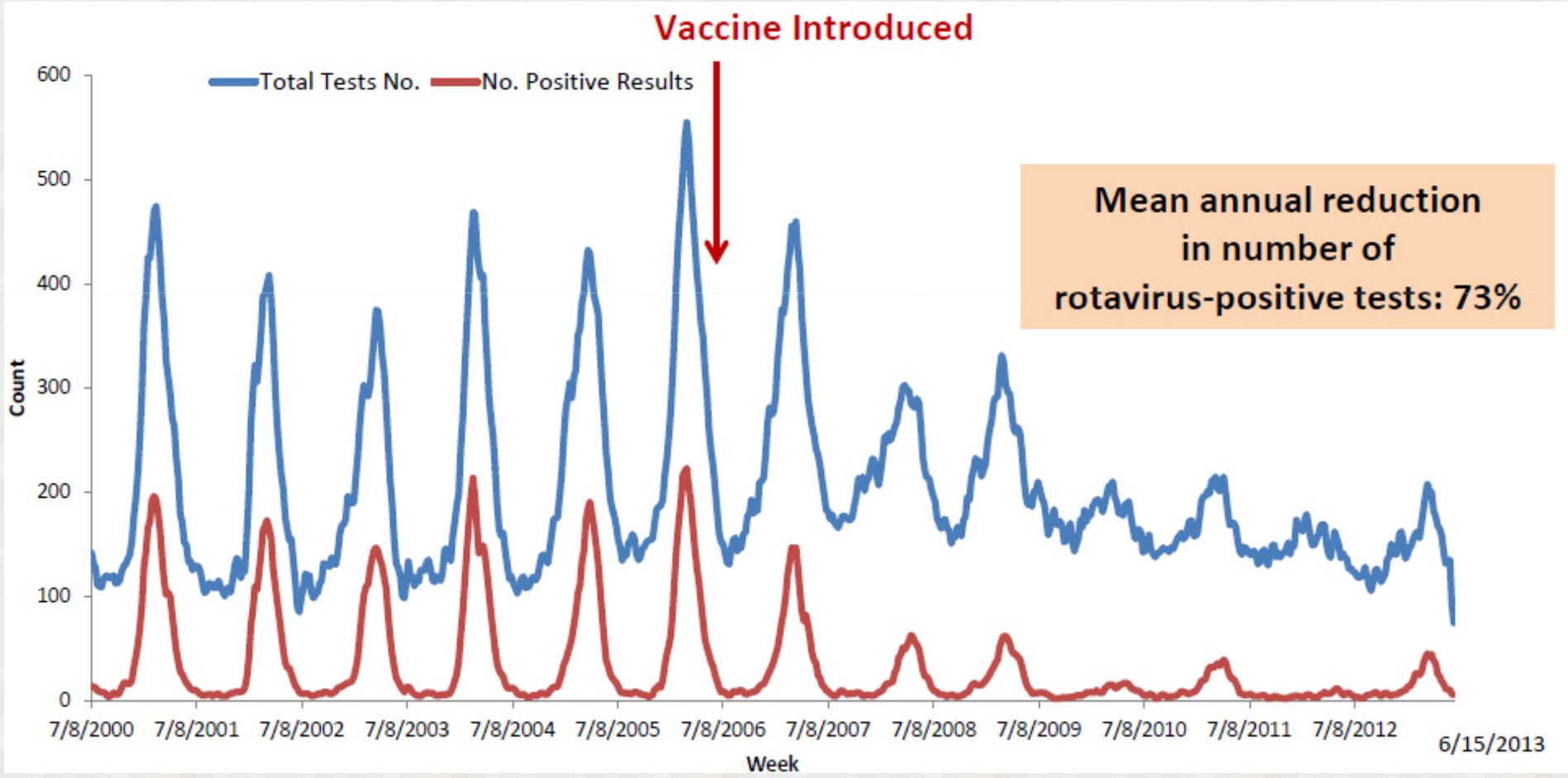
Age group	MenACWY-D (Menactra)	MenACWY-CRM (Menveo)	HibMenCY-TT (MenHibrix)
11-21 years	• Routinely recommended	• Routinely recommended	• Not approved in this age group

Rotavirus Vaccines

Recommendations
Overview of Ages and Intervals

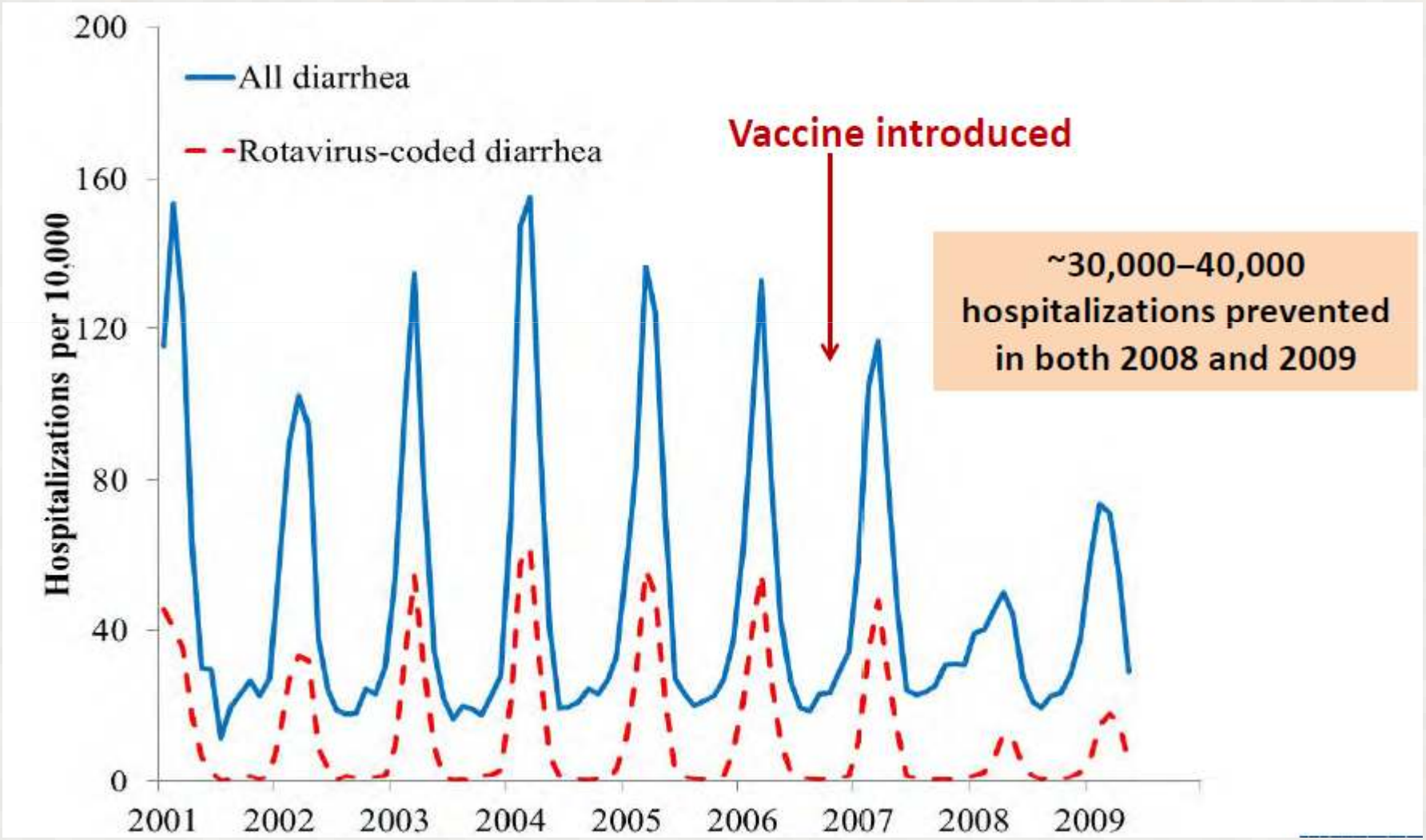
	RV1 (Rotarix®)	RV5 (RotaTeq®)
Number of doses in series	2	3
Recommended ages for doses	2 and 4 months	2, 4 and 6 months
Minimum age for Dose 1	6 weeks	
Maximum age for Dose 1	14 weeks (14 weeks 6 days)	
Interval between doses	4 weeks or more	
Maximum age for last dose	8 months, 0 days	

Rotavirus Tests at Reporting Laboratories
Number of tests and number of rotavirus-positive
July 2000-June 2013



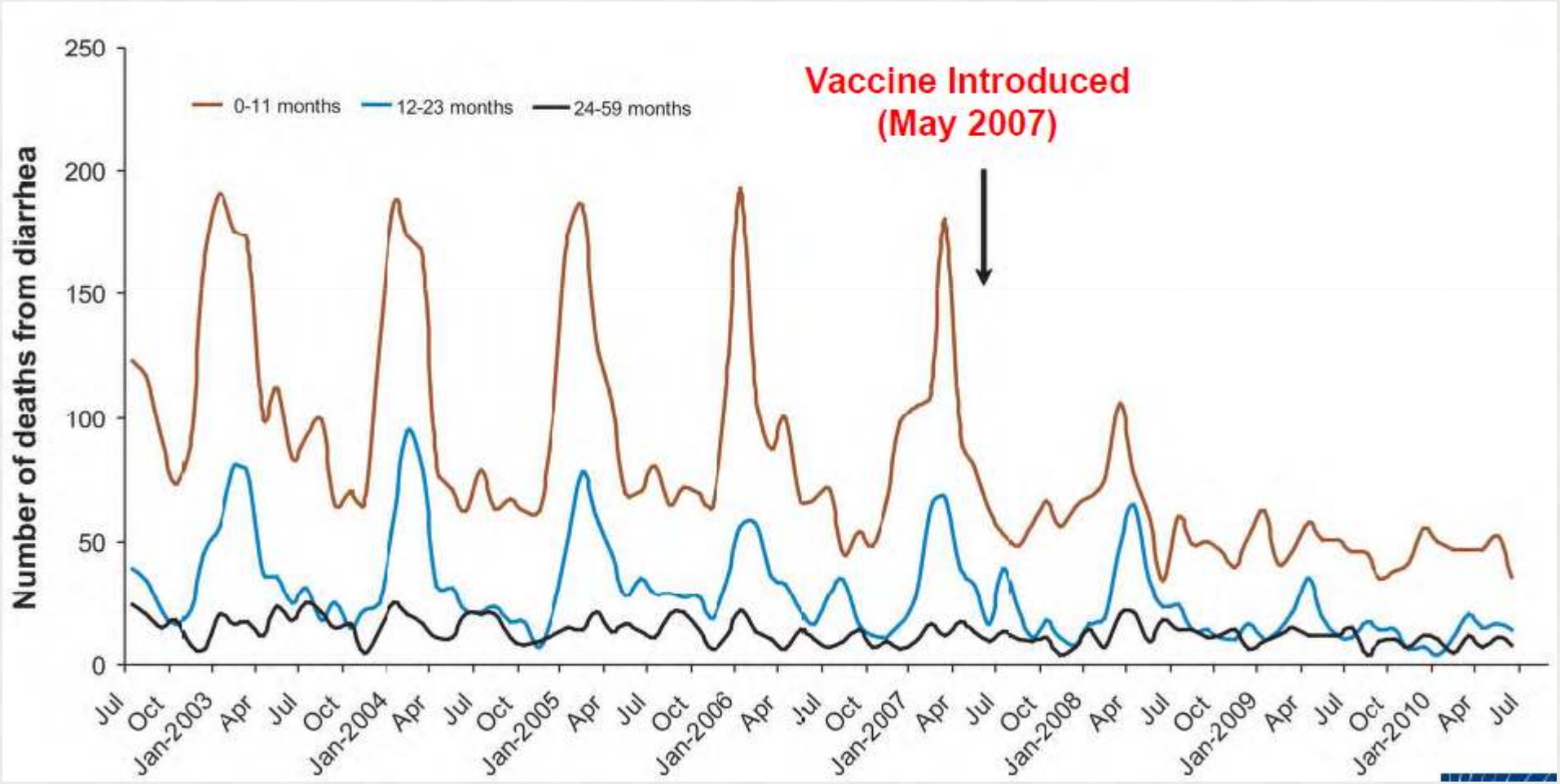
Tate J, Haynes A, Payne D, et al. *PIDJ* 2013; Tate J, et al, Preliminary

Hospitalization Data from MarketScan Database: Diarrhea and Rotavirus-coded Hospitalizations Children aged <5 yrs, 2001-2009



Cortes J, Curns A, Tate J, et al. *N Engl J Med* 2011

Large Reductions in Diarrhea Deaths after Vaccine Introduction in Mexico



Richardson VJ, et al *N Engl J Med* 2010; Richardson V, Parashar U, Patel M *N Engl J Med* 2011

Age-Specific Rotavirus Hospitalization Rate Reduction and Vaccine Coverage, NVSN

Age	Rotavirus vaccine coverage in 2008 (≥1 dose)	Decline in rotavirus hospitalization rate (2008 vs. 2006)
< 1 year	56%	66%
1 to < 2 years	44%	95%
2 to < 3 years	<1%	85%

Herd Immunity

Payne D et al. *CID* 2011

Rotavirus Vaccine: Evidence of Herd Immunity

- **Reductions in unspecified gastroenteritis hospital discharges in following age groups:**

0 – 4 years

5 – 14 years

15 – 24 years

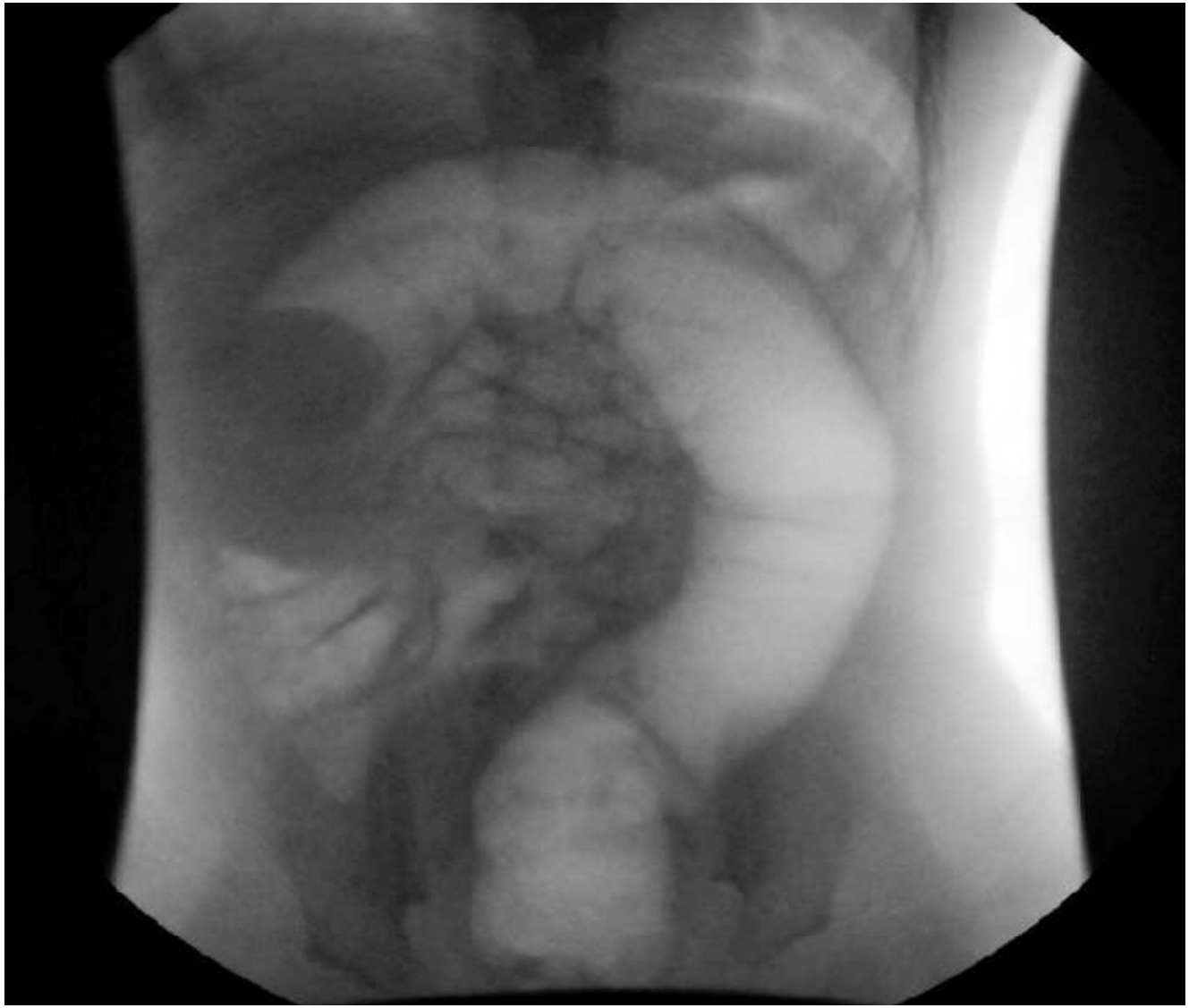
25 – 65 years

>65 years

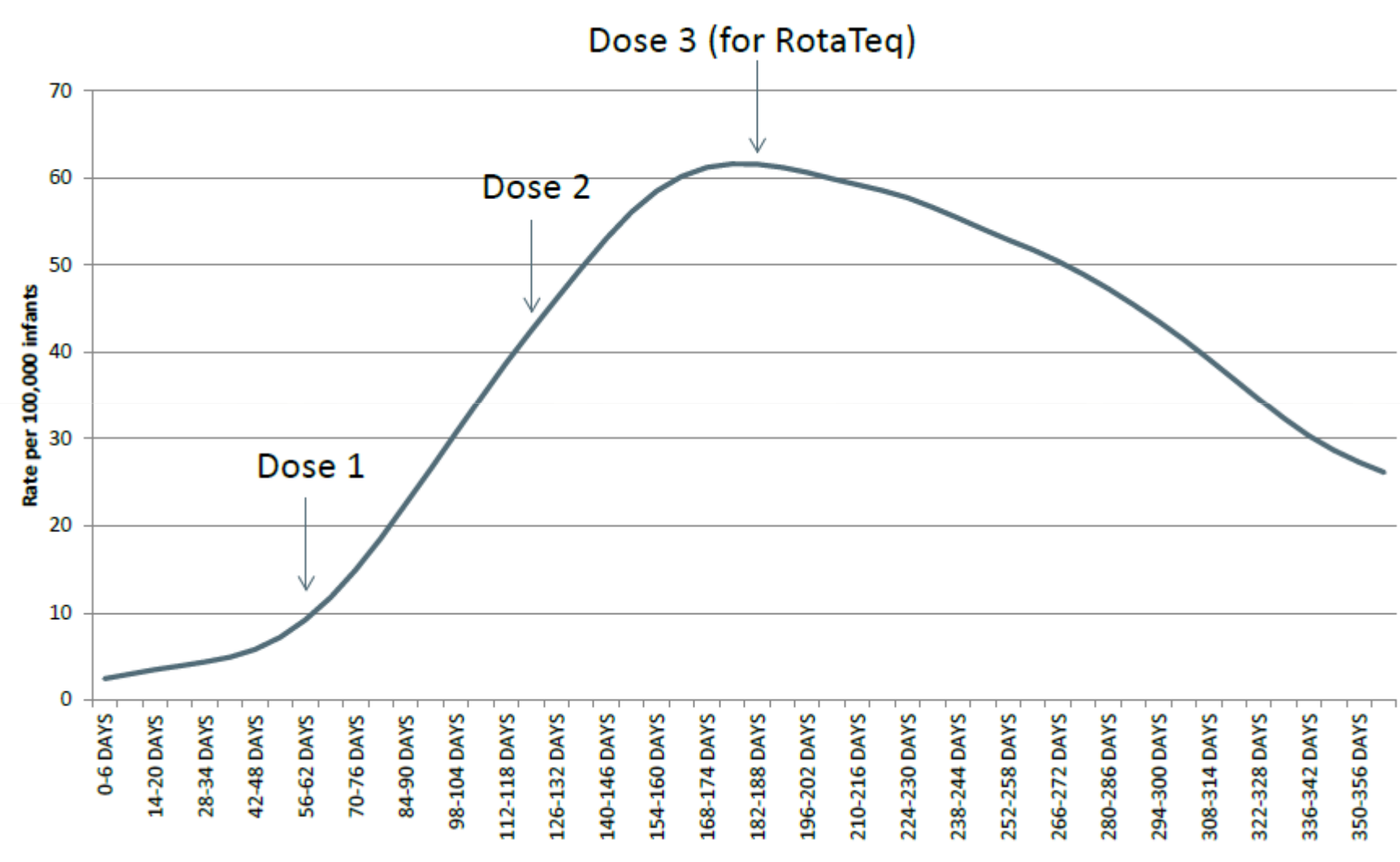
- **Greatest reductions in month of March**

Lopman BA, et al. *JID* 2011

X-ray showing ileocecal intussusception as it telescopes
into the ascending colon.



Intussusception incidence by age



Tate J, et al. Trends in IS hospitalizations… *Pediatrics* 2008;121(5):e1125-1132.

info@mini-sentinel.org

Intussusception Risk Following Rotavirus Vaccine in U.S.

Surveillance Activities

VAERS – CDC – Passive reporting by providers of adverse events (retrospective; causal relationship difficult to assess)

VSD – CDC – Active reporting from 9 managed care organizations in US (prospective; greater ability to assess causal vs. temporal relationship)

PRISM – FDA – Post-licensure surveillance

Rotavirus Vaccine and Intussusception

- Increased risk of intussusception in the immediate period following vaccination seen with original rotavirus vaccine – Rotashield
- Prelicensure studies with >70,000 children did not show evidence of increased risk of intussusception with either Rotatek (RV5) or Rotarix (R1)
- No increased signal in US – VAERS by 2010
  (Vaccine administered in US: RV5>>R1)
- Increased risk of intussusception noted in 7 days following RV1 administration in Mexico (1st dose only) and Brazil (second dose only)

Patel MM. *NEJM* 2011; 364:2283

Rotavirus Vaccine and Intussusception

Attributable increased annual impact of RV1 in Mexico and Brazil:

- **96 cases of intussusception**
- **5 deaths**

Annual Benefit of RV1 in Mexico and Brazil:

- **80,000 fewer hospitalizations due to rotavirus**
- **1,300 fewer deaths due to rotavirus**
- **? reduction in intussusception 7 days after vaccine**

Patel MM. *NEJM* 2011; 364:2283

Intussusception Risk Following Rotavirus Vaccine in U.S.

- **Preliminary estimates based on the 3 surveillance systems**
  - **1 increased case of intussusception following rotavirus vaccine per 20,000 to 100,000 children**
  - **1st dose >> 2nd >> 3rd dose**
  - **Most cases of intussusception possibly related to vaccine occur 3 to 7 days after the vaccine is administered**
  - **Rotarix (RV1) > Rotateq (RV5) (not statistically significant)**

Intussusception Risk Following Rotavirus Vaccine in U.S.

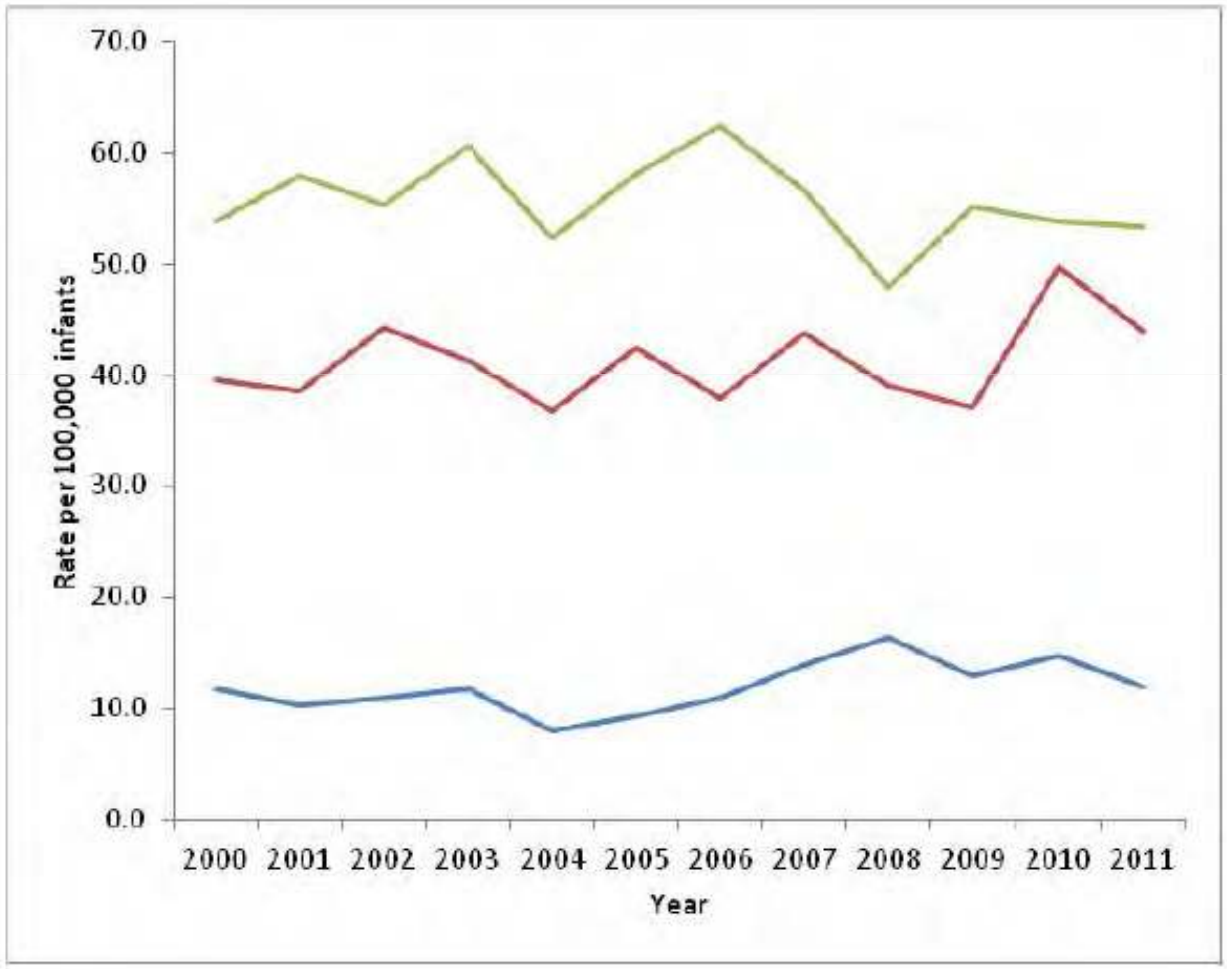
- **Slight increase intussusception in 8-11 week old infants since availability of new rotavirus vaccines**

- **No increase in intussusception at a population level in children <1 year of age**

Yen C, et al. *J Infect Dis* 2012;206:41-48.
Zickafoose JS, et al. *Arch Pediatr Adolesc Med* 2012;166:350-355.

Trends in Intussusception Hospitalizations among US infants, 2000-2011

By Specific Age Group



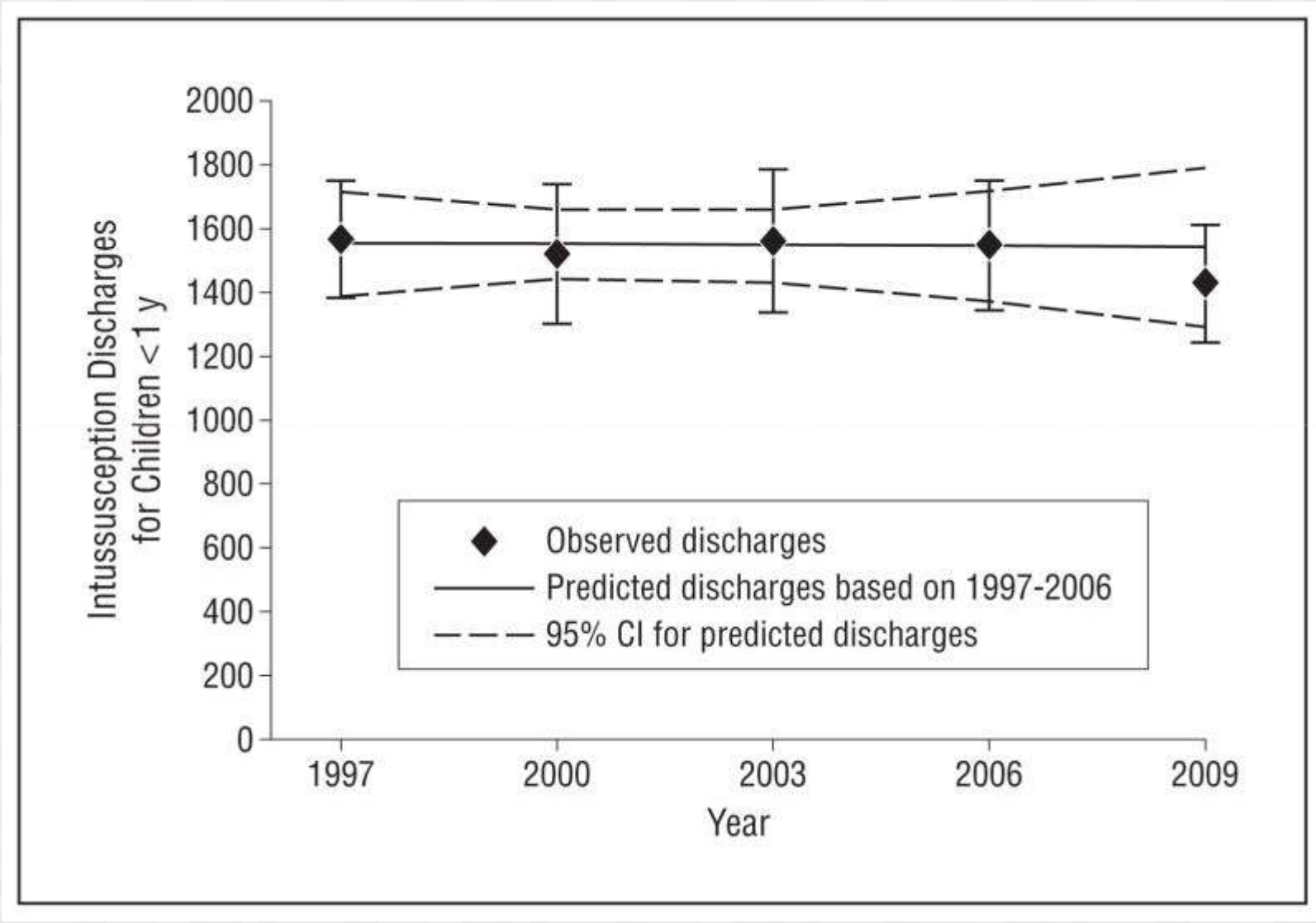
Age 25–34 weeks (Dose 3)

Age 15–24 weeks (Dose 2)

Age 6–14 weeks (Dose 1)

Yen C, Tate J, Steiner C, et al. *J Inf Dis* 2012; Tate J, Steiner C, et al, Preliminary

Hospitalizations for Intussusception in U.S.



Zickafoose JS, et al. *Arch Pediatr Adolesc Med* 2012;166:350-355.

AAP/ACIP Rotavirus Vaccine Recommendations

- No change from original recommendations
  - Same age ranges/same # of doses
- No preference of vaccine product

Intussusception Risk Following Rotavirus Vaccine in U.S.

New VIS

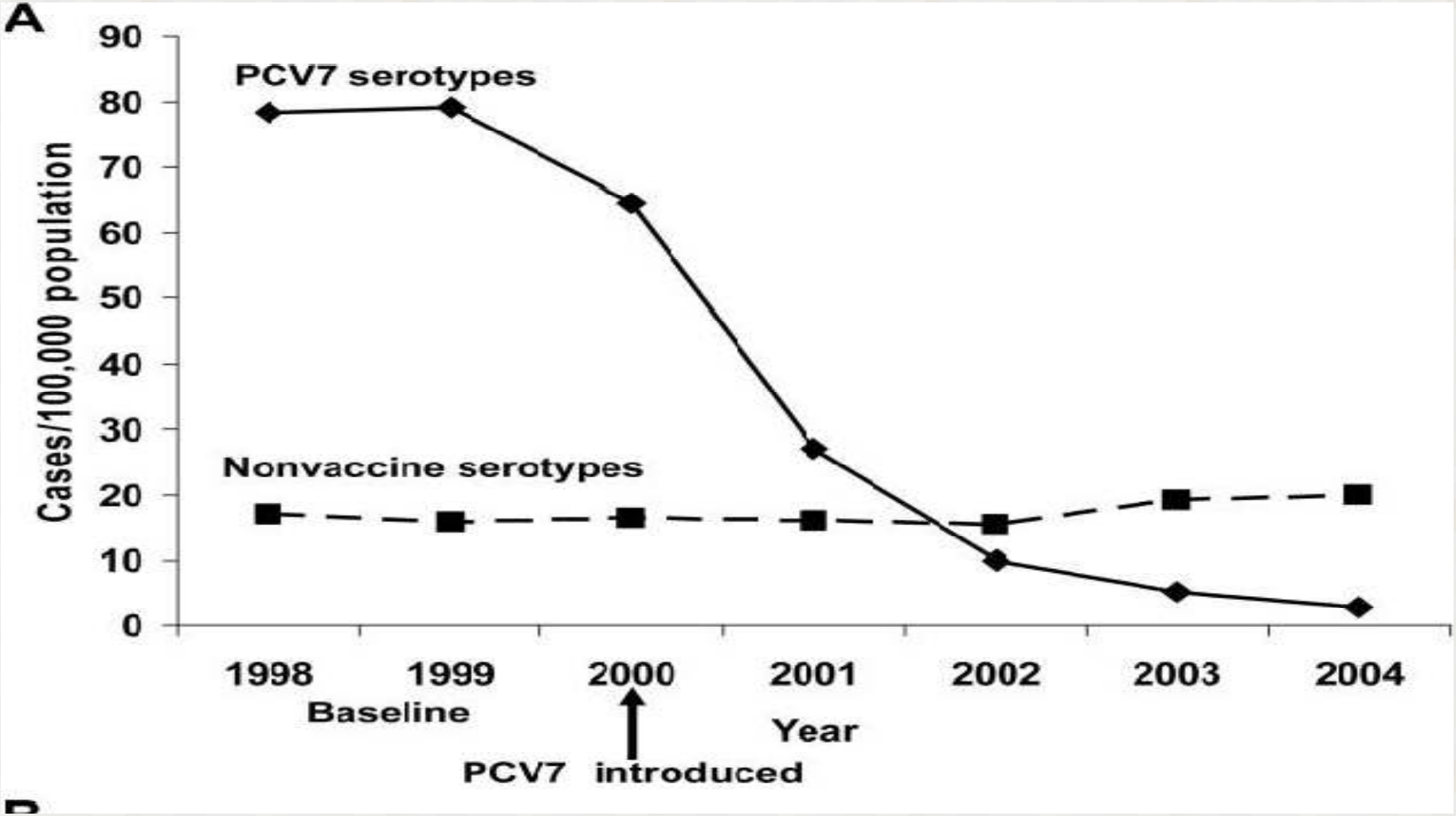
"There is a small risk of intussusception from rotavirus vaccination, usually within a week after the 1st or 2nd vaccine dose. The additional risk is estimated to range from about 1 in 20,000 U.S. infants to 1 in 100,000 U.S. infants who get rotavirus vaccine. Your doctor can give you more information."

Pneumococcal Vaccines

Incidence of Pneumococcal Disease in <5 yr olds following PCV7

77% decrease in all IPD - level after 2002

98% decrease in VT IPD; 29% increase in non-VT IPD



Hicks LA. *J Infect Dis* 2007;196:1346.

CDC. *MMWR* 2008;57:144.

The Next Step was PCV 13

- By 2008, less than 2% of cases of invasive pneumococcal disease in children < 5 were due to PCV 7 serotypes

- 61% of cases of invasive disease in children < 5 were due to serotypes covered in PCV 13 but not in PCV7 (19A, 7F and 3 accounted for 99% of these cases)

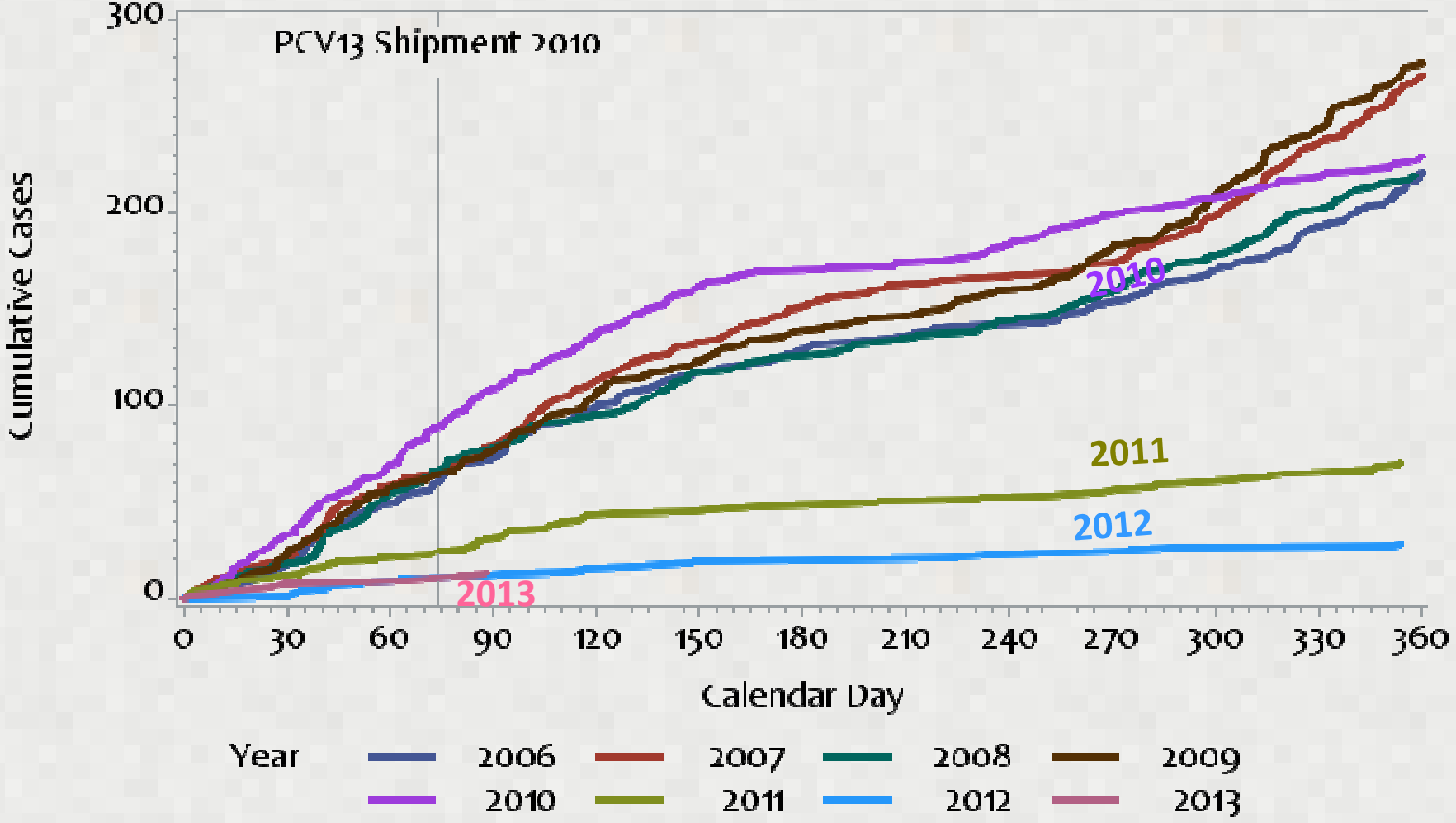
PCV 13

(contains PCV7 serotypes plus 6 additional serotypes)

(1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F)

- **Licensed by the FDA February 2010 based on a randomized, double-blind trial in over 600 U.S. infants showing comparable immunogenicity to PCV 7**
- **Recommended by the ACIP and AAP shortly after licensure**
- **Routine vaccination of all children 2-59 months**
- **Vaccination of children 60-71 months with underlying medical conditions**
- **Supplemental dose of PCV 13 to eligible children who have received 4 doses of PCV 7 previously**

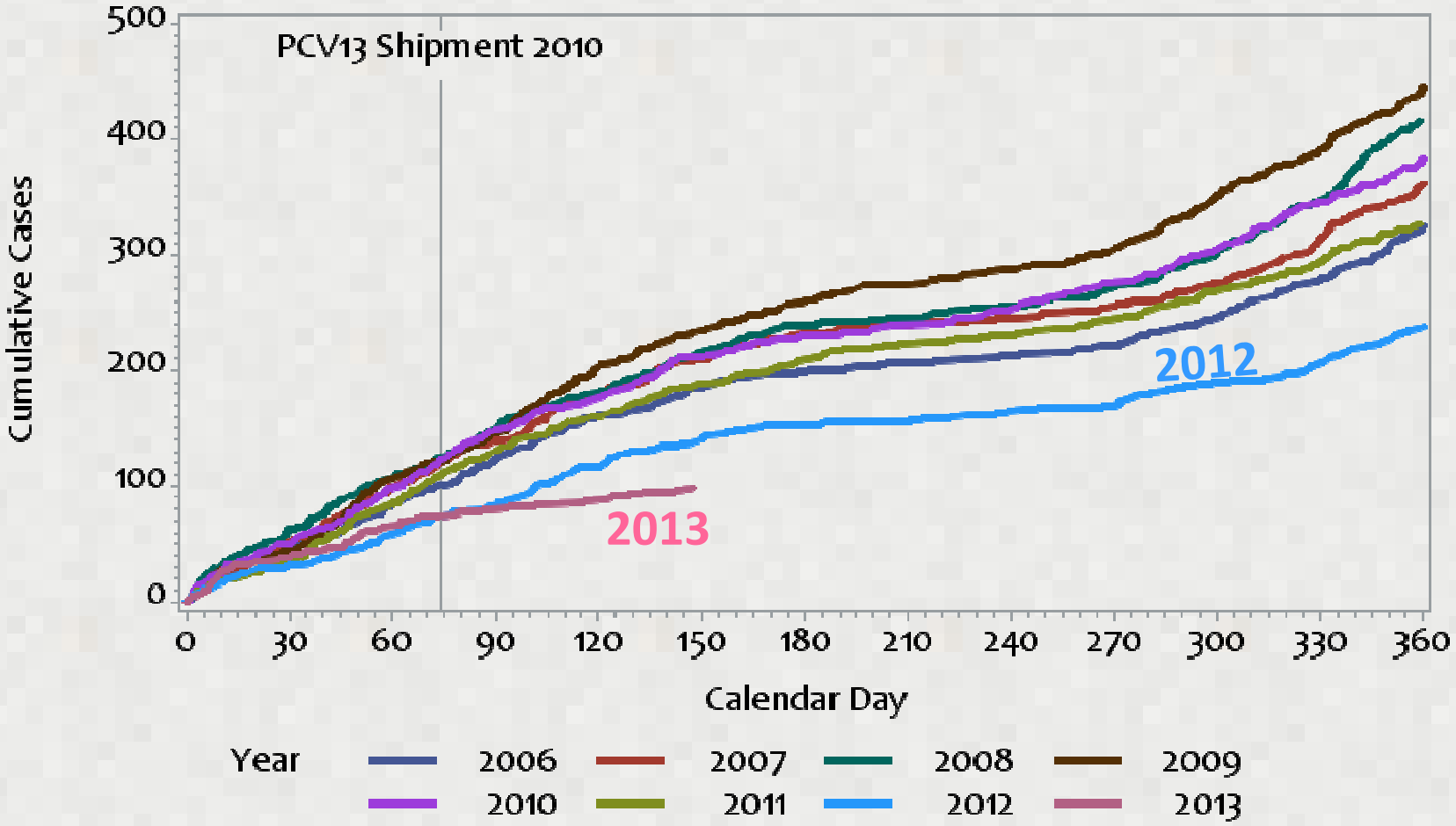
Cumulative Cases of PCV13 Serotypes not in PCV7-type IPD Among Children <5 Years Old, 2006-2013



Clear evidence of persistent direct effect….

Source Matt Moore (CDC< unpublished) *"PCV5" types include those in PCV13 but not in PCV7*

Cumulative Cases of PCV13 Serotypes not in PCV7-type IPD Among Adults >64 years old, 2006-2013



… and indirect effects.

Source Matt Moore (CDC, unpublished)

"PCV5" types include those in PCV13 but not in PCV7.

HPV Vaccines

Human Papillomavirus (HPV)

- Most common STI in men and women in US
- 150 different types of HPV; 40 are transmitted through sexual contact
- US Prevalence:
  - 79 million persons currently infected
  - 14 million persons newly infected each year

- HPV types 16/18 cause:
  - 66% of cervical cancers
  - 55% of vaginal cancers
  - 79% of anal cancers
  - 62% of oropharyngeal cancers

Disease Associations with Most Frequent Types of HPV

Diseases	HPV Type
Cutaneous warts	1, 2, 3, 4, 10 others
Cervical cancer	16, 18, 45, 31, 33, 35
Condyloma acuminata (anogenital warts)	6, 11
Recurrent respiratory papillomatosis	6, 11

Burd. *Clin Microbiol Rev* 2003;16:1-17

Human papillomavirus (HPV) vaccines licensed in the United States

Vaccines	Viral types	Date FDA Licensed
Quadrivalent (HPV4) (Gardasil)	6, 11, 16, 18	Females: June 2006 Males: October 2009
Bivalent (HPV2) (Cervarix)	16, 18	Females: October 2009

Estimated HPV and HPV 16/18-Associated Cancers, Both Sexes, 2004-2007

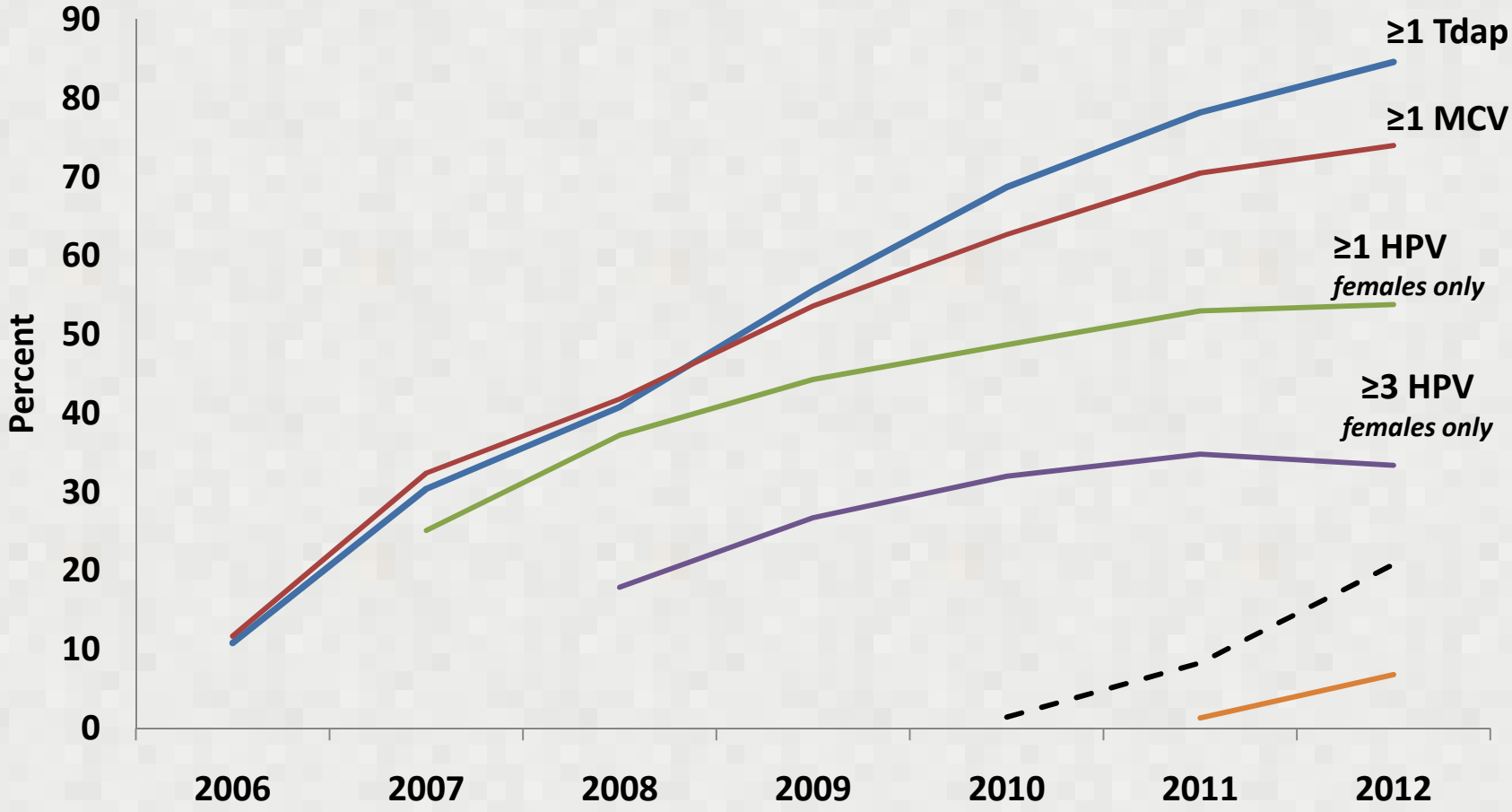
		Estimated+	
Anatomic Area	Average annual Number of cases*	HPV associated	HPV 16/18 Associated
Cervix	11,845	11,370	9,000
Vagina	714	460	400
Vulva	3,062	1,560	1,350
Anus & rectum (W)	2,977	2,770	2,590
Orpharynx (W)	2,306	1,450	1,380
Total (Females)	20,903	17,610	14,720
Penis	1,000	360	310
Anus & Rectum (M)	1,618	1,500	1,410
Oropharynx (M)	8,936	5,630	5,360
Total (Males)	11,553	7,490	7,080

- Defined by histology and anatomic site; Watson M, et al. *Cancer* 2008. Data source: National Program of Cancer Registries and SEER, covering 83% coverage of US population.

+ Gillison ML, et al. *Cancer* 2008.

- ACIP Meeting February 2011

Adolescent Vaccine (13-17 years old) United States, 2006-2012



MMWR. August 30, 2013; NIS-Teen

HPV Vaccine Effectiveness

- **Clinical trials that were performed to achieve FDA approval showed the following reductions:**
  - **HPV 16/18-related CIN 2/3 or AIS were reduced by 100%**
  - **Genital warts (females) were reduced by 97%**
  - **Genital warts (males) – were reduced by 89% after 3 doses; and 67% after one dose**

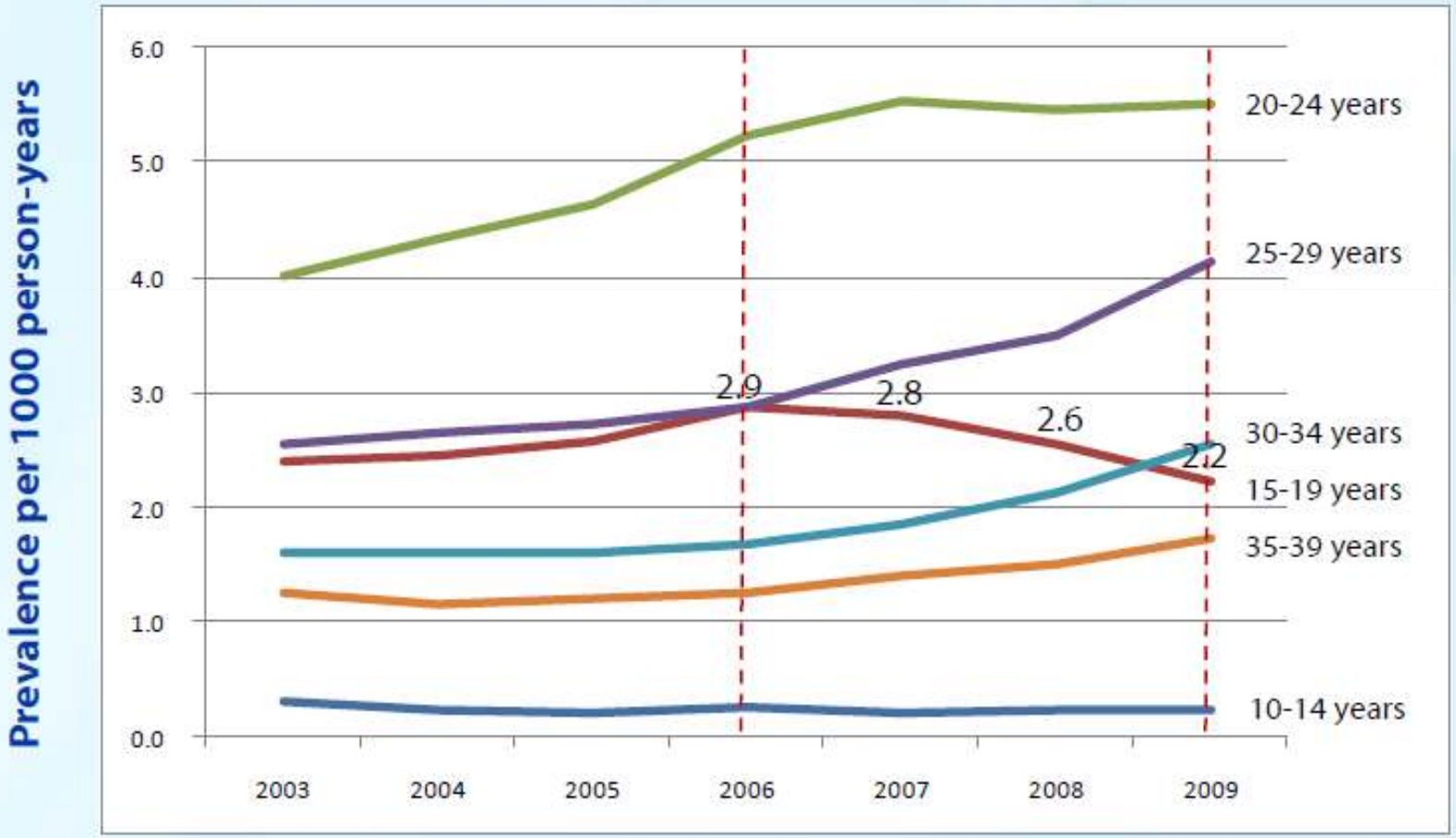
HPV Vaccine Effectiveness

- **Post-marketing surveillance in "real world" settings showed dramatic benefit already:**
  - **56% reduction in prevalence of HPV strains 6, 11, 16 & 18 in adolescent girls in United States (NHANES) despite low HPV immunization rates in the United States of 33% of girls receiving 3 doses**
  - **77% reduction in prevalence of HPV strains 6, 11, 16 & 18 in adolescent girls in Australia within 3 years vaccine introduction (3 dose immunization rates of 70%)**
  - **75% reduction in low grade cervical abnormalities in Australian girls <18 years of age within 3 years of vaccine introduction**

HPV Vaccine Effectiveness

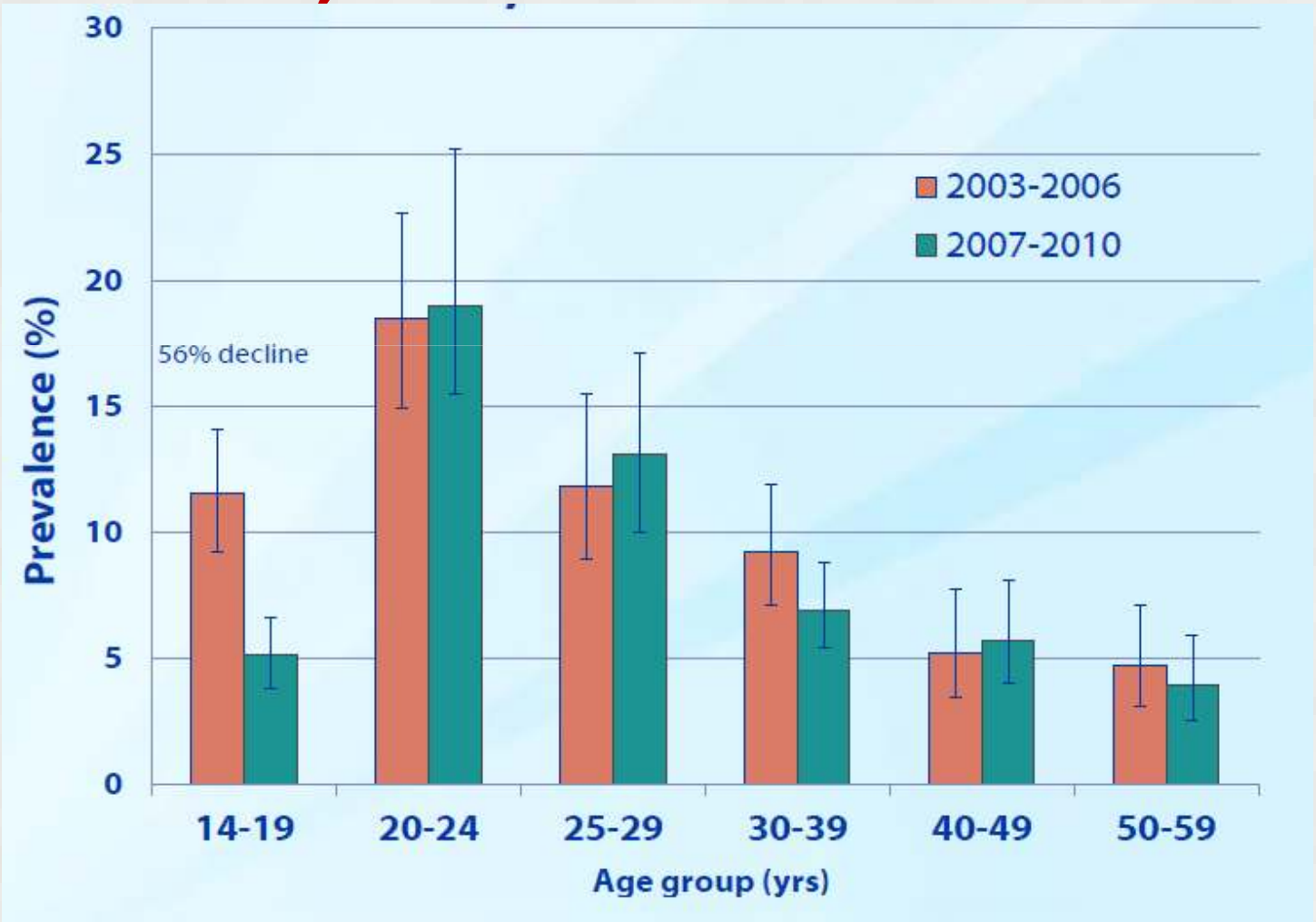
- **Post-marketing surveillance in "real world" settings showed dramatic benefit already:**
  - **45% reduction in genital warts in girls 16-17 years of age in Denmark**
  - **36% reduction in genital warts in girls 15-19 years of age in US despite low HPV immunization rates**
  - **88% reduction in genital warts in Australian females <21 years of age**
  - **Data on cervical cancer reduction will take a longer time to obtain due to the time between HPV infection and development of cancer. But data on prevention of pre-cancerous lesions make it clear that the HPV vaccine is having its desired effect.**

Prevalence of anogenital warts by age 2003-2009, US females



Flagg E. National STD Prevention Conference, May 2012

Prevalence of HPV 6, 11, 16, 18* in cervicovaginal swabs, by age group NHANES, 2003-2006 and 2007-2010



Markowitz, et al. *JID* 2013 (in press) *weighted prevalence

HPV Vaccine Safety

- **Safety**
  - **More than 57 million doses of HPV vaccine have been given in the United States through 2013.**
  - **More than 175 million doses have been given worldwide.**
  - **Post-marketing surveillance has not identified any new safety concerns in female or male HPV vaccine recipients.**
  - **Injection site discomfort is the most common adverse event.**
  - **Syncope is the most common safety concern. Adherence to a 15-minute observation period after vaccination should prevent significant adverse consequence due to syncope.**

HPV Vaccine Safety

- **Safety**
  - **Reports of adverse events to VAERS have declined dramatically since 2008 with no serious adverse events reported in 2013.**
  - **Post-marketing surveillance has not shown any increased risk following HPV vaccine and the following conditions: Guillain-Barre Syndrome, seizures, stroke, venous thromboembolism, appendicitis, anaphylaxis or other allergic reactions.**
  - **While not approved to be given during pregnancy, there have been no identified safety concerns in the HPV pregnancy registry. (Reports of girls who have been immunized with HPV vaccine while pregnant).**

HPV Vaccine Safety

- **Safety**
  - **There is no evidence to suggest that HPV vaccine is responsible for ovarian failure. Genetic, infectious, inflammatory, autoimmune and toxin-related conditions are most likely responsible for ovarian failure in adolescent girls who have received HPV vaccine. (The relationship of ovarian failure and HPV vaccine area a temporal but not causal relationship).**

HPV Vaccine Safety

- **Safety**
  - **As of June 2013, 85 deaths have been reported to VAERS in individuals who have received HPV vaccine. A majority of these deaths have been reviewed by CDC. Their findings were:**
    - **There is no diagnosis at death that would suggest that the HPV vaccine caused the death**
    - **There is no pattern of death occurring with respect to time after vaccination**
    - **There is no consistent vaccine dose number or combination of vaccines given and the death**

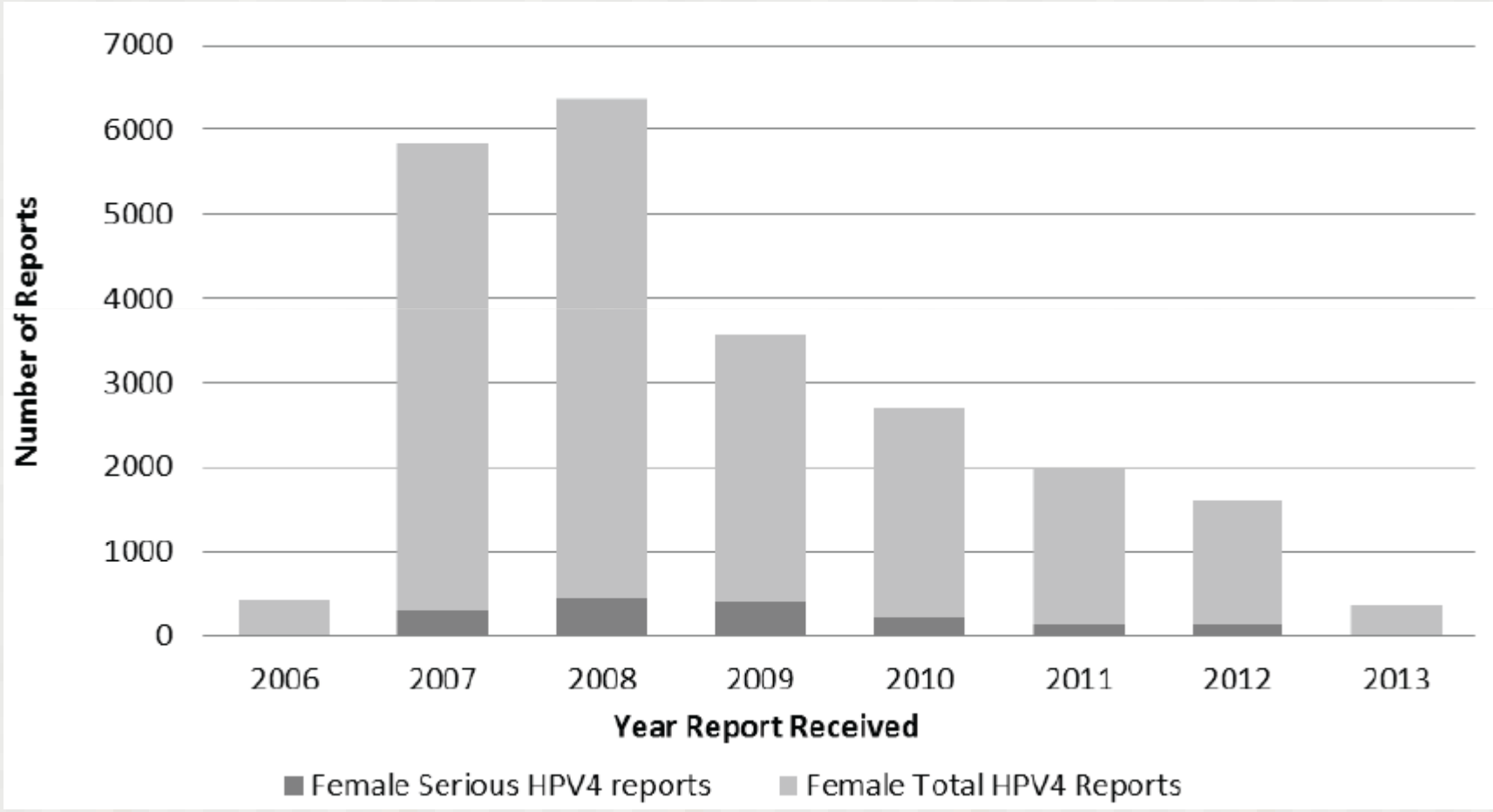
HPV vaccine safety monitoring - VAERS

- From 6/2006 through 3/2013 ~56 million HPV4 doses distributed in the United States

- No new safety concerns have been identified in post-licensure vaccine safety surveillance among male or female recipients of HPV4 vaccine
  - Among the 7.9% of reports coded as “serious”, most frequently cited are headache, nausea, vomiting, fatigue, dizziness, syncope, generalized weakness

- Syncope continues to be a frequently reported AEFI among adolescents
  - Adherence to a 15-minute observation period after vaccination is encouraged

Trends in Total and Serious Female HPV4 Vaccine Reports to VAERS by Year, 6/1/2006-3/31/2013 (N=21,194)



CDC, unpublished data

HPV4 Safety Data

- **Favorable safety profile: no association between vaccination with GARDASIL and**
  - **Congenital anomalies, miscarriages**
  - **16 pre-specified autoimmune conditions**
  - **Venous thromboembolism**
  - **Death**
  - **Any other general safety events (except syncope & possibly local skin infection)**
- **Syncope associated with GARDASIL infection-related**
- **Local skin infection (cellulitis/abscess) possibly associated with GARDASIL could be injection site reaction**
- **All safety conclusions were made by independent, external Safety Review Committee of 5 experts.**

Velcer C. Garadsil Female Safety Study Team

VAERS Serious Reports of Syncope Following HPV4*

- Total number of serious reports: 202
- Injuries resulting from syncopal event:
  - Fractures (nose, skull, maxillary)
  - Dental injuries
  - Contusions
  - Concussions
  - Intracranial hemorrhages (subdural hematoma, subarachnoid hemorrhage)
- No reports of death resulting from injury following a vasovagal syncopal event

*Unverified reports coded as syncope or syncope vasovagal

Top 5 Reasons for Not Vaccinating Daughter, Among Parents with No Intention to Vaccinate in the Next 12 Months, NIS-Teen 2012

Not needed or necessary	19.1%
Not recommended by provider	14.2%
Safety concern/side effects	13.3%
Lack of knowledge	12.6%
Not sexually active	10.1%

MMWR. 2013; 62:591-5

HPV Vaccine Communications During the Healthcare Encounter

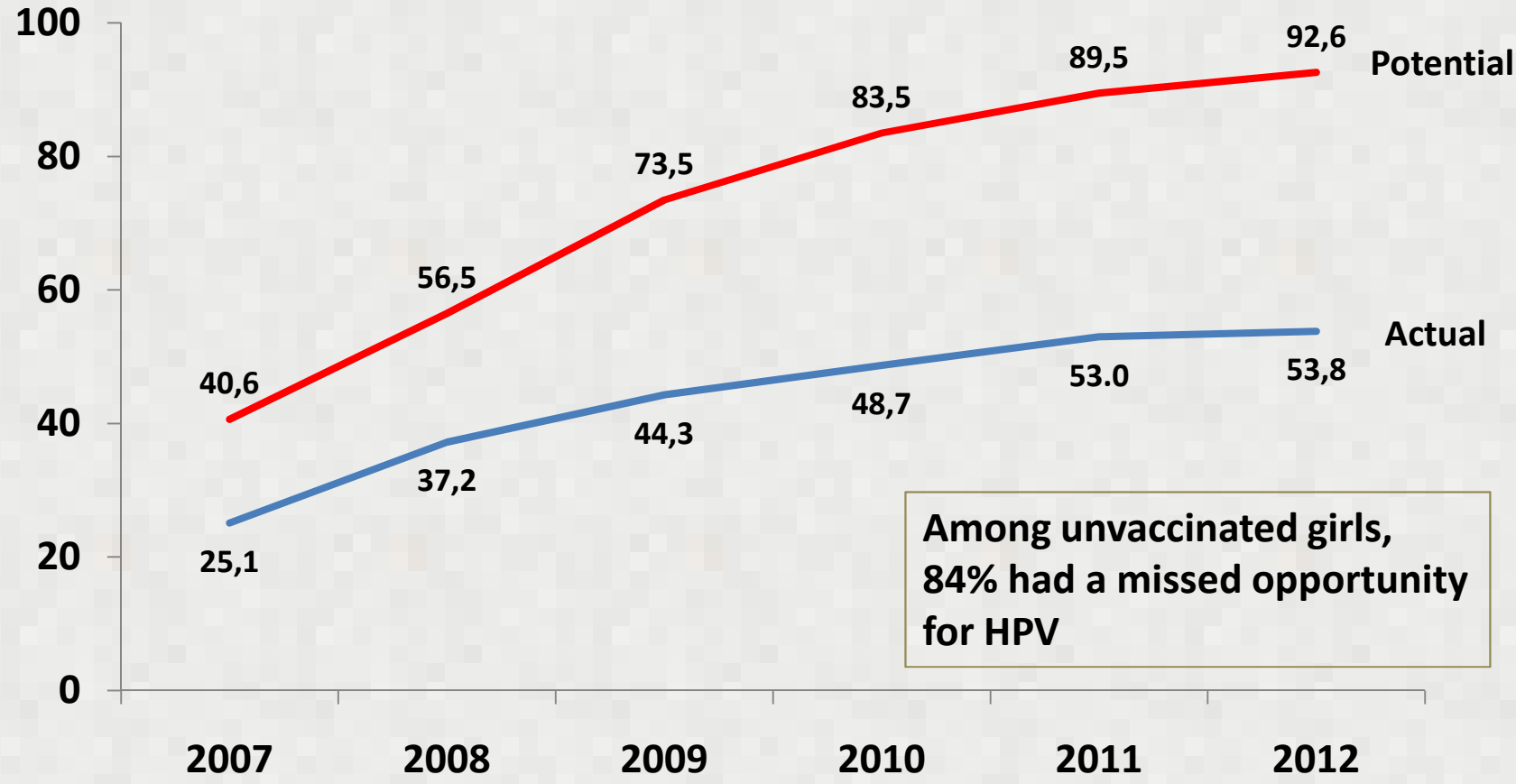
- HPV vaccine is often presented as 'optional' whereas other adolescent vaccines are recommended
- Some expressed mixed or negative opinions about the 'new vaccine' and concerns over safety/efficacy
- When parents expressed reluctance, providers were hesitant to engage in discussion
- Some providers shared parents' views that teen was not at risk for HPV and could delay vaccination until older

Goff S, et al. *Vaccine* 2011;10:7343-7349
Hughes C, et al. *BMC Pediatrics* 2011;11:74

Strategies to Improve Implementation of HPV Immunization in Adolescents

- HPV vaccine is a cancer vaccine not STI vaccine
- HPV immunization is routine and not “optional”
- Gender neutral
- Early age of administration (9-12 years) since this results in far superior immune response at this age → longer protection
- Early age of administration to ensure it predates greatest time of acquisition
- Give when giving Tdap and/or MCV4
- Give whenever opportunities arise

Actual and potentially achieve vaccination coverage of ≥ HPV among adolescent girls if missed opportunities* were eliminated, NIS-Teen

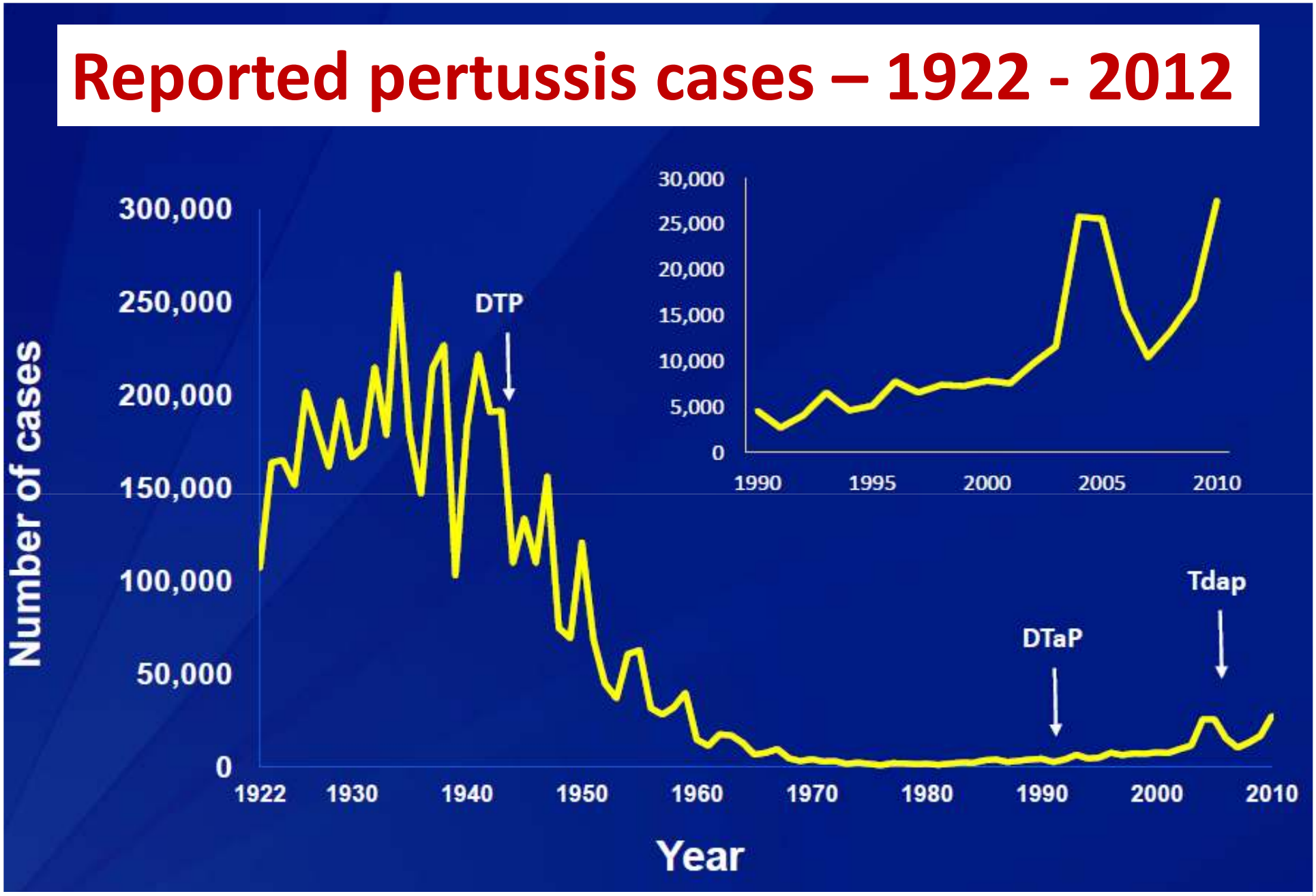


*Missed opportunity defined as having a healthcare encounter where at least one vaccine was administered but HPV was not.

MMWR. 2013; 62:591-5

Pertussis Vaccine

Reported pertussis cases – 1922 - 2012

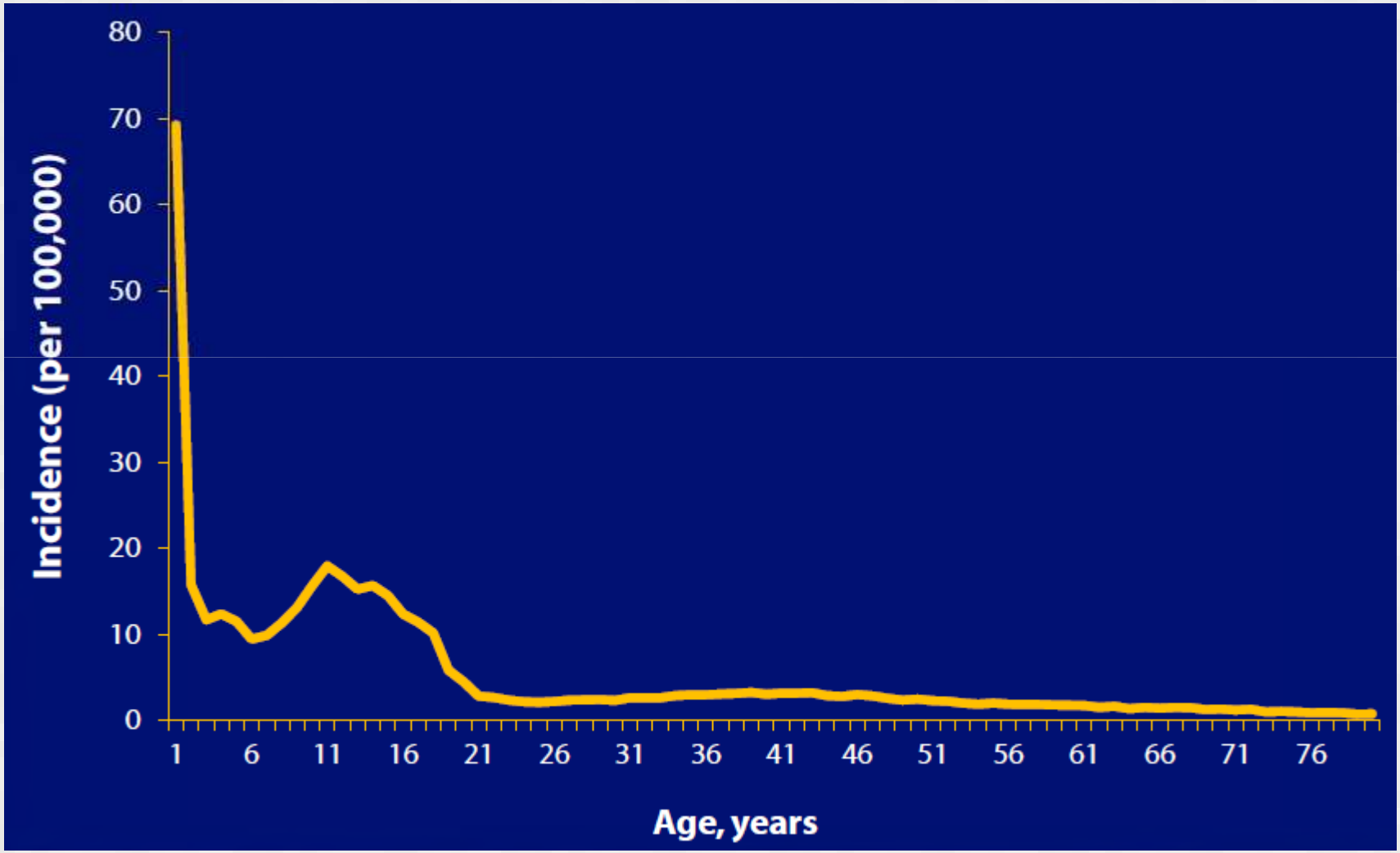


SOURCE: CDC, National Notifiable Disease Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive report to the Public health Service

Pertussis Immunization in the U.S.

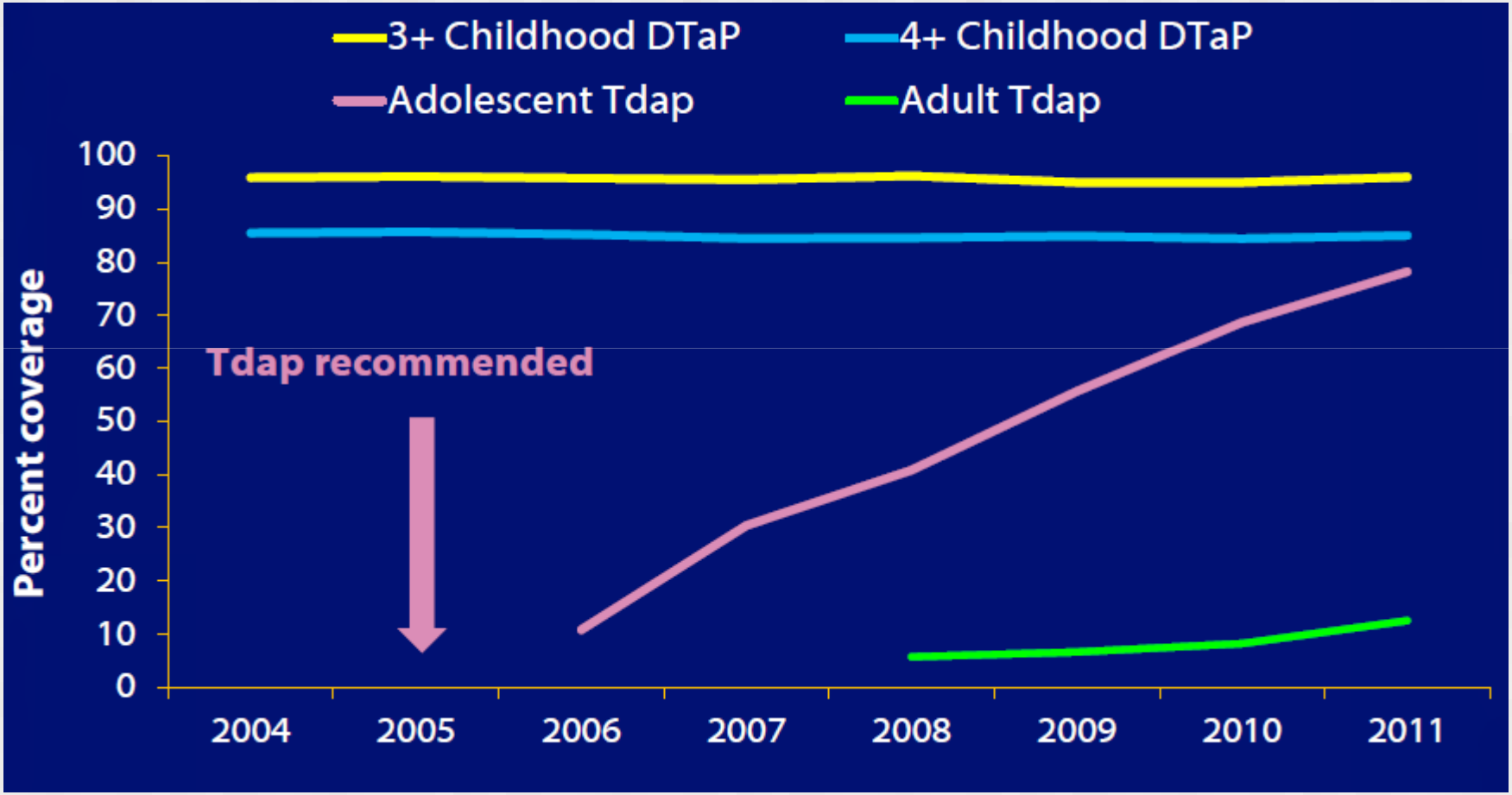
- Whole-cell vaccines/DTwP (1940s)
- DTaP (1990s)
  - Infants at 2, 4, 6 months (1997)
  - Toddlers at 15-18 months (1992)
  - Pre-school at 4-6 years (1992)
- Tdap (2005)
  - Adolescents and adults
    - Preferred administration at 11-12 years

Average Incidence of Reported Pertussis Cases in the U.S. by Age, 2002-2011



SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System

Pertussis Vaccination Coverage*† Among the U.S. Population, 2004-2011

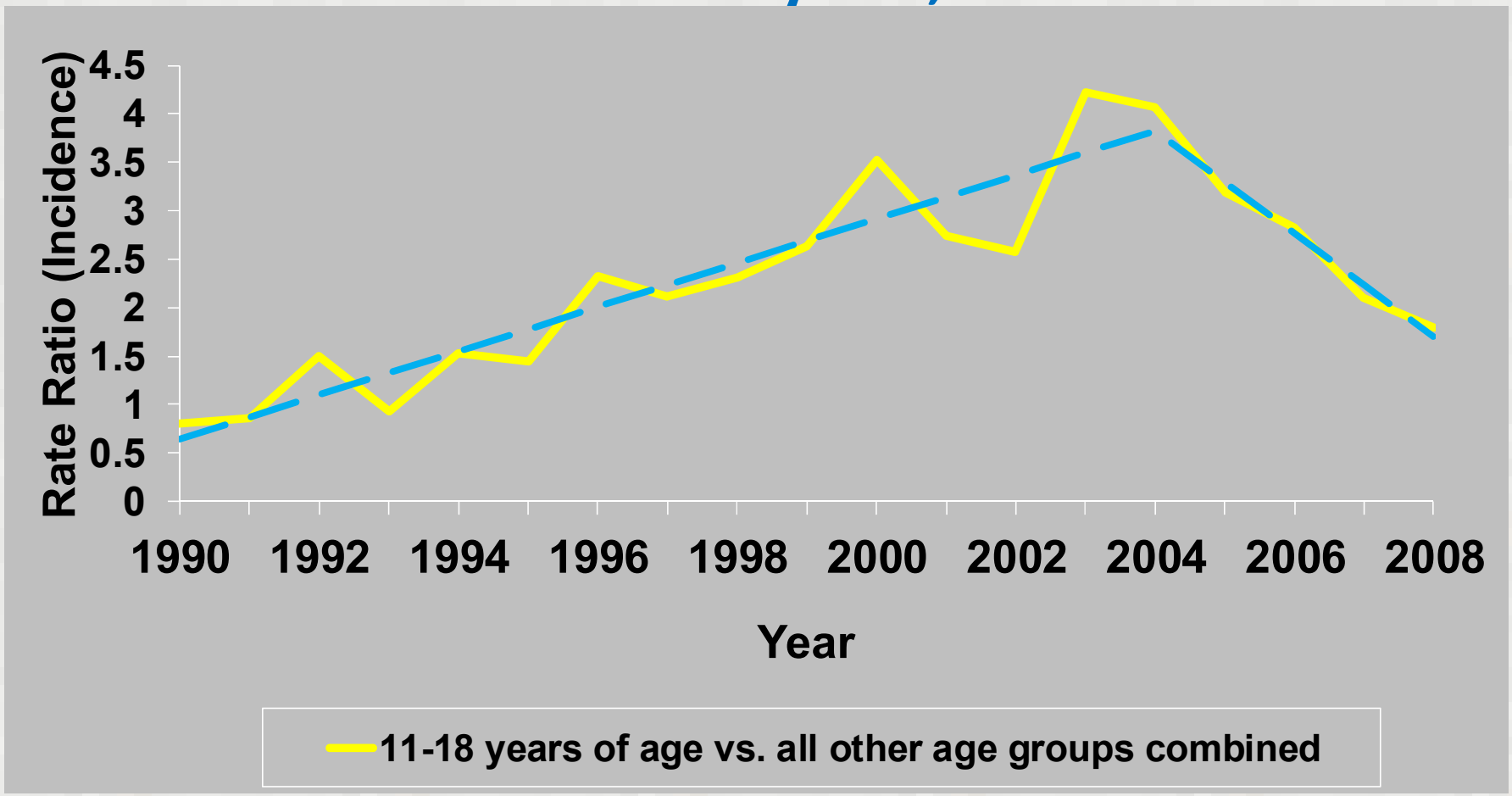


*CDC National Immunization Survey: DTaP among children aged 19 through 35 months, Tdap coverage among adolescents aged 13 through 17 years

†National Health Information Survey: Tdap coverage among adults aged 19 through 64 years

Accelerated Decline of Pertussis

Rate ratios of pertussis incidence among adolescents 11-18 years, 1990-2008

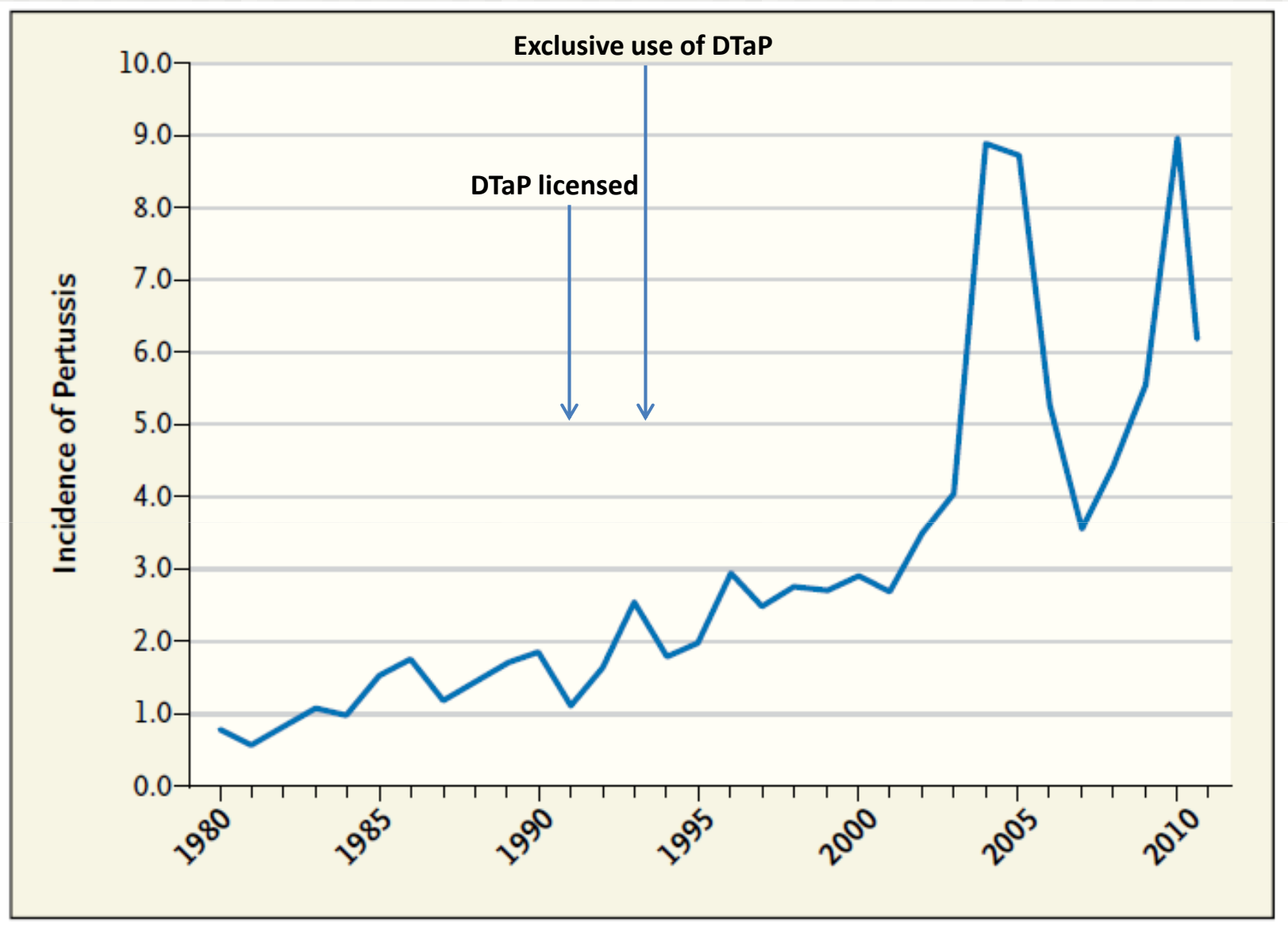


Skoff et al. *Arch Pediatr Adolesc Med.* 2012 Jan 11. [ePub ahead of print]

Vaccine Effectiveness of Acellular Pertussis Vaccine (Outbreak in Oregon)

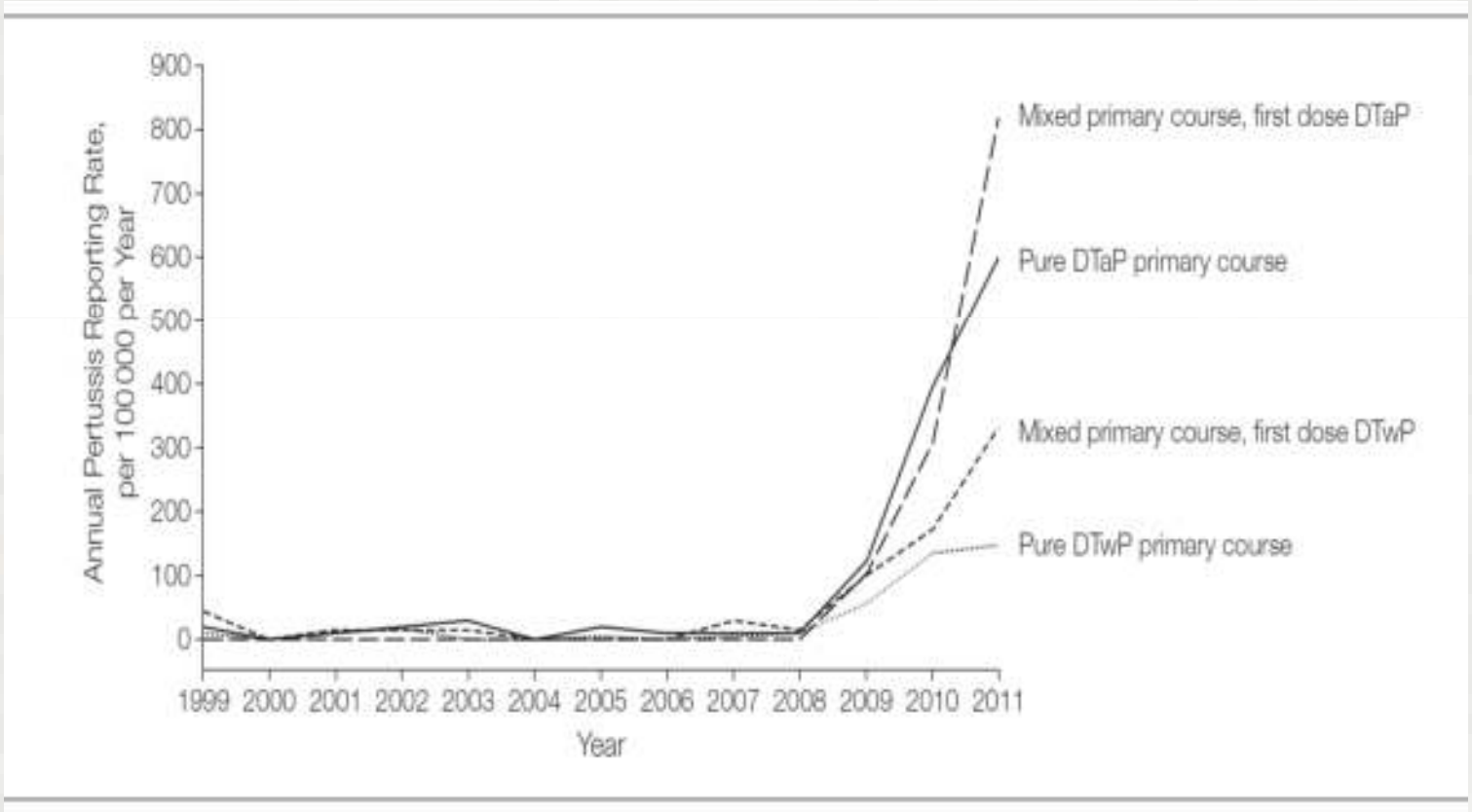
- **Vaccine Effectiveness by age group:**
  - **15-47 months of age – 95% (92-97%)**
  - **13-16 years of age - 47% (19-65%)**
- **Relative Risk of Pertussis**
  - **1.9 to 20.6 times more likely in unvaccinated**
  - **1.3 to 3.0 times more likely in partially-vaccinated**

Clin Infect Dis published online April 18, 2014



Incidence of Pertussis per 100,000 Population in the United States, 1980-2011.
Data are from the Centers for Disease Control and Prevention.

Pertussis Reporting Rates 1999-2011 by Primary Pertussis Vaccine(s) Received fro Children Born in 1998, Australia



More gel to the concept of greater longevity of Protection if primed DTwP

Epidemiology and Control of Pertussis

- **Excellent initial 5-dose DTaP VE (98%)**
- **Modest but immediate waning immunity post DTaP (95% → 83% @ 1 → 5 yrs)**
- **Pertussis burden in children <11 years appears to be a "cohort effect" from change to all aP vaccines (susceptibility *despite* vaccination)**
- **Tdap program has reduced the burden of pertussis in young adolescents**
- **No evidence of Tdap herd protection**

Thomas Clark, MD, MPH *ACIP* 2/12

Enlightenments from the Baboon Model

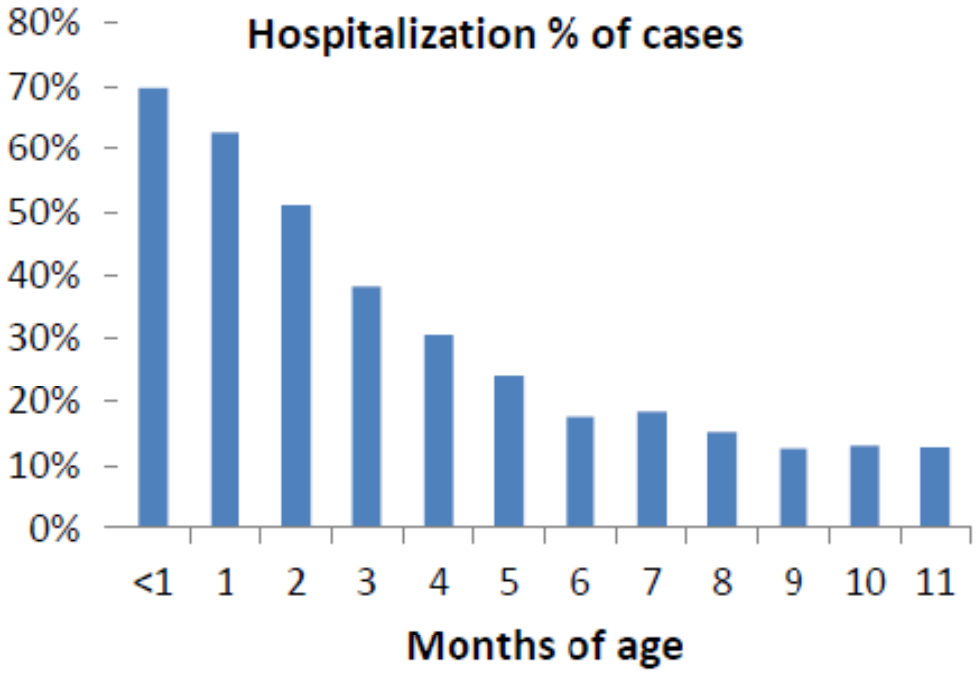
- **Baboons under experimental inoculation:**
  - **are infected and excrete *B. pertussis* x 21 days**
  - **produce antibodies to PT (3rd wk)**
  - **once infected, exhibit leukocytosis (peak 2nd wk) and cough illness (peak 1st to 2nd wk)**
  - **once infected are protected against subsequent challenge (no replication org; but Ab boost)**
  - **exhibit immunologic memory ≥24 mos (IL-27 & IFN-γ secreting memory T cells)**
- **Acellular Vaccines (DTaP):**
  - **protect against disease**
  - **do *not* protect against infection (i.e. replication of org) by experimental or natural transmission**
  - **does not prevent infected animal from transmitting**
- **Whole Cell Vaccines (DTwP):**
  - **confer protection against infection (i.e. replication of org) to a degree >aP and <disease**

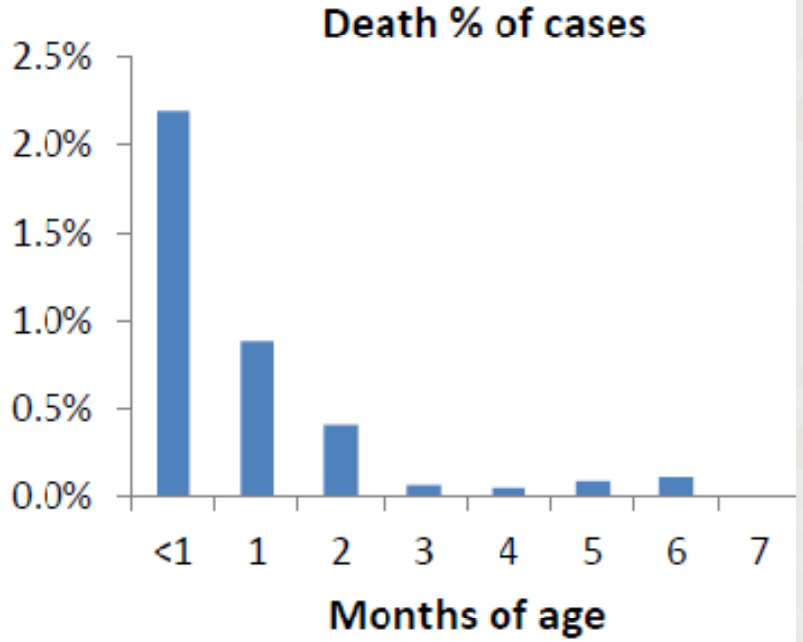
Tod Merkel. CBER, FDA 10/18/13

Enlightenments from the Baboon Model (2)

- **Immunologic Response**
  - aP → strong Th2 (no Th1)
  - wP → mod Th1 and Th2
- **Mechanism of Protection**
  - Clearance of airway bacteria requires Th-17 response
  - Protection requires Ab vs toxins

Hospitalizations and Deaths
% Total Cases, 2001-2009





Source: CDC, National Pertussis Surveillance System and Supplemental Pertussis Surveillance System (2010)

Maternal Transfer of Pertussis Antibody (IgG ELISA EU/ml)

Antigen	Maternal Delivery	Cord	Infant 2 Month
PT	2.4 (1.9-3.1)	4.1 (3-5.5)	1.4 (1.2-1.7)
FHA	6.9 (5-9.5)	12.3 (8.8-17.3)	3 (2.3-3.8)
FIM	13 (9.2-18.5)	20.4 (14-29.6)	5.8 (4.5-7.4)

J Infect Dis. 2004 Jul 15;190(2):335-40

Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine (Tdap) in Pregnant Women - - Advisory Committee on Immunization Practices (ACIP), 2012

AAP/ACIP Recommendations for Pregnant Women

AAP/ACIP recommends that providers of prenatal care implement a Tdap immunization program for all pregnant women. Health-care personnel should administer a dose of Tdap during each pregnancy, irrespective of the patient's prior history of receiving Tdap.

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