

# Cocooning: The US Experience and Current Strategies

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**BACKGROUND**

# Reported pertussis-related deaths by age-groups - 1980-2009\*

Age-Group	1980-1989 <sup>1</sup>	1990-1999 <sup>1</sup>	2000-2009 <sup>2</sup>
0-1 month	38	68	119
2-3 month	11	16	56
4-5 month	5	5	6
6-11 month	7	4	1
1-4 years	13	2	2
5-10 years	1	6	2
11-18 years	0	0	2
>18 years	1	2	6
Total	77 <sup>†</sup>	103	195*

\*2009 Data are provisional

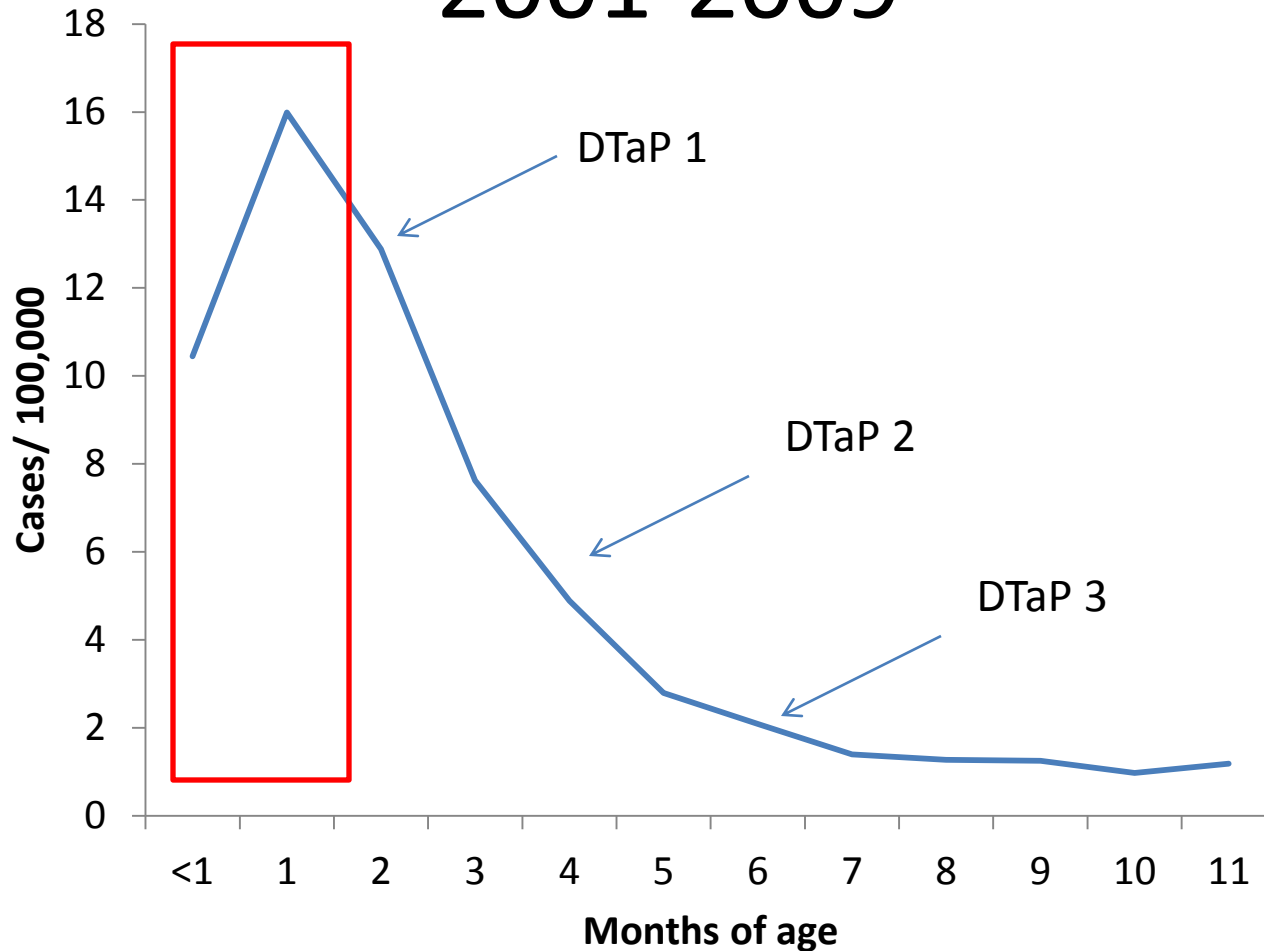
<sup>1</sup> Vitek CR et al. *Pediatr Infect Dis J* 2003; 22(7):628-34.

<sup>2</sup> National Notifiable Diseases Surveillance System, CDC, 2009\*

<sup>†</sup> Includes one case with unknown age

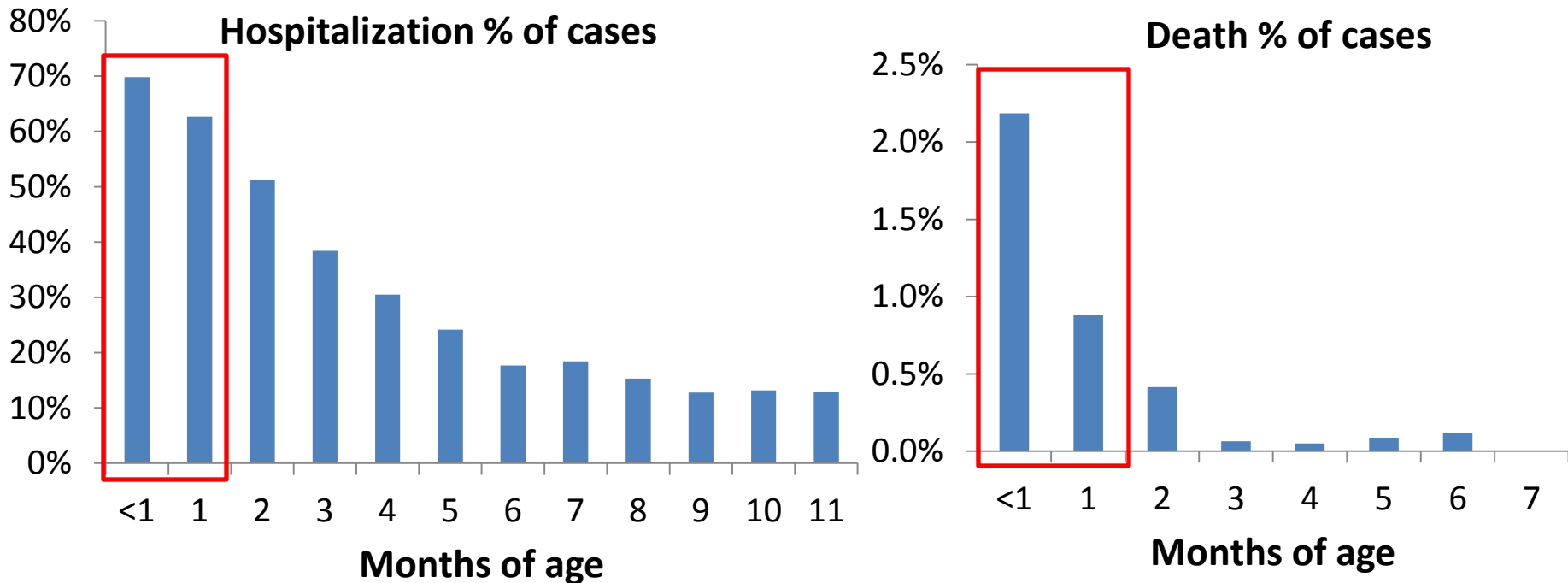


# Pertussis Incidence among Infants 2001-2009



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

# Hospitalizations and Deaths % Total Cases, 2001-2009



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

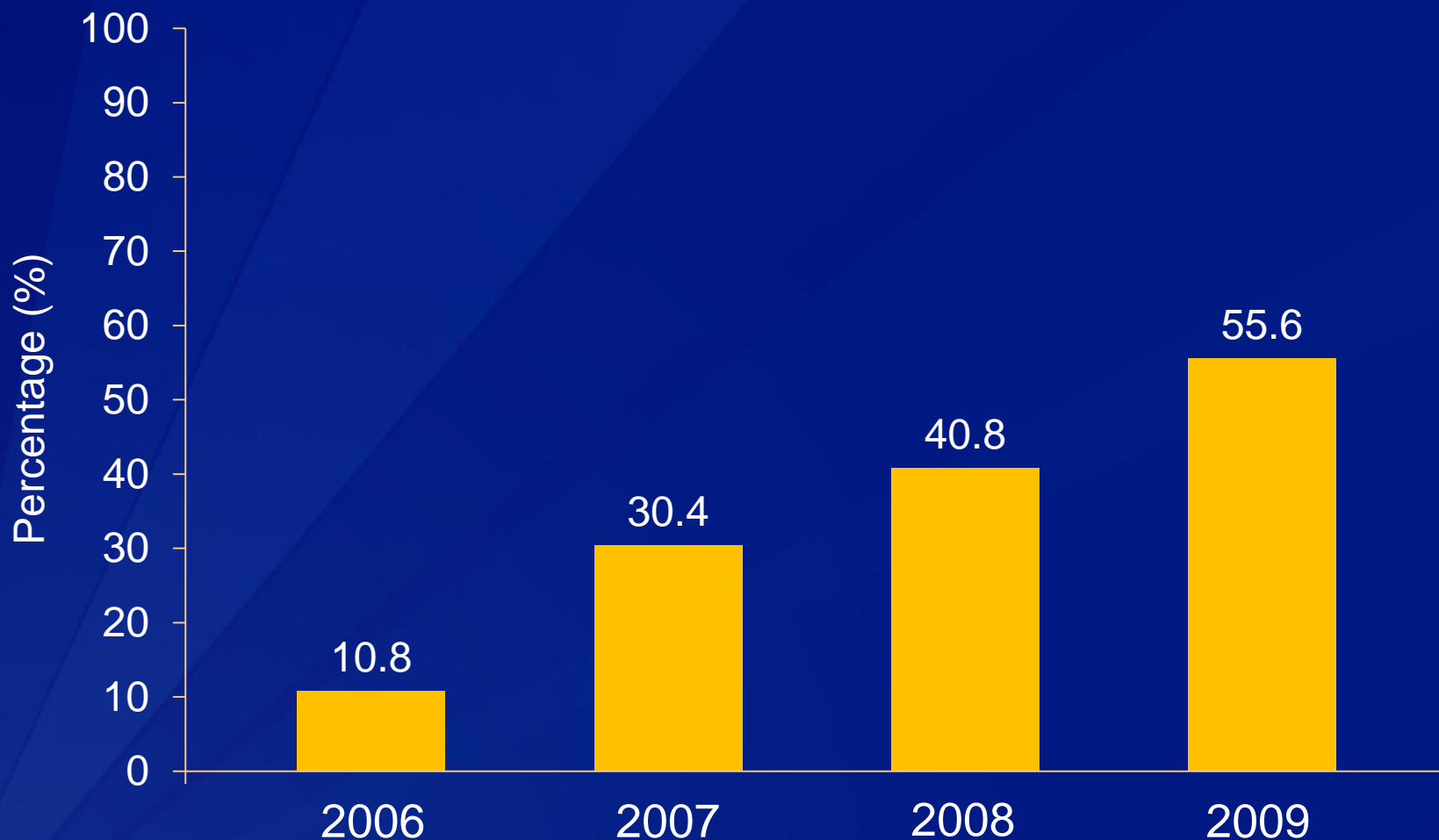
# Source of Infant Pertussis

- ❑ **Household members 75%–83%**
- ❑ **Parents and siblings most common sources**
  - Parents (55%)
  - Siblings (16%-20%)
  - Aunts/uncles (10%)
  - Friends/cousins/others (10%-24%)
  - Grandparents (6%)
  - Caretakers (2%)

Wendelboe AM., et al. Transmission of Bordetella pertussis to Young Infants. *Pediatr Infect Dis J* 2007;26: 293–299

Bisgard KM, Pascual FB, Ehresmann KR, Miller CA, Cianfrini C, Jennings CE et al. Infant pertussis: who was the source? *Pediatr Infect Dis J* 2004; 23(11):985-989.

# Tdap coverage among adolescents aged 13-17 years – 2006-2009



CDC. National, State, and Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2008. MMWR 2009;58(36):997-1001.

CDC. Vaccination Coverage Among Adolescents Aged 13-17 Years – United States, 2007. MMWR 2008;57(40):1100-1103.

CDC. Vaccination Coverage Among Adolescents Aged 13-17 Years– United States, 2006. MMWR 2007;56(34):885-888.

CDC. National, State, and Local Area Vaccination Coverage among Adolescents Aged 13-17 Years - United States, 2009 MMWR 2010 ;59(32):1018-1023.

# Tdap Vaccine Effectiveness

- Bridging studies of ADACEL and BOOSTRIX<sup>1</sup>
  - 85-89%
- APERT study<sup>2</sup>
  - 92% (95% CI: 32.0-99.0)
- Australia<sup>3</sup> – screening method
  - 78.0% (95% CI: 60.7-87.6)
- St. Croix outbreak<sup>4</sup> – case-control study
  - 65.6% (95% CI: -35.8-91.3)
- MN case-control study (poster #80)
  - 72.3% (95% CI: 38.8-87.4)

<sup>1</sup> Schmitt HJ et al. JAMA 1996;275:37-41; Gustafsson LH et al. NEJM 1996;334:349-355

<sup>2</sup> Ward JI et al. N Engl J Med. 2005 Oct 13;353(15):1555-63.

<sup>3</sup> Rank C, et al. Pediatr Infect Dis J. 2009 Feb;28(2):152-3.

<sup>4</sup> Wei SC, et al. CID 2010; 51(3):315-321.

# **IMPLEMENTATION AND EVALUATION**

# Cocooning Can Be Successful

- ❑ **Demonstration projects**
  - Houston, TX – Ben Taub General Hospital
  - Nevada - 18 birthing hospitals
- ❑ **Important success factors**
  - “Champion” for the cause
  - Donated healthcare provider time
  - Free Tdap

# Challenges to implementation of postpartum immunization

- ❑ **New immunization platform**
- ❑ **Pertussis awareness**
- ❑ **Two populations**
  - Postpartum women
  - Other family members
- ❑ **Vaccine history**
- ❑ **New immunization providers**
- ❑ **Reimbursement issues**



# Five years later, is cocooning working?

## ❑ **No, not at a national level**

- Very limited success of vaccinating fathers or other family members
- Poor uptake of Tdap when made available at birthing hospitals
- No demonstration of program sustainability or scale-up
- No program of support at Federal level

## ❑ **Not fully successful examples**

- Jefferson County, NY: free Tdap
- California: during an epidemic, free Tdap

## Effectiveness of cocooning

### Limited data available

- ❑ One ecological study found no impact of only maternal postpartum Tdap on infant disease.<sup>1</sup>
- ❑ Pertussis incidence in infants born at CA hospitals with a postpartum Tdap policy was lower compared to hospitals without a postpartum Tdap policy<sup>2</sup>
- ❑ No system to measure coverage

<sup>1</sup> Castagnini L, *et al.* Impact of maternal post-partum Tdap vaccination on pertussis illness in young infants. IDSA , Vancouver Canada. Presented on October 23, 2010

<sup>2</sup> Winter K, *et al.* Effectiveness of postpartum Tdap vaccination in California hospitals. CSTE, Portland Oregon. Presented June 2010.

# ACIP Conclusions about Cocooning

- ❑ Recommend vaccination of all contacts of infants
- ❑ Cocooning is an insufficient national strategy to prevent pertussis morbidity and mortality in newborn infants
- ❑ Consideration of pregnancy immunization at June ACIP meeting

**A NEW STRATEGY**

# Overview of ACIP Workgroup Considerations

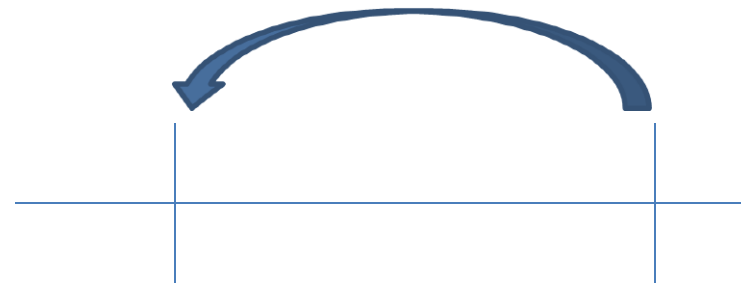
- ❑ **Safety in mothers and newborns**
  - Vaccine Adverse Event Reporting System (VAERS)
  - Pregnancy registry data (GSK and sanofi pasteur)
  - Recent studies
- ❑ **Immunogenicity of Tdap use in pregnancy**
  - Recent studies
- ❑ **Interference by maternal antibodies**
  - Recent studies
  - Currently registered trials
- ❑ **Programmatic considerations**

# Evaluation of Tdap use in pregnant women

	Favorable to maternal vaccination
Safe to pregnant women	Yes
Safe to newborn	Yes
Transplacental transfer of pertussis antibodies to neonates	Yes
Adverse impact on primary DTaP response	?
Programmatic considerations	Yes

# Tdap during pregnancy?

- Move mother's dose to the 3<sup>rd</sup> trimester
  - Protect infant against transmission from mother (similar to postpartum)
  - Likely benefit -- direct immunity to infant through maternal antibodies<sup>1</sup>



During pregnancy  
(3<sup>rd</sup> trimester)

Postpartum

<sup>1</sup> Healy et al 2004; Van Savage et al 1990; Gall et. Al. 2011; Leuridan, et al. 2008; Shakib et al 2010.

# Methods

## Pregnancy

- Mothers vaccinated in 3<sup>rd</sup> trimester of pregnancy
- Increase in risk of disease during 2<sup>nd</sup> and 3<sup>rd</sup> month to model “blunting”

## Postpartum dose

- 2 week delay in booster immune response
- Additional cocooning doses given before birth of infant

- Vaccine cost same for all Tdap doses:  
\$37.55 dose cost<sup>1</sup> + \$20 administrative cost<sup>2</sup>

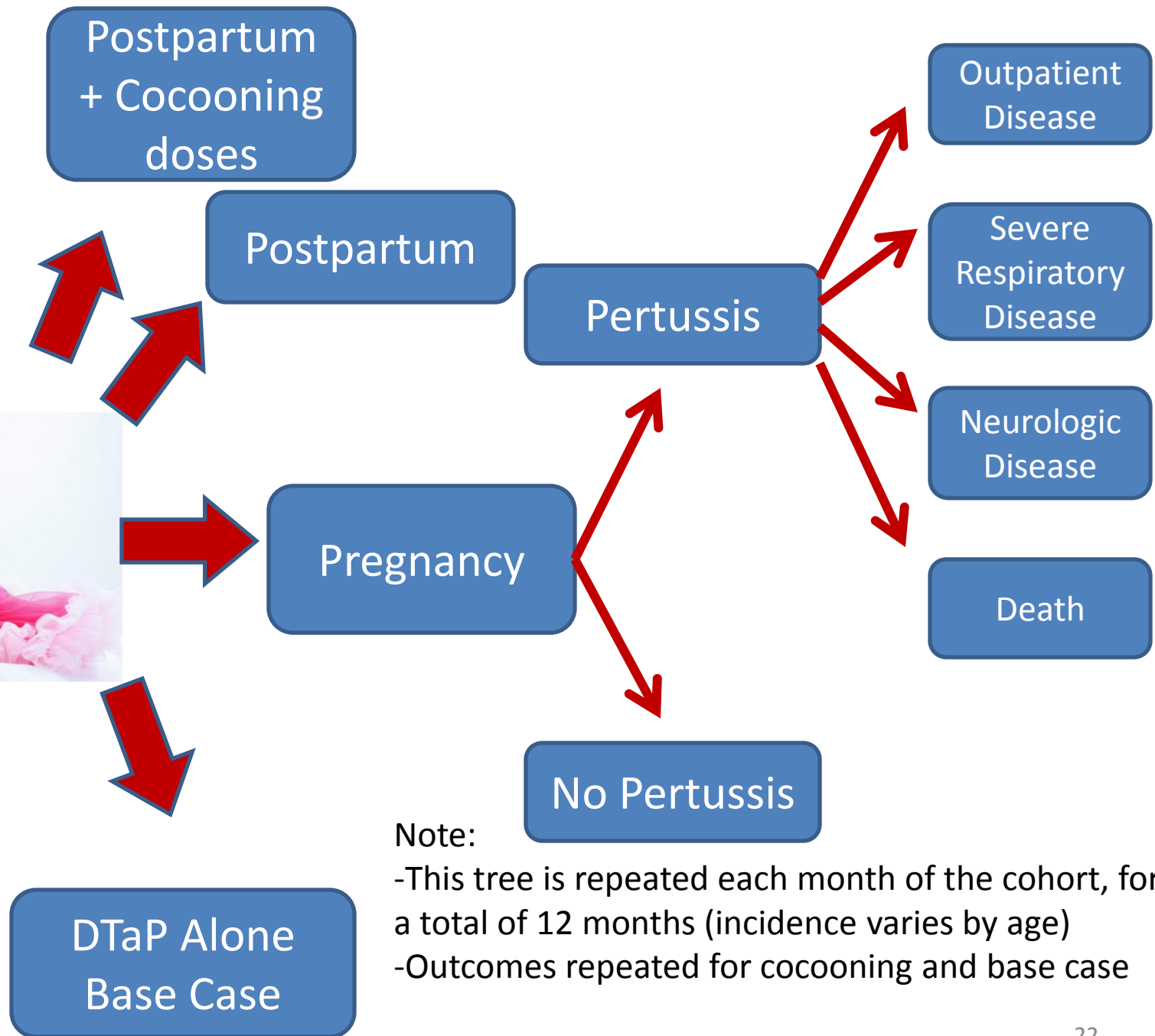
<sup>1</sup> CDC 2011a.

<sup>2</sup> Caro 2005.

# Model

- A simulated birth cohort
  - 4,131,019 (2009 birth cohort size) infants followed for one year<sup>1</sup>
- Monthly incidence, hospitalization, and death rate
- Societal costs perspective for infants only
- Analytic horizon
  - Direct disease costs totaled over first year of life
  - Life years lost, 2009 average life expectancy (77.9 years<sup>2</sup>)

Source: 1. Hamilton 2010; 2. US Census Bureau 2011.

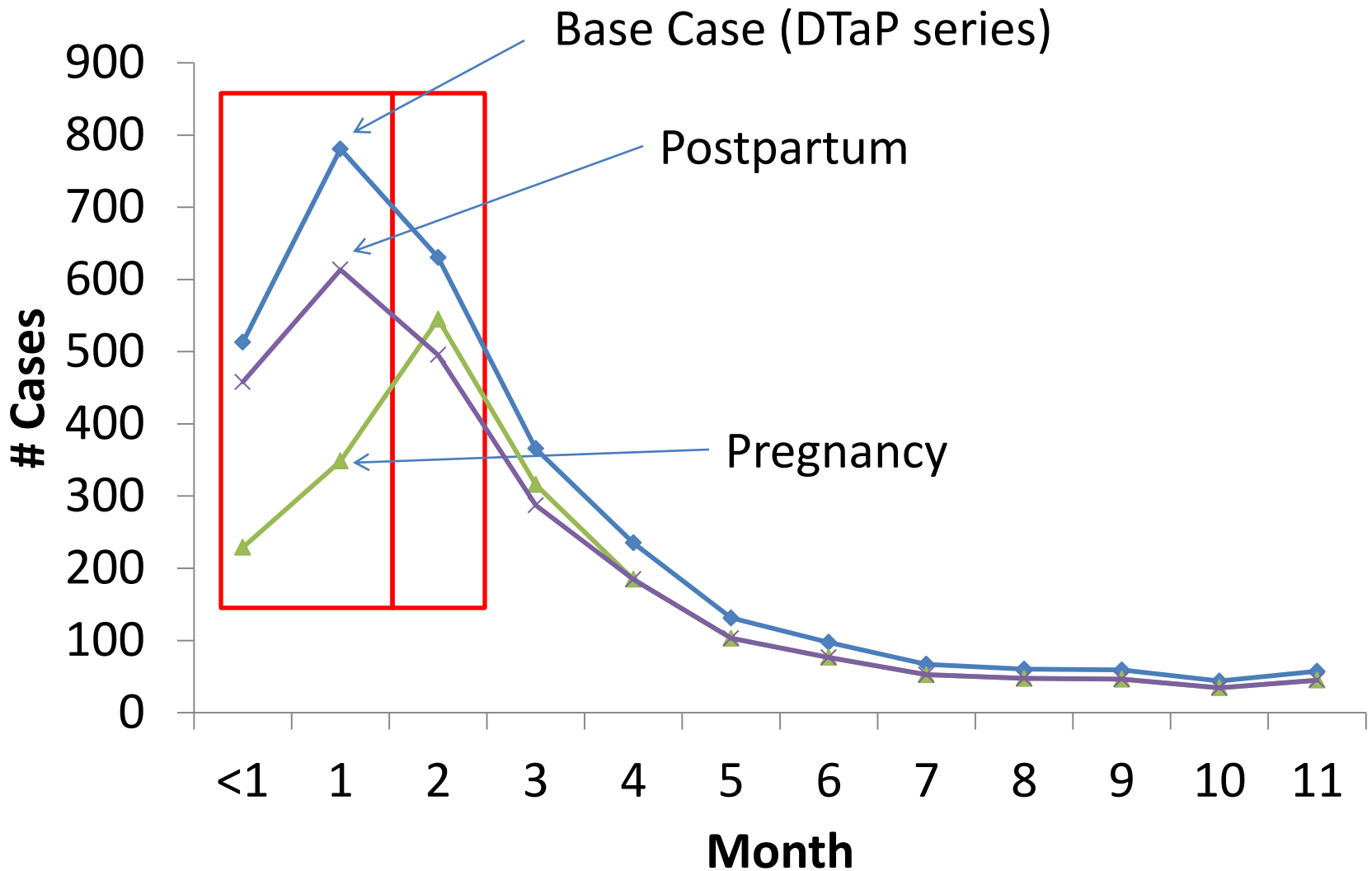


Note:

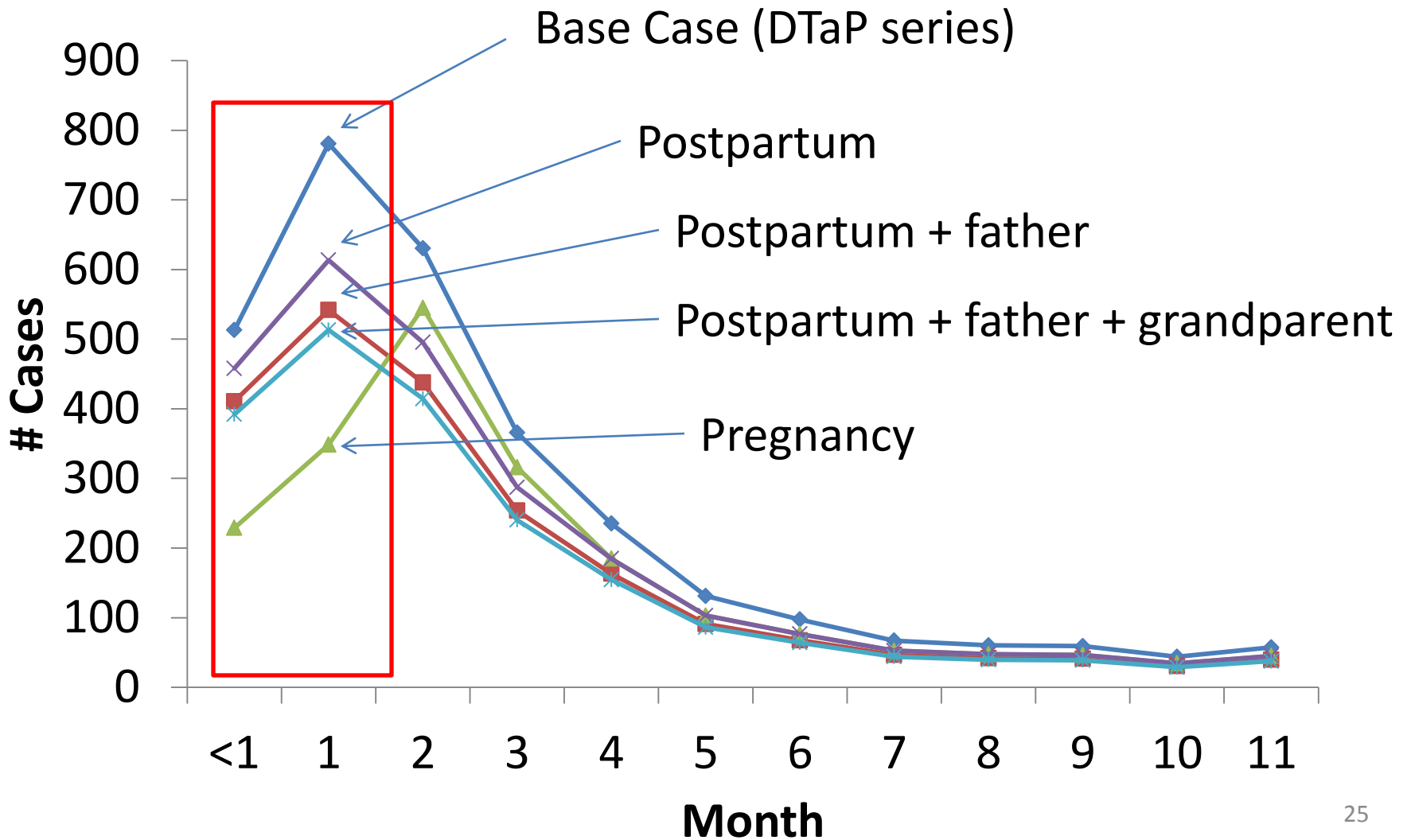
- This tree is repeated each month of the cohort, for a total of 12 months (incidence varies by age)
- Outcomes repeated for cocooning and base case

# Results

# Postpartum vs. Pregnancy



# Pregnancy vs. Postpartum + Father + Grandparent



# Mean % Reductions from Base Case (all interventions)

	Pregnancy	Postpartum	+ father	+grandparent
Cases	33%	20%	29%	32%
Hospitalizations	38%	18%	28%	32%
Deaths	49%	16%	25%	29%
Program cost (72% coverage)	171 million	171 million	342 million	513 million

# Cost Effectiveness Summary

Incremental Cost Effectiveness Ratio	Pregnancy*	Postpartum*	+ father**	+ grandparent***
Cost per case averted	162,298	280,947	606,966	1,526,713
Cost per hospitalization averted	294,114	606,179	1,261,757	3,173,722
Cost per QALY saved	415,442	1,174,143	2,154,170	5,418,427
Cost per life year saved	498,960	1,569,926	2,753,358	6,925,576

\*Relative to base case, \*\*Relative to postpartum , \*\*\*Relative to postpartum + father

# Conclusions

- Two factors drive pregnancy cost effectiveness
  - Mother fully protected at birth (for a given vaccine efficacy)
  - Maternal antibody transfer to infant
- Additional cocooning doses are predicted to be less cost effective



# Next Steps

- ❑ **Planned case-control study evaluating cocooning and post-partum vaccination effectiveness**
- ❑ **Building on success of H1N1 campaign to achieve coverage**
- ❑ **Addressing revaccination with Tdap**

# Thank You

**For more information please contact Centers for Disease Control and Prevention**

1600 Clifton Road NE, Atlanta, GA 30333

Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: [cdcinfo@cdc.gov](mailto:cdcinfo@cdc.gov) Web: [www.cdc.gov](http://www.cdc.gov)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

National Center for Immunization & Respiratory Diseases

Meningitis and Vaccine Preventable Diseases/Division of Bacterial Diseases





# Safety of Tdap in pregnancy in VAERS - January 1, 2005 – June 30, 2010

- **129 (1.2%) of 10,350 (US) reports after Tdap vaccines involved pregnant women**
  - 3.1% (4) of 129 reports classified as “serious”†
  - No maternal deaths
- **Most commonly reported pregnancy-related AEs:**
  - Spontaneous abortion (N=20; 15.5% of all Tdap pregnancy reports)
  - Six (4.7%) gestational diabetes
  - 3 each (2.3%) of oligohydramnios and pregnancy toxemia (nausea and vomiting)
  - Two (1.6%) each of stillbirths and congenital anomalies (gastroschisis, patent foramen ovale and peripheral pulmonic stenosis)
- **Most commonly reported non-pregnancy-related AEs:**
  - Six (4.7%) each of injection site reactions and acute respiratory infections
- **Summary: no unexpected patterns or unusual events**

\*CDC/ISO unpublished data

† Serious reports are coded as such based on Code of Federal Regulations if they result in: death, life-threatening illness, hospitalization, prolongation of hospitalization, persistent or significant disability, congenital anomaly

# General Model Inputs

Parameter	Base Case (Min, Max)	Sources
Coverage for all doses	72% (25, 85) (min father 6%)	Healy (2009)
Tdap efficacy	85% (50, 92)	Schmitt (1996); Skoff (2011); Ward (2005)
Incidence infants < 1 yr	Mean 2000-2007 incidence	CDC (2010)
Hospitalization probability	Mean 2000-2007 hospitalizations % total cases	CDC (2010)
Death probability	Mean 2000-2007 deaths by month % total cases	CDC (2010)
Underreporting	15% (0, 30)	Cortese (2008); Sutter (1992)
Discount rate	3% (0, 5)	

# Intervention Model Inputs

Parameter	Base Case (Min, Max)	Source
Efficacy maternal antibodies	60% (15, 85)	Authors' Assumption; Gall (2011)
Duration antibody effectiveness	2 months (1, 3)	Van Savage (1990); Healy (2009); Shakib (2010)
Blunting (months 2 and 3)	10% (0, 20)	Van Savage (1990)
Transmission mother	35% (30, 40)	Bisgard (2004); Wendelboe (2007); Westra (2010)
Transmission father	15% (10, 20)	Bisgard (2004); Wendelboe (2007)
Transmission grandparent	6% (0, 10)	Wendelboe (2007)

# Costs (US 2009\$) and QALYs\*

Cost Category	Medical	Non-medical**	QALY
Outpatient visit <sup>1</sup>	110	47	0.85
Inpatient respiratory illness <sup>1</sup>	7,323	487	0.58
Inpatient neurologic illness <sup>1</sup>	7,032	745	0.51
Death (medical cost) <sup>1</sup>	15,808	735	0
Public health response <sup>2,***</sup>	\$2,162 (min 1,081; max 3,243)		

\*Quality Adjusted Life Year (QALY).

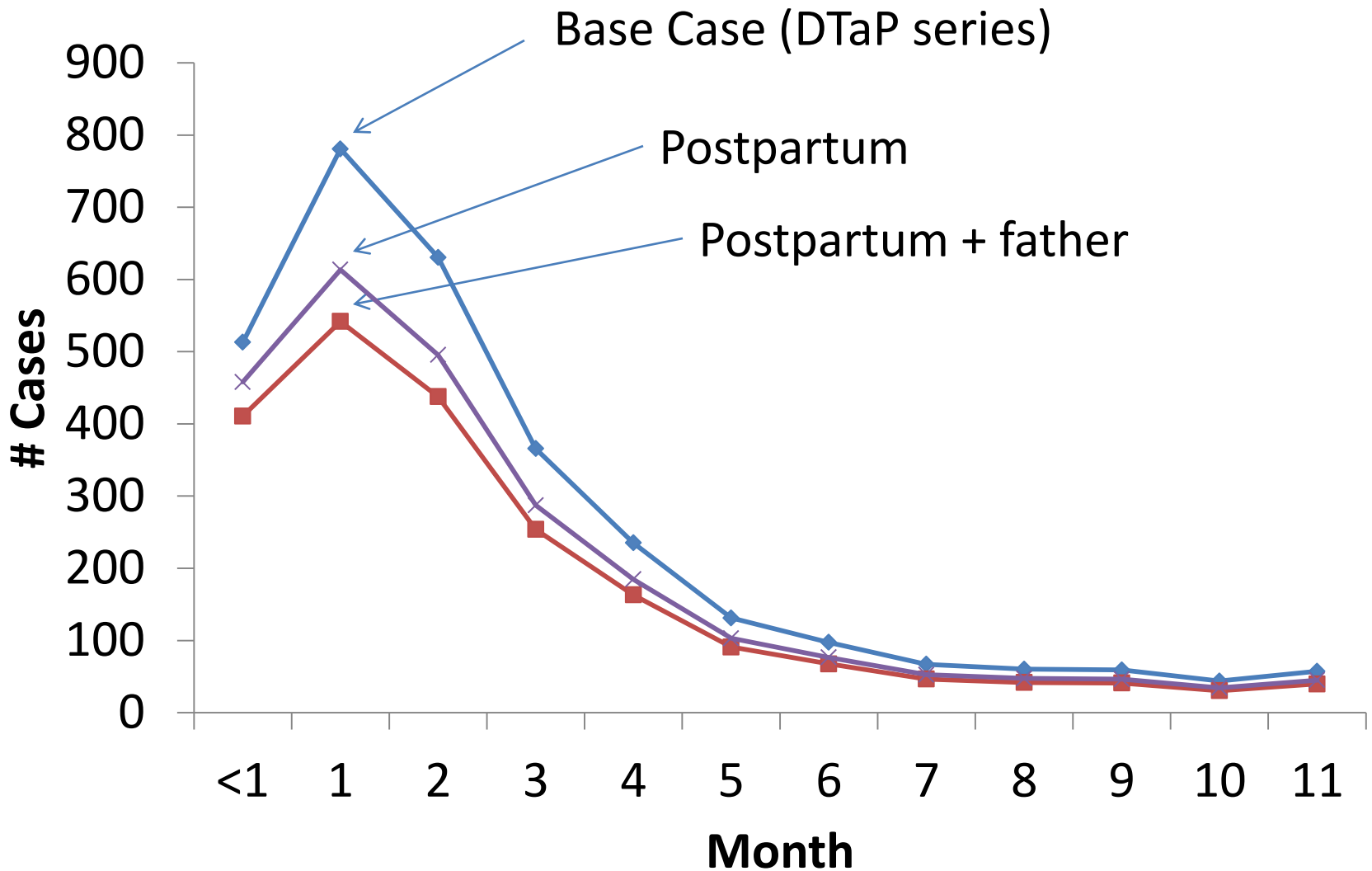
\*\* Parent's lost work, transportation, over-the-counter medications

\*\*\* Public health labor time spent tracing contacts, reporting cases, etc.

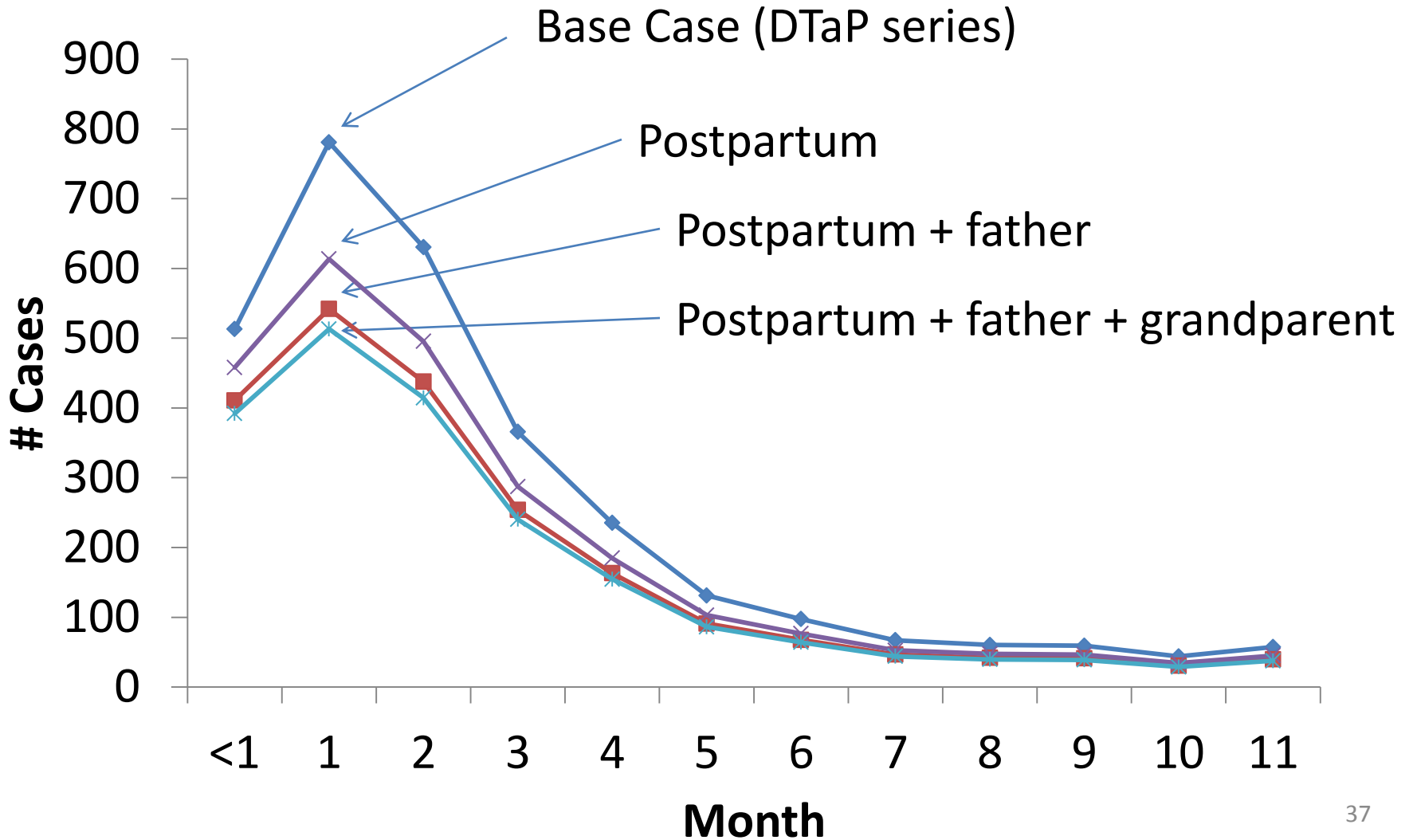
<sup>1</sup>Lee et al. 2007 and Lee et al. 2005.

<sup>2</sup>CDC 2011b.

# Postpartum + Father



# Postpartum + Father + Grandparent



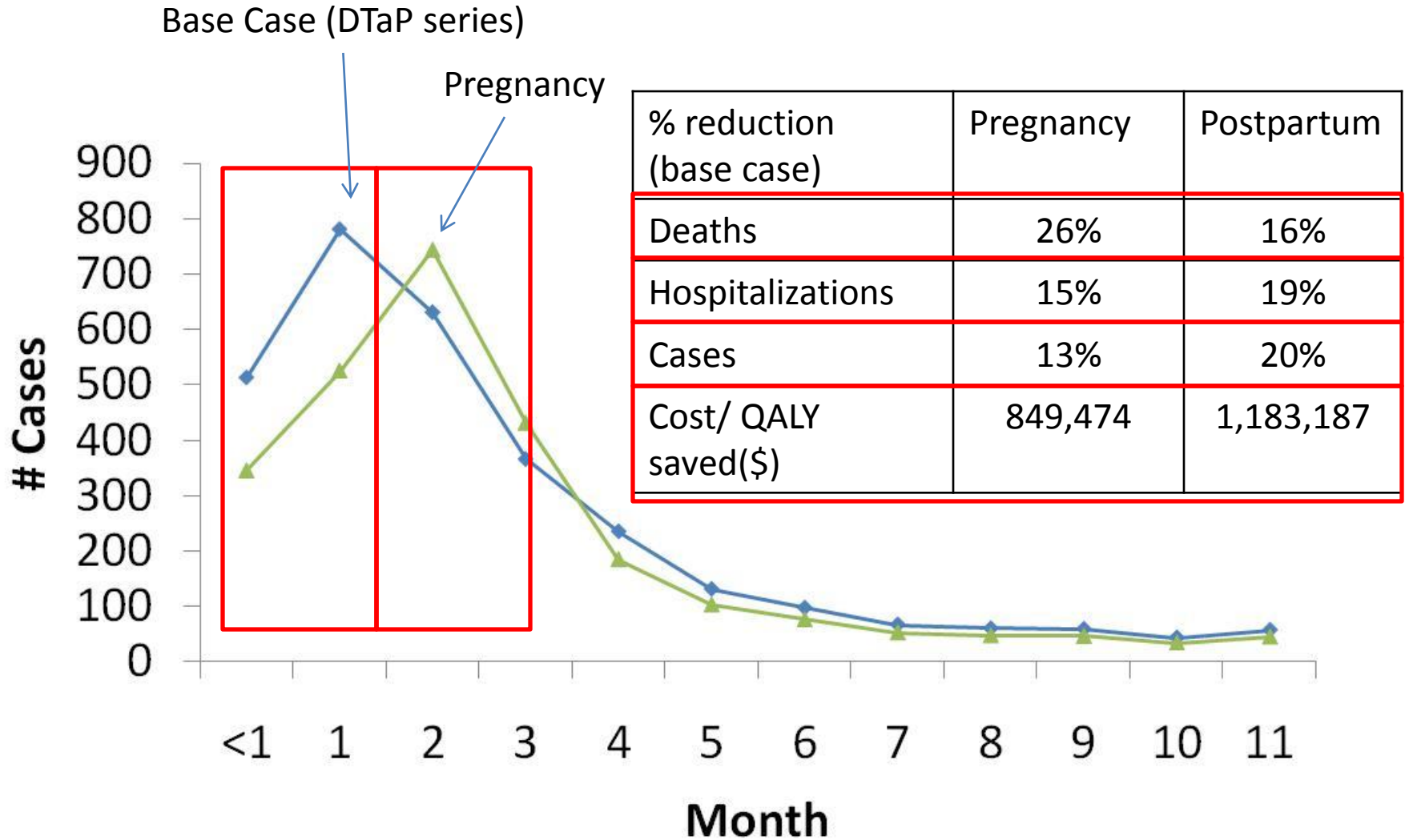
# Sensitivity Analyses

# Worst Case Scenario

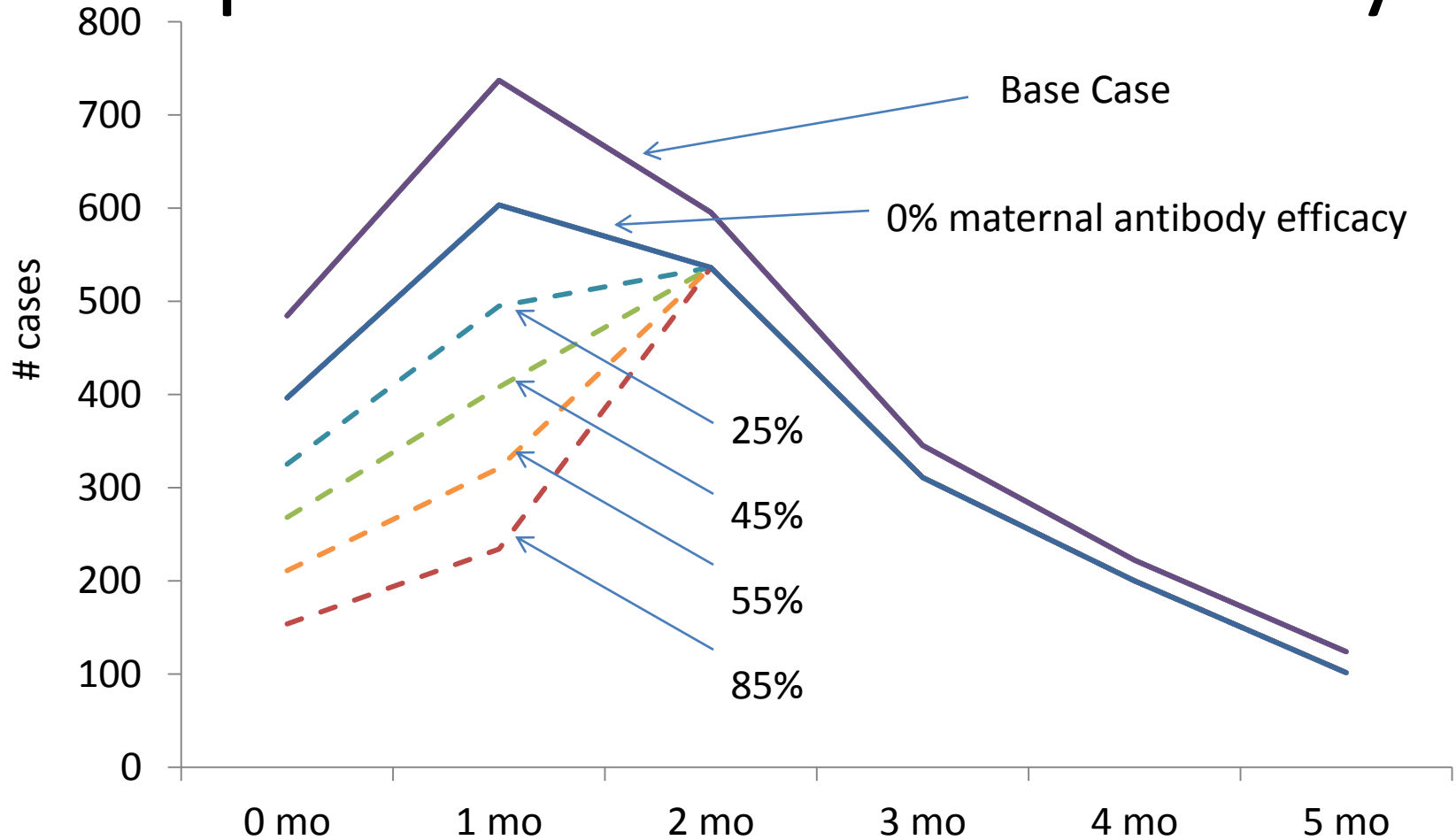
- 50% increase in risk of disease in months 2 and 3
- 20% efficacy of maternal antibodies

# Worst Case Scenario

**50% increase in risk of disease (months 3,4) & 20% maternal antibody effectiveness**



# Varying the efficacy of transplacental maternal antibody\*



\*Efficacy in mother held constant, 10% blunting