

SERVE VACCINARE GLI ADOLESCENTI E GLI ADULTI CONTRO LA PERTOSSE?

Susanna Esposito, Maria Francesca Patria

**Pediatria ad Alta Intensità di Cura, Università degli Studi di
Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore
Policlinico, Milano**

Agenda

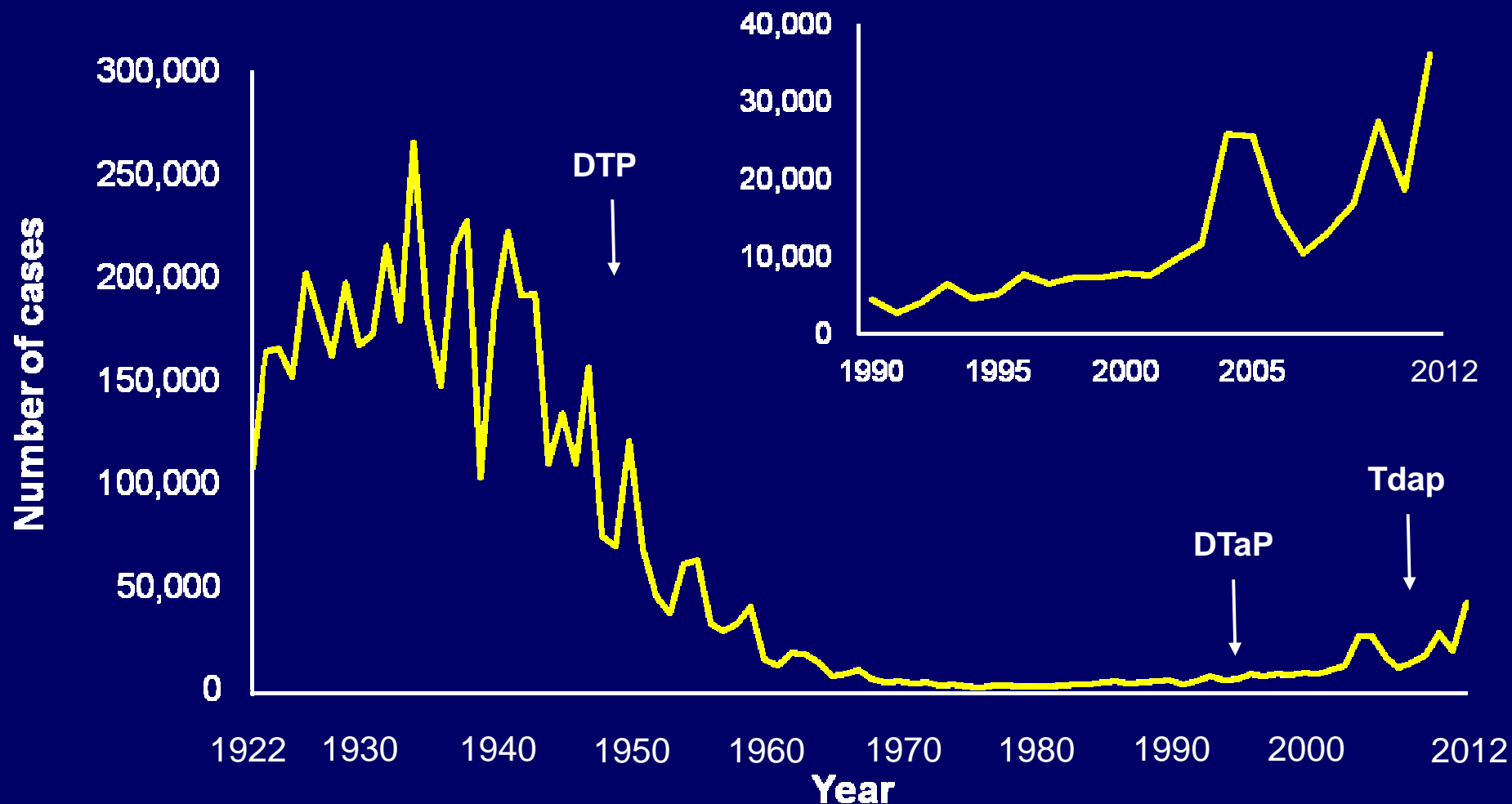
- **Global burden of pertussis**
- **Burden of pertussis in infants, adolescents and adults**
- **Reservoir of *Bordetella pertussis* and disease transmission**
- **Pertussis prevention strategies**
- **Cost-effectiveness of pertussis vaccination**
- **Conclusions**

Pertussis – The Global Problem

- Remains endemic worldwide
 - Estimated 20–50 million cases and 300 000 deaths each year¹⁻³
- Major public health problem, even in countries with sustained high vaccination coverage⁴
 - Incidences (2/100,000) in Japan to 124/100,000 in Switzerland)^{1,5}
- Vaccination has reduced the global burden of pertussis by over 90% compared to the pre-vaccine era⁶
- However, major pertussis epidemics have been reported over the last decades in many countries, including Europe, Japan, North and South America, Australia and New Zealand¹⁻¹¹

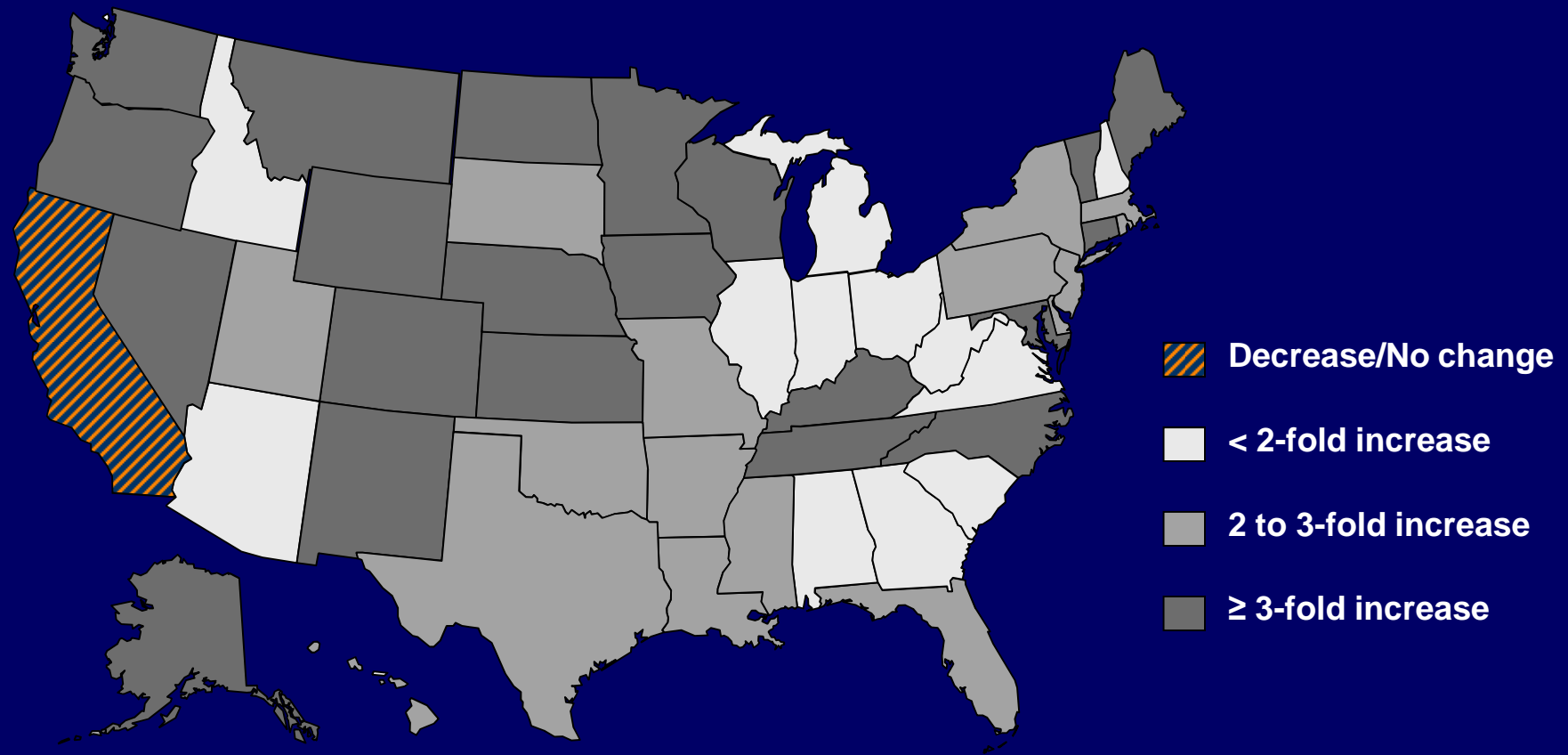
1. Celentano LP, et al. *PIDJ* 2005;24:761–5. 2. Crowcroft NS, Pebody RG. *Lancet* 2006;367:1926–36. 3. WHO. WHO-recommended surveillance standard of pertussis. Available at: http://www.who.int/immunization_monitoring/diseases/pertussis_surveillance/en/ (last accessed April 2013). 4. Tan T, et al. *PIDJ* 2005;24:S10–18. 5. Sato Y & Sato H. *Biologicals* 1999;27:61–69. 6. *Wkly Epidemiol Rec* 2010;85:385–400. 7 Sato H, Sato Y. *Clin Infect Dis* 1999;28(suppl 2):S124–30. 8. Kamiya H, et al. *EID* 2012;18:1166–1169. 9. Hozbor D, et al. *J Infect* 2009;59:225–31. 10. Hellenbrand W, et al. *BMC Infect Dis* 2009;9:22. 11. Grant CG & Reid S. *NZ Med J* 2010;123:46–61

Reported NNDSS Pertussis Cases: 1922–2012*



*2012 data are provisional

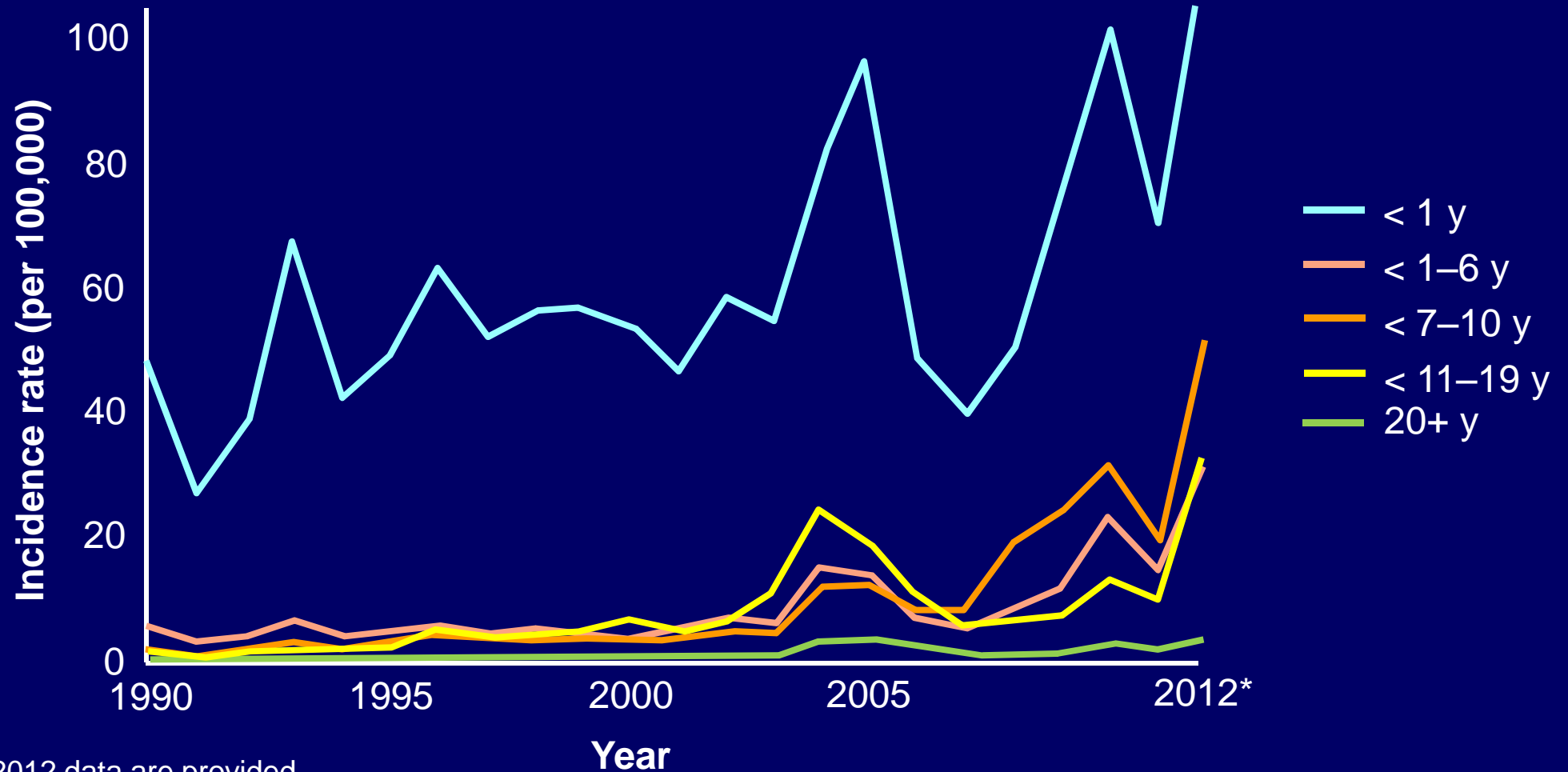
Changes in Pertussis Reporting by State 2011–2012*†



In 2012, the United States experienced one of the most severe pertussis epidemics seen in the last 50 years. There were almost 42,000 cases of the disease and 18 deaths. 15 of the deaths occurred in infants less than 2 months of age

**Data for 2012 are provisional and subject to change. †Cases reported through W 46 in 2011 were compared with cases reported through W 46 in 2012; fold-changes were calculated for each state*

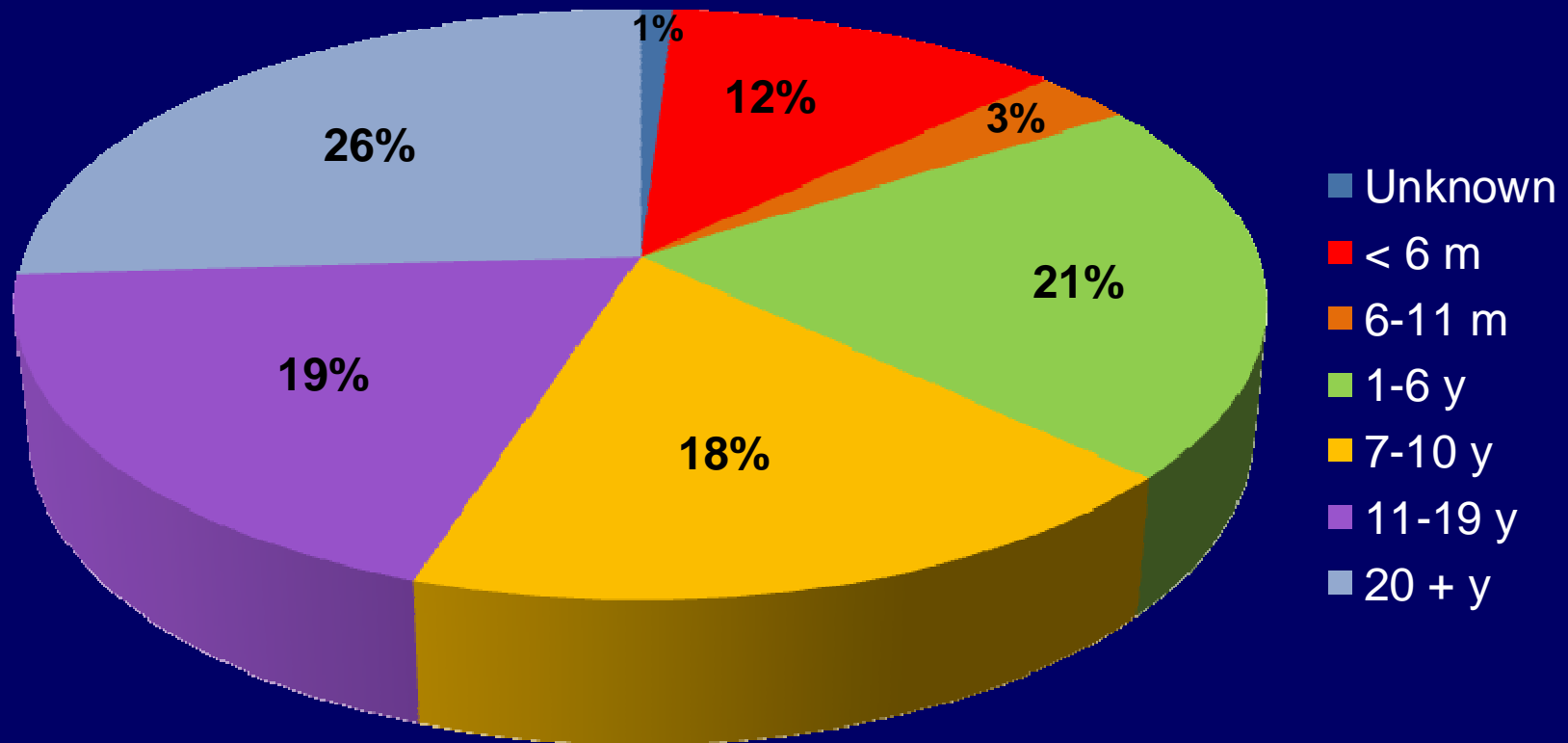
Reported Pertussis Incidence by Age Group: 1990–2012*



*2012 data are provided

Reported Pertussis Cases by Age Group – US 2010–2011

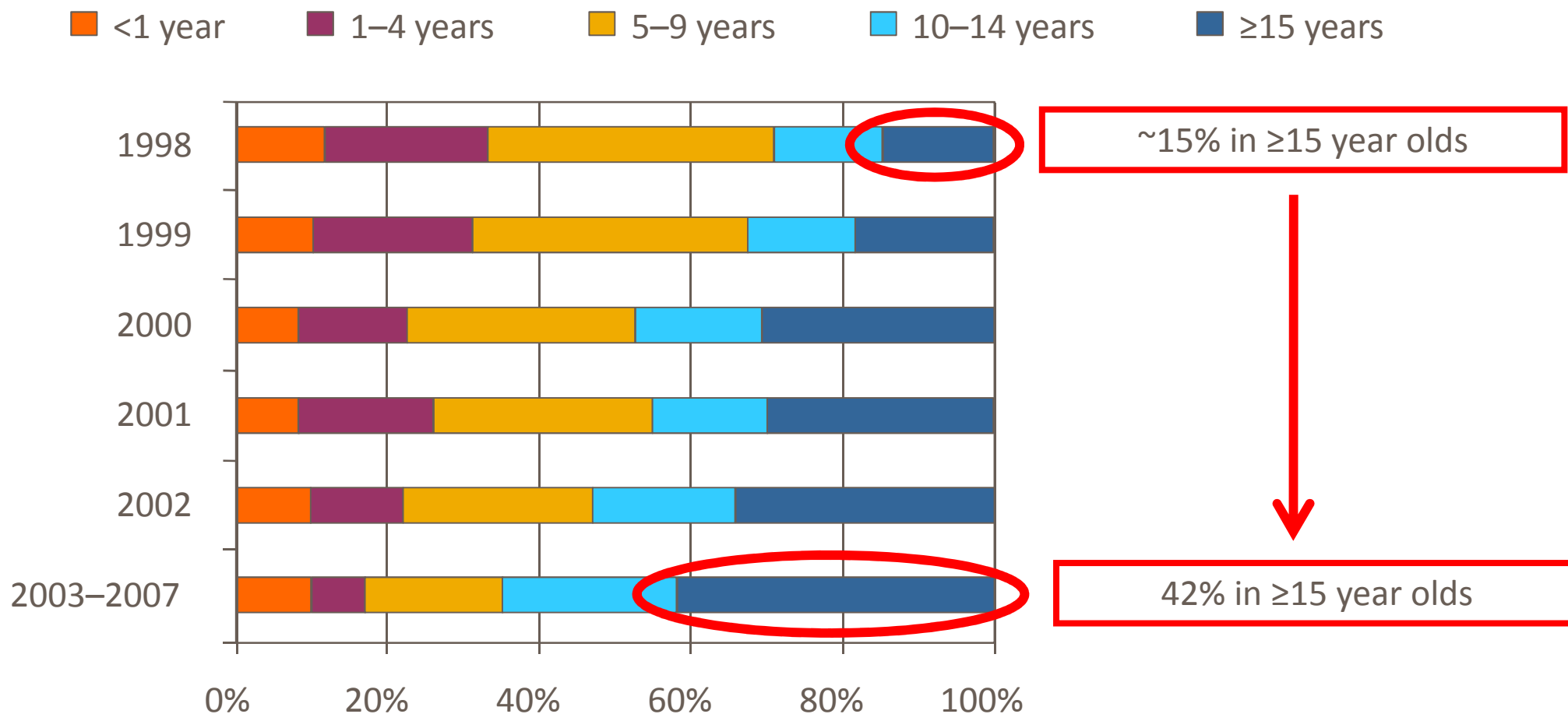
46,269 cases reported, 2010-2011



1. CDC. Data on file (2010 Final Pertussis Surveillance Report), Nov 2011.

2. MKT24380 and CDC. Data on file (2011 Final Pertussis Surveillance Report), Oct 2012.MKT26067.

Pertussis is shifting to older children and adults: Europe 1998–2007



Pertussis Morbidity and Mortality in Infants

- Highest incidence of morbidity and mortality consistently in infants < 6 months of age who are too young to have completed their primary immunization series
 - Of the estimated 300 000 deaths yearly worldwide, most are in young infants; 90% in developing countries with case-fatality rates estimated to be as high as 4% of infants < 12 months of age
 - In 2010, pertussis incidence in US infants < 6 months was 417.8/100,000 - which is 19.5 X the incidence of the general population (21.4/100,000)
 - Highest complications and hospitalization rate (70%)
 - Annually since 1990, 93–100% of pertussis-related deaths in the US have occurred in < 4 months of age
- The number of deaths being reported in the infant population has been steadily rising since the 1980s

Health Burden in Adolescents and Adults

- In adolescents and adults, pertussis is common, endemic and epidemic; its incidence is increasing^{1,2}
- Proportion of pertussis cases in ≥ 10 y in the US has increased from 15.1% in the late 1970s, to 49% in the early 2000s³
- Proportion of adults contaminated by Pertussis in Germany has increased from 20% in 1995 to 68% in 2007⁴
- True adult burden estimated at ~800,000 to 3.3 million cases annually in the US⁵
 - **Waning naturally induced and vaccine-induced immunity (~5-10 y)⁶⁻⁹**
 - **Increasing recognition**

1. Rothstein E, Edwards K. *Pediatr Infect Dis J* 2005;24:S44-7. 2. Tan T, et al. *Pediatr Infect Dis J* 2005;24:S10-18. 3. *MMWR* 1982;31(25):333-336. 4. Hellenbrand W, et al. *BMC Infect Dis* 2009;25:9:22. 5. Cherry JD. *Pediatrics* 2005;115:1422-1427; 6. *MMWR* 2006;55(RR-3):1-43. 7. Von Konig CHW, et al. *Lancet Infect Dis* 2002;2:744-750. 8. Lugauer S, et al. *Eur J Pediatr* 2002;161(3):142-146. 9. Salmaso S, et al. *Pediatrics* 2001;108(5):E81

Clinical Symptoms of Pertussis in Adolescents and Adults

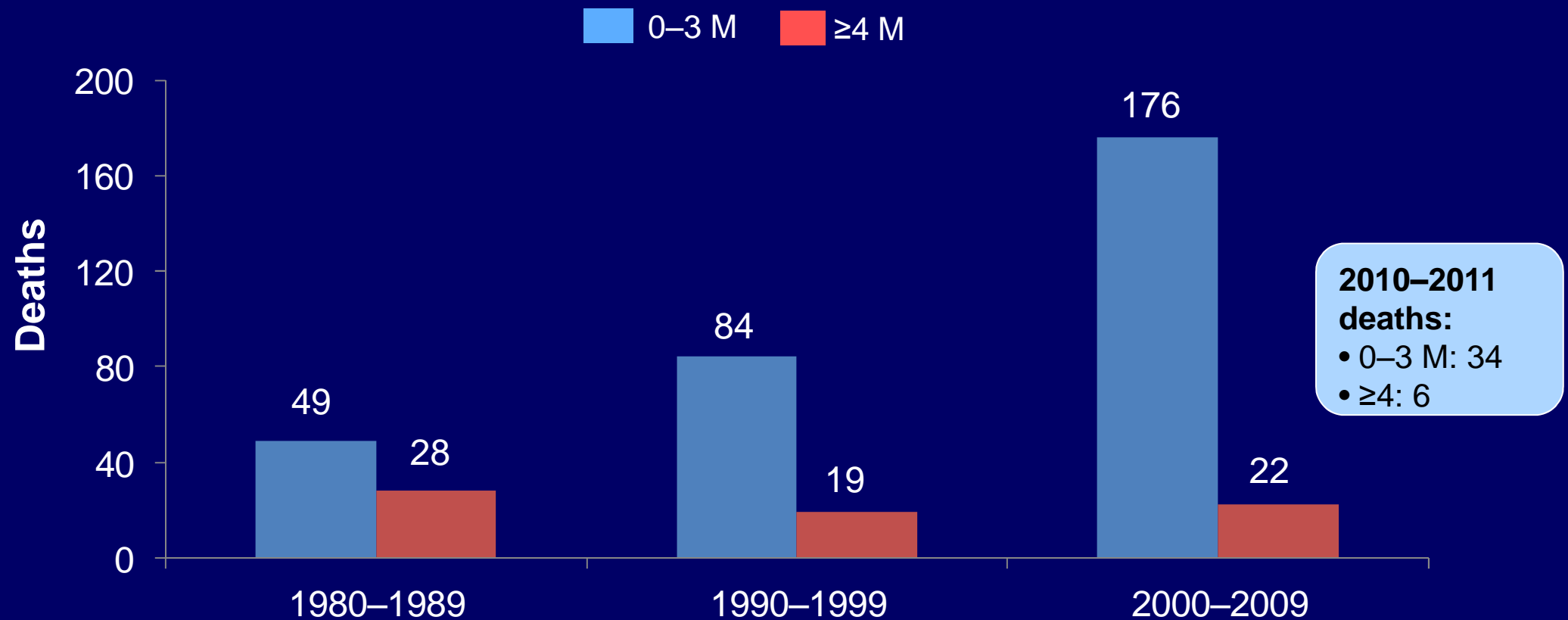
Clinical characteristic	Age group	
	Adolescents (%) (10–19 years)	Adults (%) (≥ 20 years)
Paroxysms	82–100	74–100
Whoop	30–67	8–82
Apnea	19–86	29–92
Cyanosis	6–15	0–12
Vomiting	45–71	10.5–70
Hospitalization	1.4–7.5	3.5–5.7

1. Aoyama T, et al. *AJDC* 1992;146:163–166; 2. Farizo KM, et al. *Clin Infect Dis* 1992; 14:708–719; 3. Postels-Multani S, et al. *Infection* 1995;23:139–142; 4. Schmitt-Grohé, et al. *Clin Infect Dis* 1995;21:860–866; 5. Trollfors B & Rabo E. *Br Med J Clin Res Ed* 1981;283:696–697.; 6. Yih WK, et al. *J Infect Dis* 2000;182:1409–1416; 7. DeSerres G, et al. *J Infect Dis* 2000;182:174–179

Complications of Pertussis in Children ≤ 4 Years of Age in the US, 1997–2000

Age	Hospitalization	Pneumonia	Seizures	Encephalopathy	Death	No. with Pertussis
< 6 M	4,543	847	103	15	56	7,203
6–11 M	301	92	7	1	1	1,073
1–4 Y	324	168	36	3	1	3,137

More Pertussis Deaths Occur in Infants ≤ 3 M: Death Rate Decreased from 2009 to 2010–2011



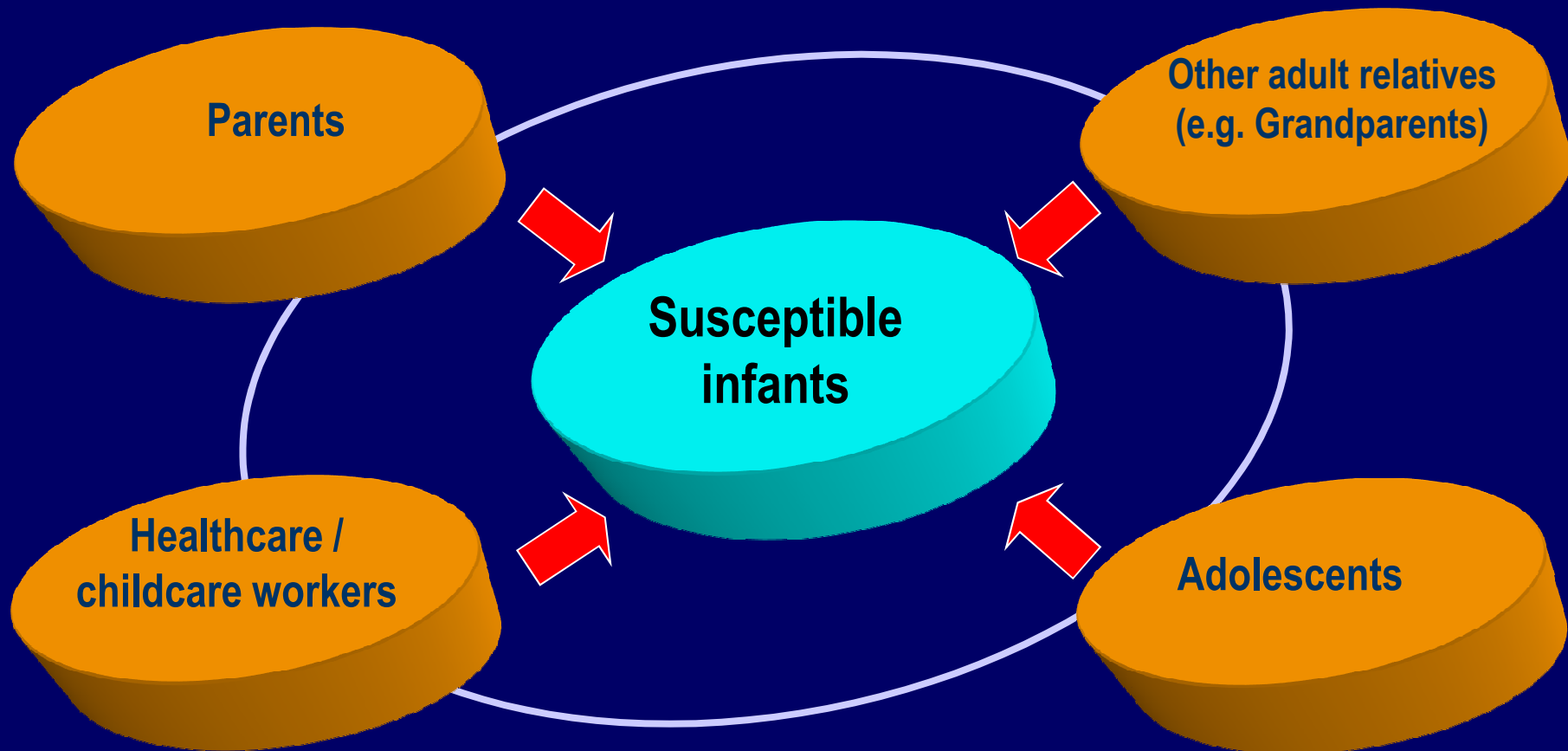
Notes: 1980–1989: Includes one case of unknown age. 2009: provisional

Liang JL. Pertussis in the United States. Slide presentation at National Cocooning Summit. Las Vegas, NV. March 15 2012.

Available at:

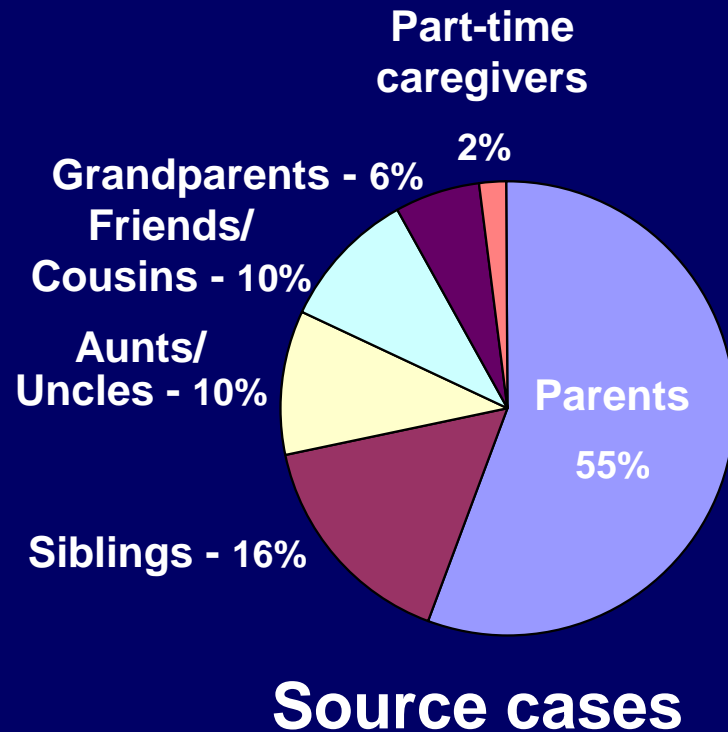
http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=2&ved=0CDkQFjAB&url=http%3A%2F%2Fsnicnv.org%2Fsnihc%2520Powerpoint%2FPertussis%2520in%2520the%2520United%2520States%2C%2520Jennifer%2520Liang%2C%2520DVM%2C%2520MPVM%2C%2520CDC%2C%25203.15.2012.ppt&ei=ht5_UbPHYqy0QXBtYCIbW&usg=AFQjCNFawEahWpd72pAIFwNPYakAEoRdDg&sig2=DioMaW_v6VgVwuVLYQCzeQ (slide 16. Last accessed April 2013)

Adolescents / Adults a Major Source of *B. pertussis* Infection for Infants



1. Baron S, et al. *Pediatr Infect Dis J* 1998;17:412–418; 2. Cattaneo LA, et al. *J Infect Dis* 1996;173:1256–1259; 3. Deen JL et al. *Clin Infect Dis* 1995;21:1211–1219; 4. Izurieta HS, et al. *Clin Infect Dis* 1996;22:503–507; 5. Nouvellon M, et al. *Infect Control Hosp Epidemiol* 1999;20:758–760; 6. Bisgard K, et al. *Pediatr Infect Dis J* 2004;23:985–989; 7. Wendelboe AM, et al. *Pediatr Infect Dis J* 2007;26:293-299

Pertussis Transmission to Young Infants



- Prospective international multicenter study of laboratory confirmed pertussis cases in ≤ 6 M and their household and non-household contacts – France, Germany, US, Canada
- 95 index cases and 404 contacts – source case was identified for 61.5% of index cases
 - mean age of the infant index case was 2.9 M (35 - < 2 mos; 38 - 2 to 3 mos; 22 - 4 to 6 mos)

Adolescent and Adult Groups for whom CDC Strongly Recommends Tdap Vaccine

- ALL Adolescents beginning at 11–12 years of age – No minimal interval between last Td and Tdap vaccine^{1,2} – (78.2% immunized)³
- ALL Adults especially those who are Close Key Contacts of Infants < 12 months of age⁴ – including persons ≥ 65 years of age^{1,5} – (13% immunized)⁶
- Healthcare workers who have direct patient contact in any hospital or clinic setting² – (27% immunized)⁶
- Wound Care – Any adolescent or adult who gets a severe cut or burn and needs protection against tetanus infection⁵
 - Tdap should be used in place of Td if person has not had a previous dose of Tdap⁴

Adolescent and Adult Groups for Whom CDC Strongly Recommends Tdap Vaccine

- Pregnant women (after 20 weeks gestation) who have not previously received a dose of Tdap should receive a dose¹ – (2.8% immunized)¹
- Newest recommendation: dose of Tdap should be given during each pregnancy between 27 weeks and 36 weeks regardless of the interval since the last pregnancy¹
- Postpartum administration of Tdap as soon as possible after delivery and before hospital discharge remains a viable option for those women who did not receive the vaccine during pregnancy and have never received a dose of Tdap vaccine in the past^{1,2}
 - Postpartum administration of Tdap is ONLY a one time dose^{1,2}

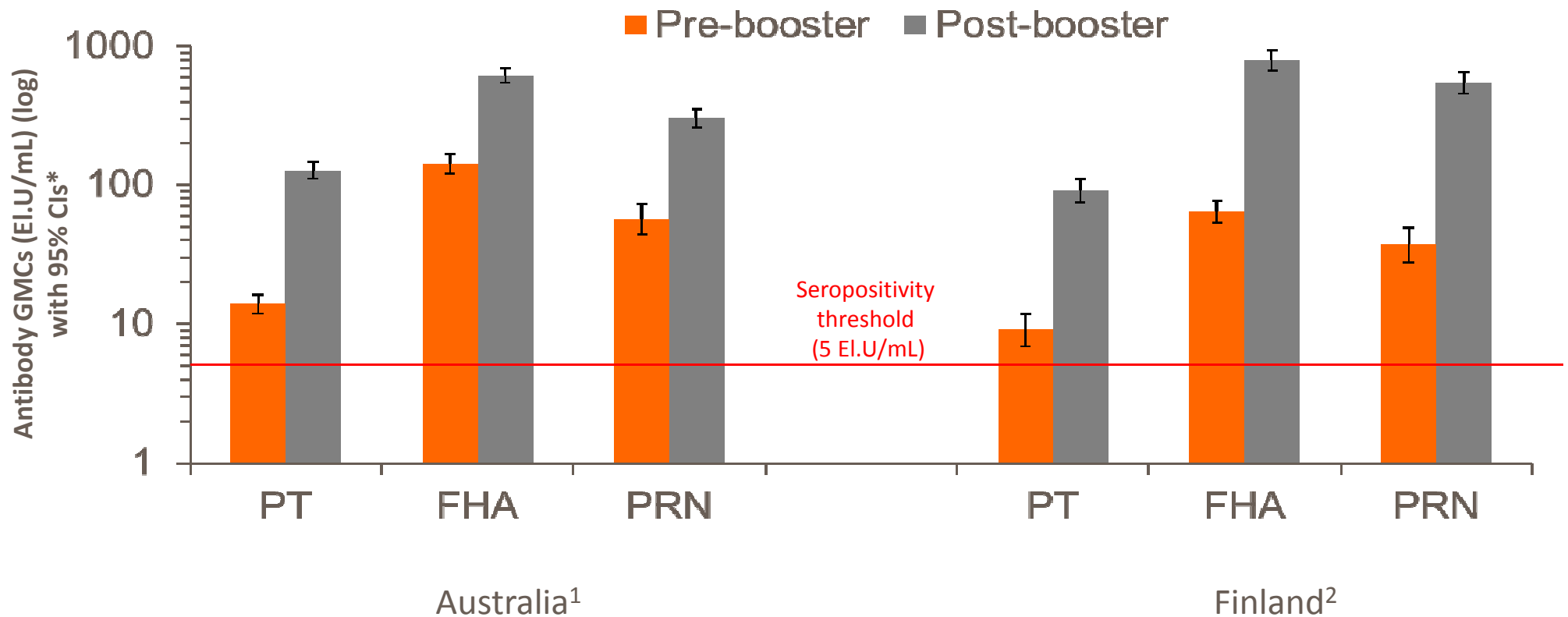
Adult and Adolescent Tdap Booster

- **ap booster vaccines specifically formulated for and licensed for use in the adolescent and adult populations**¹
- **Tdap has a similar safety profile to Td vaccine**^{2,3}
- **APERT (multicenter, randomized, double-blind trial) showed that ap boosters**⁴:
 - **Confer protection for adolescents and adults against symptomatic pertussis**
 - **Likely confer protection against mild and asymptomatic infections**
- **ap boosters contain lower amounts of diphtheria and ap antigens to prevent systemic and injection site adverse reactions**^{1,2}
 - **Td and Tdap can be given concomitantly or sequentially**⁵
 - **No minimal interval between Td and Tdap vaccines**⁶
- **ap boosters have been introduced for adolescents and adults in a number of countries including Italy, France, Germany, Australia, Canada, US, Argentina**^{1,7}

dTpa elicited a robust increase in pertussis antibodies when administered as a decennial booster



Ambro/FreeDigitalP
hotos.net

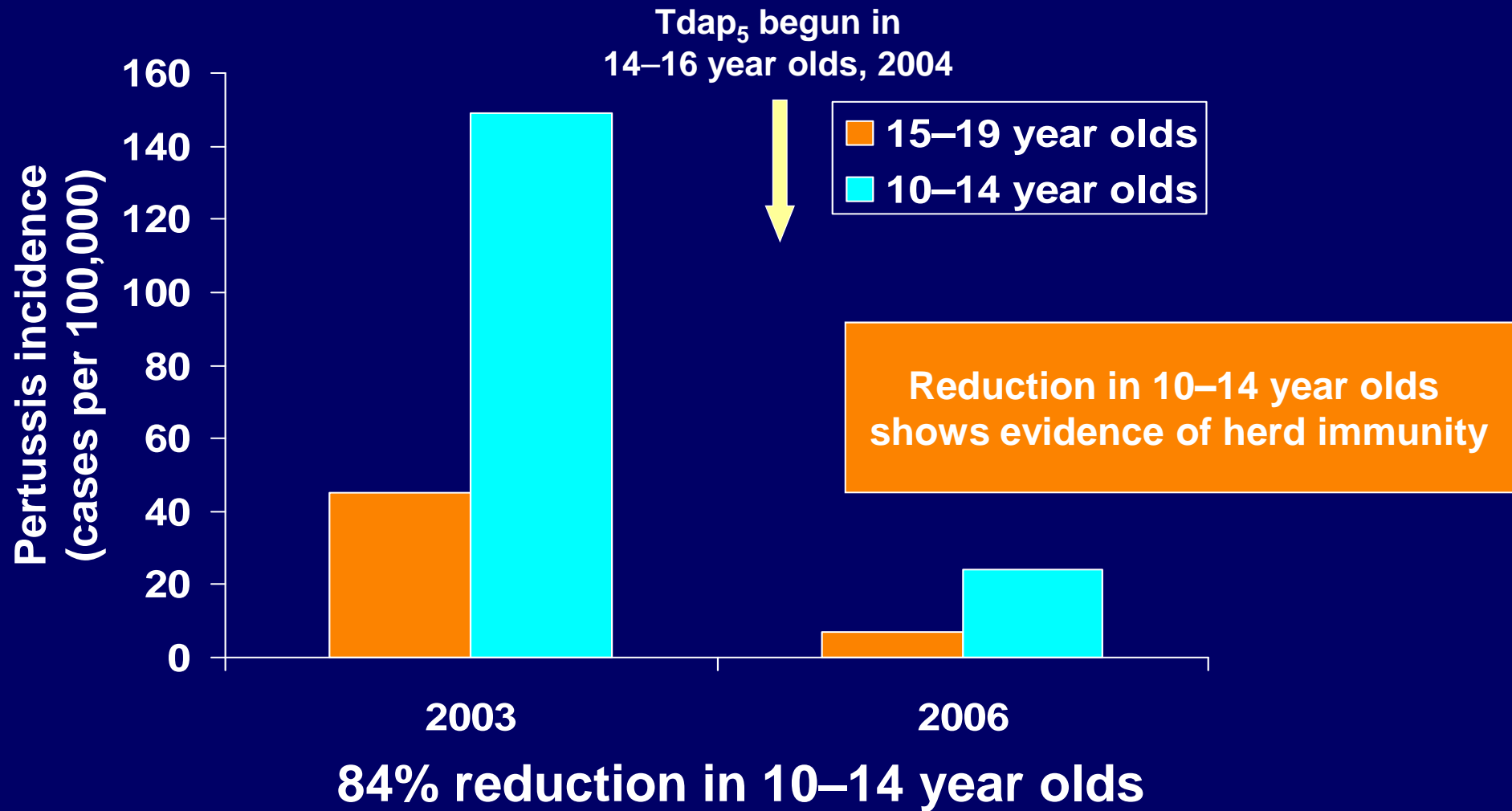


- In both studies, the decennial booster was generally well tolerated

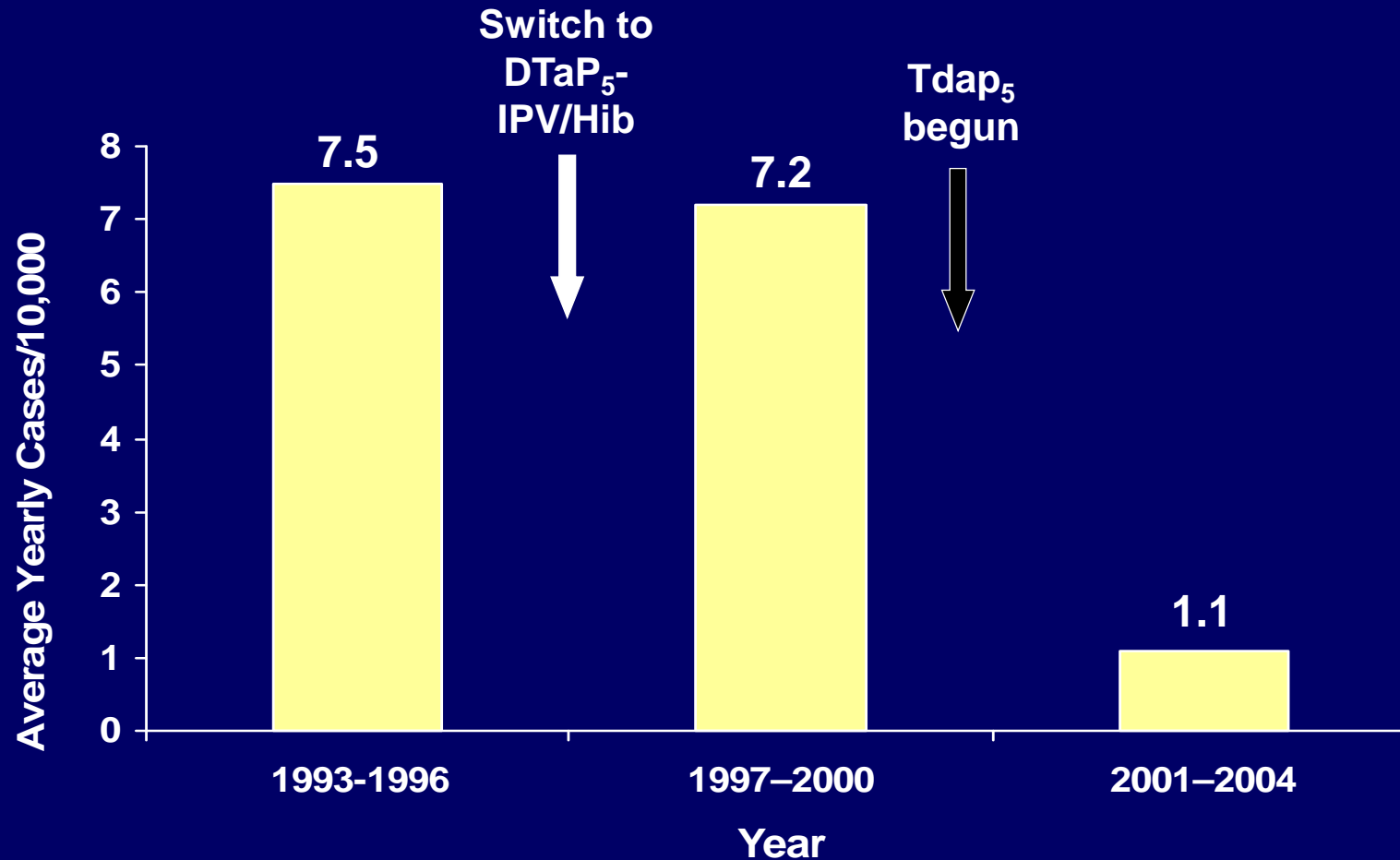
1. Booy *et al. Vaccine* 2011; 29: 45–50
2. Mertsola *et al. Clin Infect Dis* 2010; 51: 656–62

*Data are presented for group originally vaccinated with dTpa

Pertussis Incidence, British Columbia



Pertussis Incidence, Northwest Territories, 1993–2004



DTaP₅-IPV/Hib vaccine was adopted for infants and children in Northwest Territories 1997 and Tdap₅ vaccine was adopted for adolescents in early 2001

Adolescent and Adult Pertussis Vaccine Recommendations in Europe

Country	Pertussis containing vaccine
Austria	Tdap 13 years, Tdap 18-20 years, Tdap every 10 years until 60 years, then every 5 years
Belgium	Tdap 14-16 years, cocoon
Finland	Tdap 14-15 years
France	DTaP-IPV 11-13 years or if missed catch up Tdap-IPV 16-18 years, Tdap-IPV once in adulthood, HCW, CCW, cocoon
Germany	Tdap or Tdap-IPV 9-17 years, Tdap once in adulthood, HCW, CCW, cocoon
Greece	Tdap 11-12 years, if missed Tdap once in adulthood
Ireland	Tdap 11-14 years
Italy	Tdap 11-12 years
Luxembourg	Tdap-IPV 15-16 years, then every 10 years
Norway	Tdap in adults every 10 years until 60 years
Sweden	Tdap 14-16 years
Switzerland	Tdap 11-15 years, Tdap 25-29 years, cocoon

Antepartum and Cocooning Programs

Major objective

- **Protect young infants, who are too young to be immunized, from getting pertussis disease** ¹⁻⁴

Rationale

- **Targeted Tdap immunization of all potential adolescent and adult contacts of infants**^{1,2}

Vaccination strategies close contacts of the infant

- **Pregnant women between 27 and 36 weeks gestation with each pregnancy and postpartum mothers**^{1,3,4}
- **Family members and relatives**^{1,2,4}
- **Babysitters, nannies, daycare providers**
- **Other close contacts**⁴

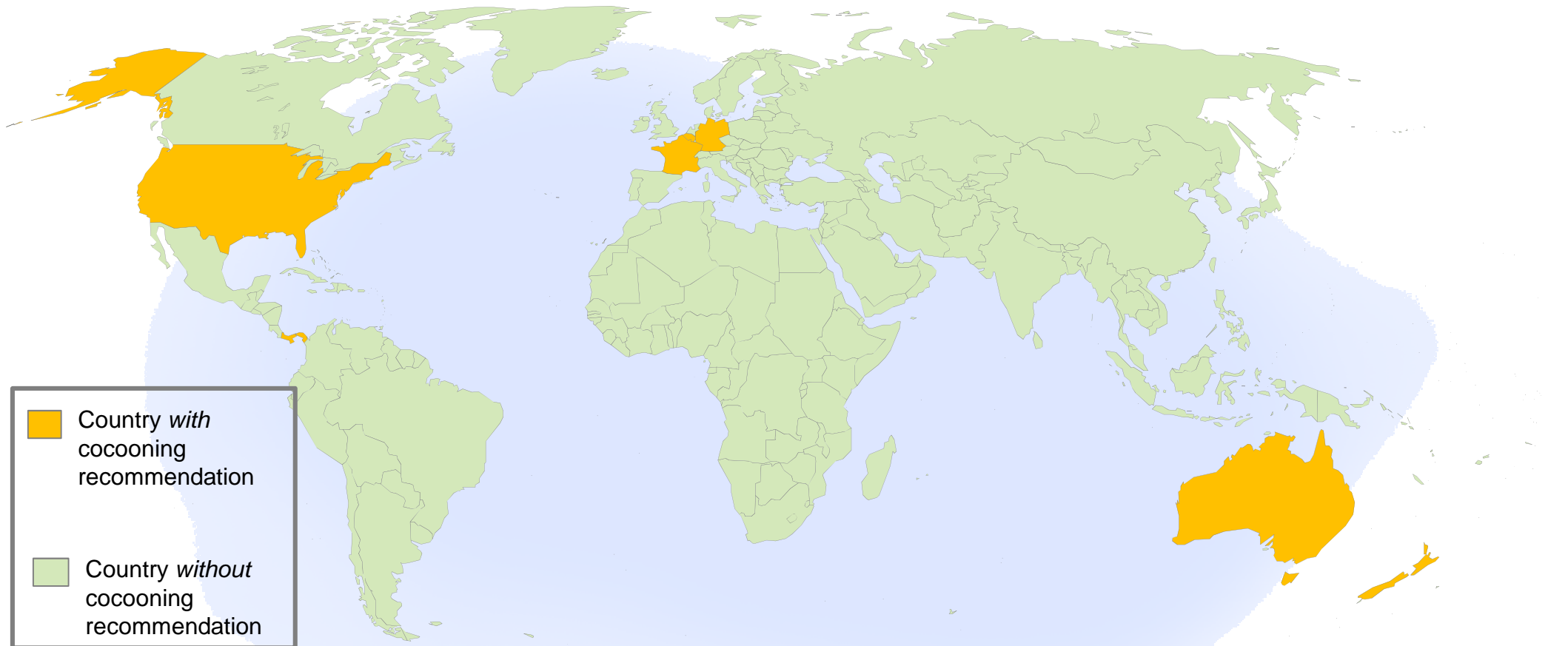
Cost-effectiveness of Adult Pertussis Vaccination

- A German model has suggested that an adult pertussis vaccination program would be cost effective
 - A one-time adult vaccination strategy would prevent 498,000 cases
 - A decennial adult vaccination strategy would prevent 1 million cases
- The programs would cost
 - €366 million and €687 million, respectively
 - €160 and €200 per case prevented, respectively

Cost-effectiveness of Pertussis Immunization Strategies Aimed at Protecting Infants

- A Dutch model evaluated the cost-effectiveness of 3 immunization strategies:
 - Infant immunization at birth (cohort of 200,000)
 - Parents immunization immediately after birth of infant (cocooning) (cohort of 401,380)
 - Maternal immunization during the 3rd trimester of pregnancy (cohort of 201,380)
- Cocooning and maternal immunization were found to be cost-effective and cost saving assuming a 200-fold underreporting factor:
 - Payer's perspective - €4600/QALY and €3500/QALY, respectively
 - Societal perspective - savings of up to €7200 and €500, respectively

Countries with cocooning recommendations



1. Australian Immunisation Handbook 9th edition 2008; Part 2.3.2, available from: <http://www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-specialgroups> (accessed June 2011); 2. Kinkhoest (pertussis) – vaccinatie. Available from: <http://www.zorg-en-gezondheid.be/Ziektes/Vaccinaties/Vaccins-A-Z/Kinkhoest-%28pertussis%29---vaccinatie/> (accessed June 2011); 3. Haut conseil de la santé publique. *Bulletin Épidémiologique Hebdomadaire* 2009;16–17:46–76; 4. Impfpfehlungen der Ständigen Impfkommission am Robert Koch-Institut/Stand: Juli 2010. *Epidem Bull* 2010;30:279–98; 5. New Zealand Ministry of Health Immunisation Handbook 2011; Ch 6; 6. CDC. *MMWR* 2011;60:13–5; 7. <http://www.cdc.gov/vaccines/recs/provisional/default.htm> (accessed August 2011); 8. WHO vaccination schedule, available from: http://apps.who.int/immunization_monitoring/en/globalsummary/ScheduleSelect.cfm (accessed June 2011)

Conclusions

- **Pertussis remains a major public health problem especially in adolescents and adults where the incidence of disease is increasing and causing a substantial disease burden**
- **Most infants are infected by an adolescent or adult contact**
- **Development of improved surveillance systems and recognition of adolescent and adult pertussis disease is needed**
- **In order to control spread of disease, vaccine strategies focused on increasing vaccination rates in the adolescent and adult populations are critical**
- **Cocooning is a cost-effective and increasingly common method to protect infants from disease**
- **Educational interventions are required for HCW and patients to increase awareness of adolescent and adult pertussis disease and importance of Tdap vaccination**