

SAGE Working Group on Pertussis Vaccines

Summary of Evidence: Strategies to Prevent Early Mortality

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WHO SAGE Meeting

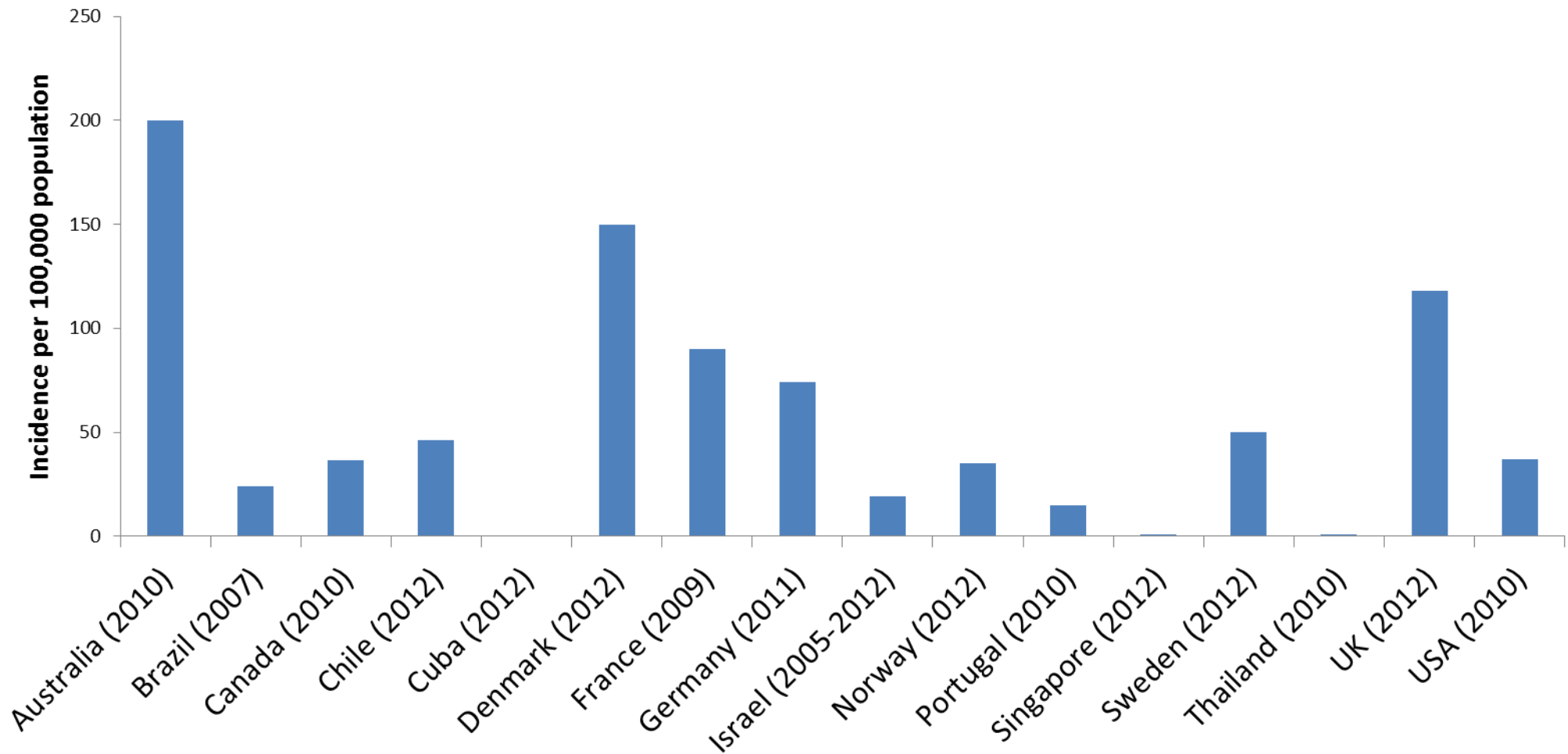
April 1-3, 2014

Strategies to Prevent Infant Mortality

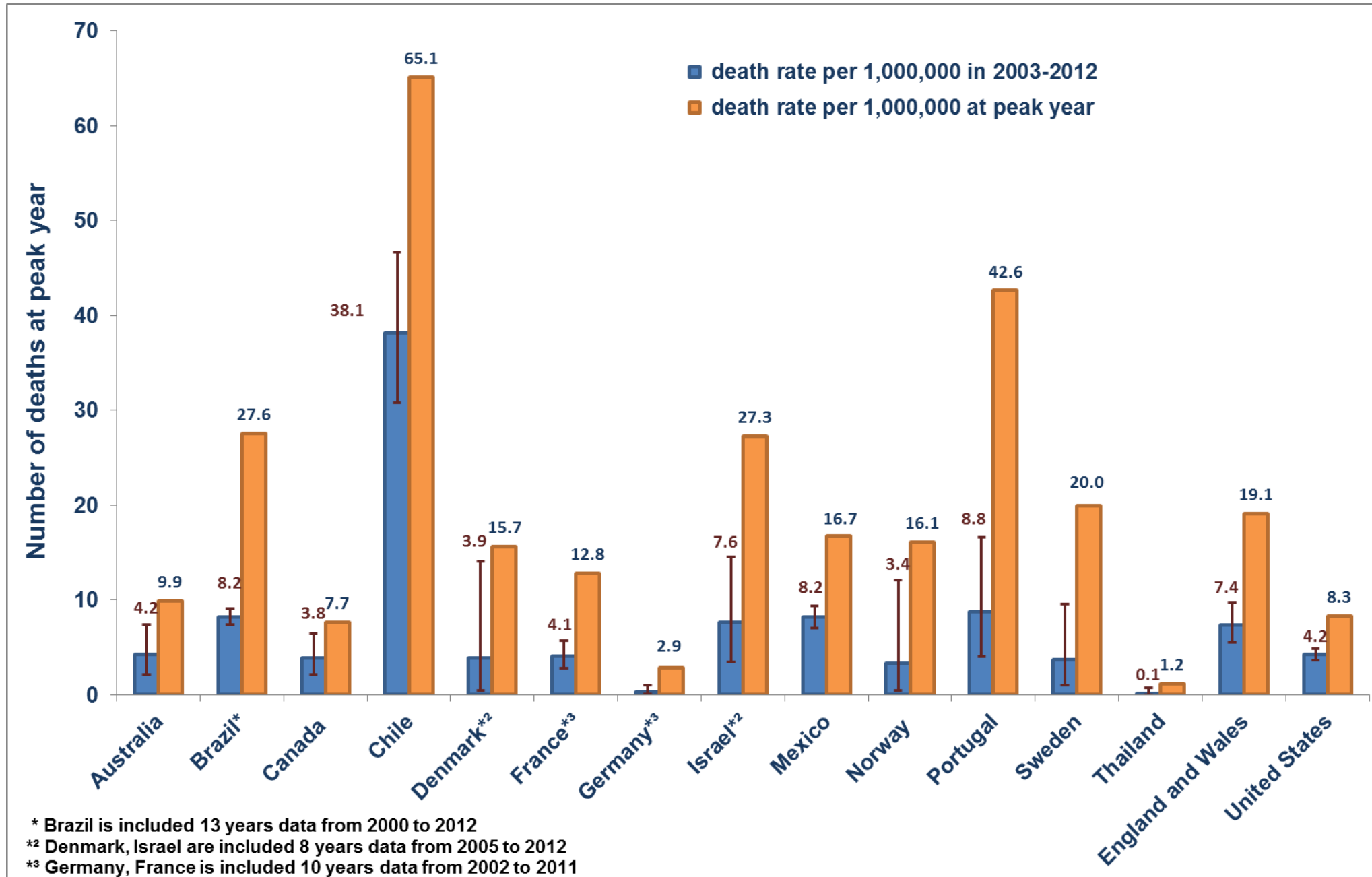
- 1 or 2 doses of pertussis vaccine
- Maternal immunization
- Newborn immunization
- Cocooning
- Health care worker immunization



Infant Hospitalizations – Recent Data



Infant Mortality – Recent Data



EFFECTIVENESS OF 1 OR 2 DOSES OF PERTUSSIS VACCINE



1 or 2 Dose Effectiveness

- Background
 - In 2009, insufficient data to determine effect of 1 or 2 doses on mortality
 - Country questionnaire included data request
 - Mortality data remain limited
 - Effect on severe infant morbidity and/or hospitalization also assessed
 - Assessment of effectiveness preliminary
 - May change with systematic review of vaccination schedules
 - However, data consistent and convergent across multiple studies

1 or 2 Dose Effectiveness

Country/ Vaccine	Single dose	Two doses
Australia (aP) Quinn et al (2014)	VE hospitalization: 55% (95%CI: 43-65%)	VE hospitalization: 83% (95%CI: 70-90%)
England (aP or wP) Campbell et al (2012)	VE against infant pertussis disease: 62% (95%CI: 53-69%)	VE against infant pertussis disease: 85% (95%CI: 77-91%)
France (wP) Briand et al (2007)	VE against infant pertussis disease: 58%	VE against infant pertussis disease: 87%
Germany (aP) Juretzko et al (2002)	VE hospitalization: 68.0% (95%CI: 45.6-81.1)	VE hospitalization: 91.8% (95%CI: 84.7-95.7)
USA (wP or aP) Unpublished data	VE against pertussis disease in ages 6-23mo: 50.5% (95% CI: -71.1-86.3)	VE against pertussis disease in ages 6-23mo: 80.1% (95% CI: 41.3-93.2)

1 or 2 Dose Effectiveness

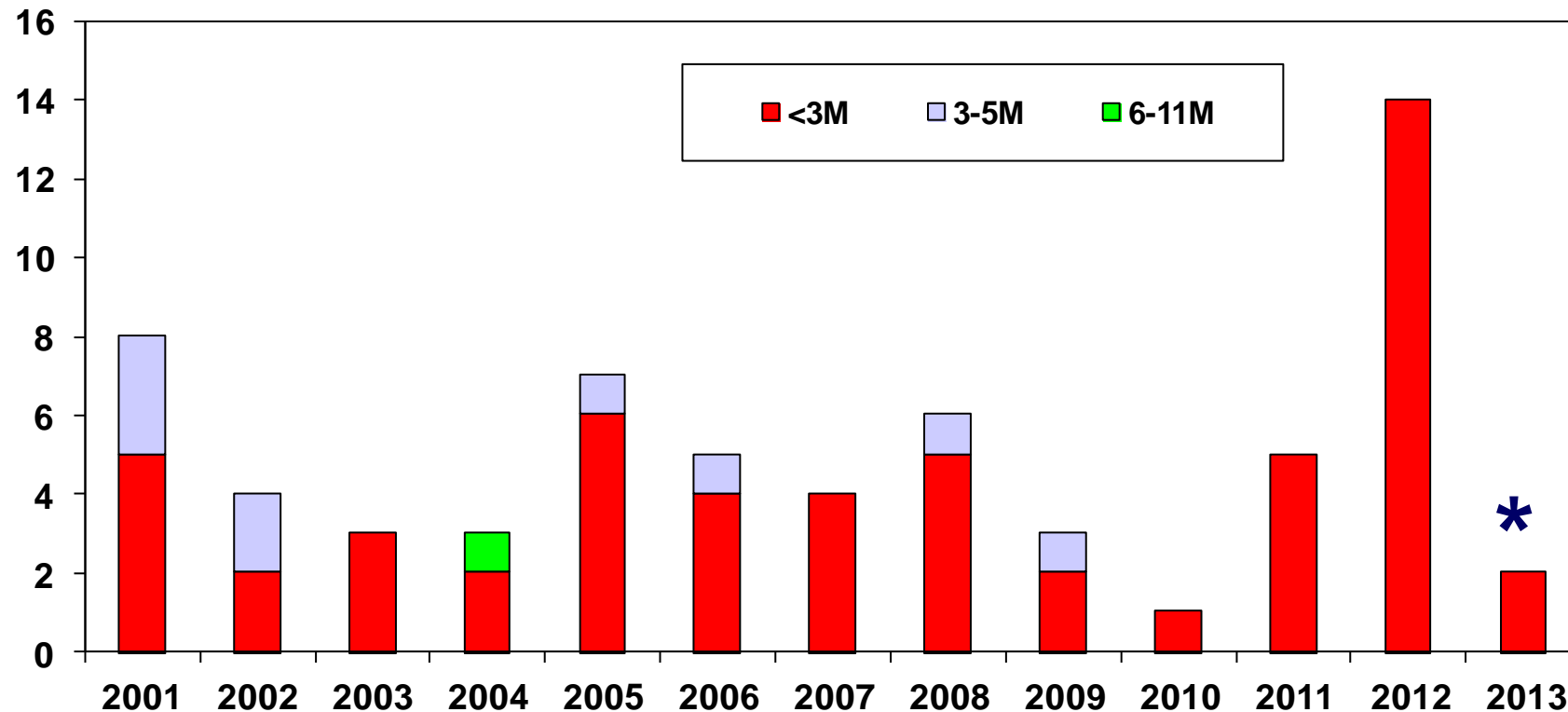
- Conclusions
 - Overall vaccine effectiveness
 - 1 dose of aP or wP >50% effective
 - 2 doses of aP or wP >80% effective
 - No evidence of superiority for any aP vaccines
 - Early first dose critical
 - As soon as possible ≥ 6 weeks
 - Pertussis incidence peaks in 2nd month prior to routine vaccination
 - Timing based on local epidemiology and vaccine delivery system
 - Must complete entire series to prevent morbidity in older age groups and prevent transmission to unvaccinated infants

MATERNAL IMMUNIZATION

RECENT UK EXPERIENCE



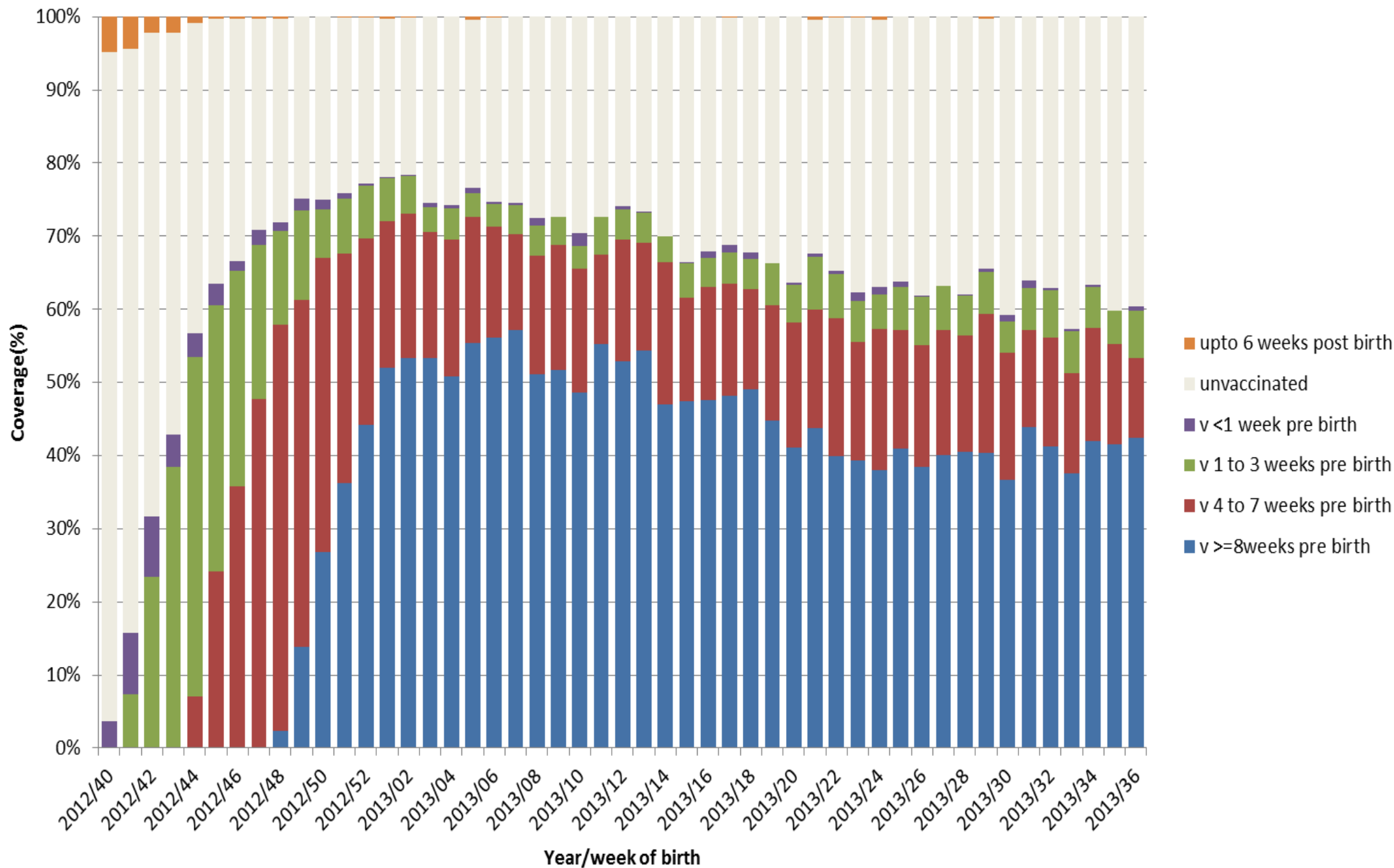
Reconciled deaths from pertussis in infants, England only



Sources: lab confirmed cases, certified deaths, Hospital episode statistics, GP registration details

* Both with unvaccinated mothers

% of mothers vaccinated by week of birth of infant (to 3/9/2013) and timing prior to delivery: Data from the Clinical Practice Research Datalink which covers 12.5 million UK patients



Laboratory confirmed cases. January to September 2008 to 2013 England only

Age group	2008	2009	2010	2011	2012	2013	% change 2013 vs 2011
<1 month	24	16	6	16	43	10	-38
1 month	67	43	22	57	161	37	-35
2 months	58	29	15	45	124	25	-44
3-5 months	33	20	6	21	62	22	5
6-11 months	8	3	3	7	22	7	0
1-4 years	21	19	7	10	58	41	320
5-19 years	184	121	59	124	1128	669	440
20+ years	307	304	186	349	4311	2984	755
Total	702	555	304	629	5909	3795	503

Maternal pertussis vaccine effectiveness by timing of vaccination in relation to delivery using the screening method: data to September 2013

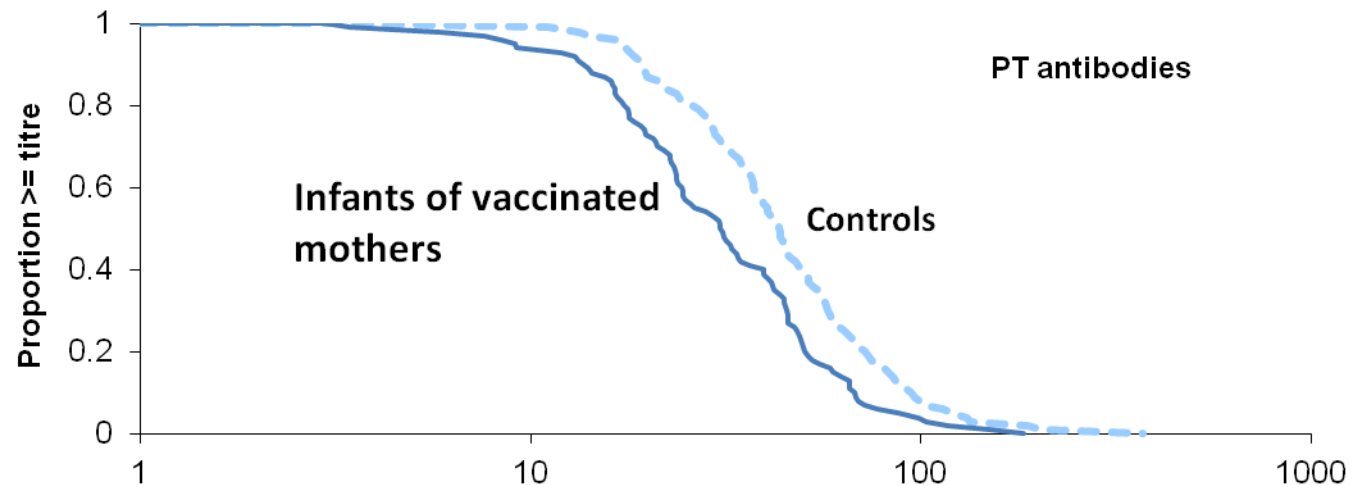
Timing of maternal immunisation	VE (95% CI)
At least 7 days before birth	91% (84% to 95 %)
At least 28 days before birth	91% (83% to 95%)
7 to 27 days before birth	91% (70% to 96%)
0-6 days before or 1-13 days after birth	38% (-95% to 80%)

Maternal Immunization

Some reduction in infants' post primary responses to pertussis antigens, diphtheria, meningococcal C conjugate and some pneumococcal serotypes

The clinical significance of these reductions is uncertain

(PT antibody response is shown here, similar results for FHA and fimbrial antibodies)

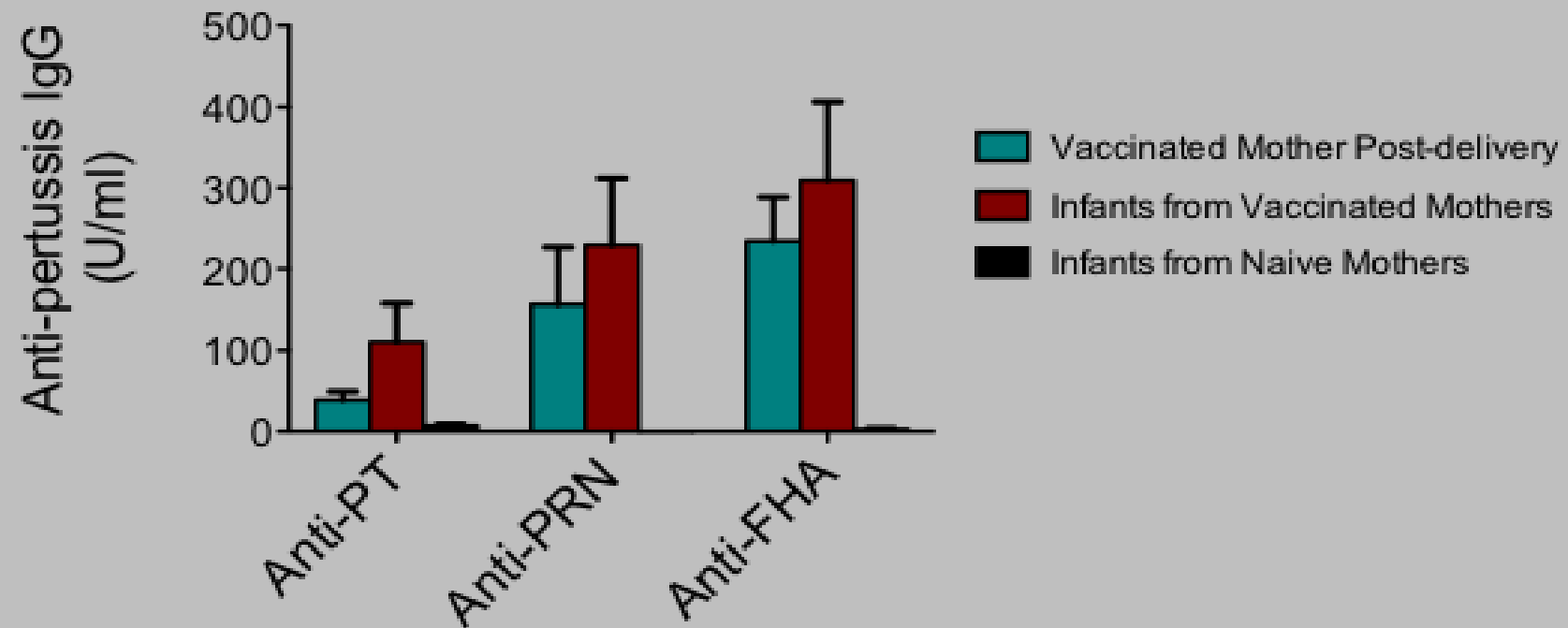


Safety assessment by Medicines and Healthcare Regulatory Agency

Pregnant women with a record for a pertussis-containing vaccination from 01/10/2012 to 31/03/2013 were identified in the Clinical Practice Research Datalink. Stillbirth rates following vaccination were compared to published national background data. A matched cohort study, using historical unvaccinated controls, examining a range of pre-defined pregnancy-related adverse events was also conducted.

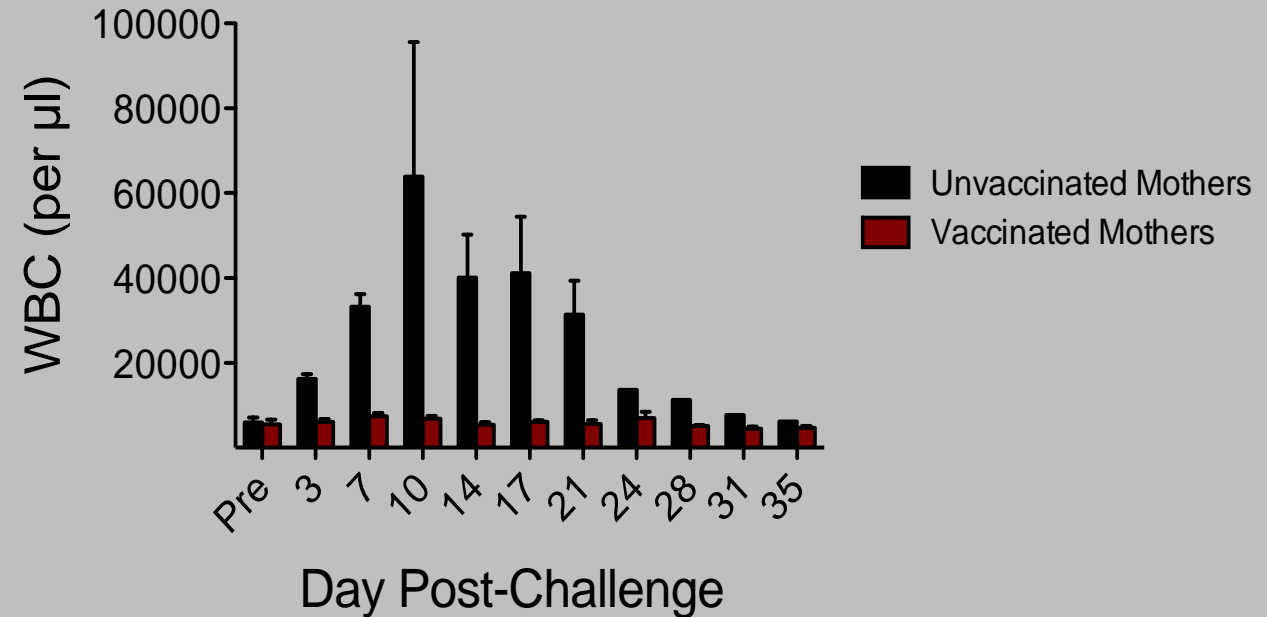
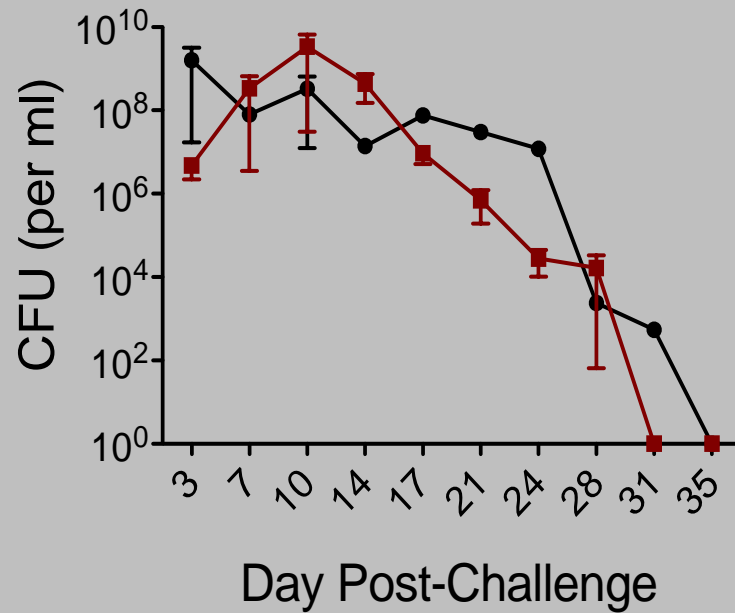
Follow up information on 17,560 vaccinated women. No adverse affects on fetal or obstetric outcomes identified

Baboon Trans-placental transfer of Maternal IgG



*Attribution: Tod J. Merkel et al
Laboratory of Respiratory and
Special Pathogens CBER/FDA*

Baboon Maternal Vaccination Confers Protection



Infants born to vaccinated mothers exhibit no signs of infection

- No leukocytosis
- No coughing
- No reduction in activity

*Attribution: Tod J. Merkel et al
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Maternal Immunization

- **Conclusions**
 - aP vaccine safe and effective for pregnant women.
 - High impact on infant pertussis incidence and mortality
 - Direct: protection via transfer of maternal antibodies
 - Indirect: Lower risk of transmission through protection of the mother
 - Some reduced post-primary antibody levels in infants of vaccinated mothers (USA, Canadian and E&W infant immunogenicity studies)
 - Clinical significance uncertain
 - No evidence so far of increased risk of pertussis in UK infants after primary immunisation
 - aP findings cannot be extrapolated to wP vaccines without additional immunogenicity and safety data

NEWBORN IMMUNIZATION



Newborn Immunization: Conclusions

- Neonatal immunization not recommended at this time
 - Evidence of immunogenicity in infants but limited data on impact and safety
 - Data from baboon infants receiving a single vaccine dose demonstrate protection against severe pertussis disease
 - Lack of availability of an aP alone vaccine
 - Window period of susceptibility
- Continued evaluation recommended
 - If data supporting immunogenicity, protection, and safety become available, it may have supplementary role along with maternal vaccination

COCOONING

Cocooning

Rationale

- Aims to protect young infants by reducing their risk of exposure to pertussis
- Requires vaccination of the most likely sources of infection for the infant
 - Parents, siblings, grandparents...

Cocooning: Conclusions

Based on unpublished data from Australia and Chile:

Quinn et al. Effectiveness of preventing infant pertussis by the 'cocooning' strategy: NSW case-control study

- May reduce severe infant morbidity
 - Timing is crucial
 - Cost-effectiveness lower than maternal or neonatal vaccination due need to vaccinate larger number of individuals
- Advantages
 - Possible better acceptability of vaccination post-partum than during pregnancy in some settings
- Disadvantages
 - Delay in protection, logistic difficulties, effectiveness of aP against transmission?

HEALTH CARE WORKER IMMUNIZATION



Health Care Worker Immunization

- Results

- Approaches include vaccination of all HCWs or those with increased pregnancy, newborn, or infant contact
- No evidence for prevention of transmission to infants
 - But case/outbreak reports HCW role in nosocomial pertussis transmission
 - Only partially effective - documented transmission from dTap vaccinated HCWs

- Conclusions

- HCW are highest priority group in adult vaccination programs
 - Implementation logistically difficult in absence of adult program
- Needs revisiting - degree of aP protection from infection unclear

Summary

- 1 or 2 doses of pertussis vaccine
 - Effective in preventing mortality/severe disease
 - Timely vaccination with start of series at 6 weeks is important
- Maternal immunization
 - Overall reduction in infant mortality
 - Direct: protection via transfer of maternal antibodies
 - Indirect: lower risk of transmission through protection of the mother
 - Issue of cost-effectiveness
 - May be cost effective in some high income settings

Summary

- **Cocooning**
 - When applied with high coverage, cocooning strategies may have an impact on infant disease
 - Degree of effect varies with setting and coverage rate
- **Newborn immunization**
 - Not currently recommended due to limited data on impact and safety, gap in protection, and lack aP alone vaccine
- **Health care worker immunization**
 - Existing adult programs should prioritize health care workers to reduce risk of transmission to infants