Using the Wisconsin Immunization Registry to Estimate Tdap Effectiveness for Preventing Pertussis

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Disclosures

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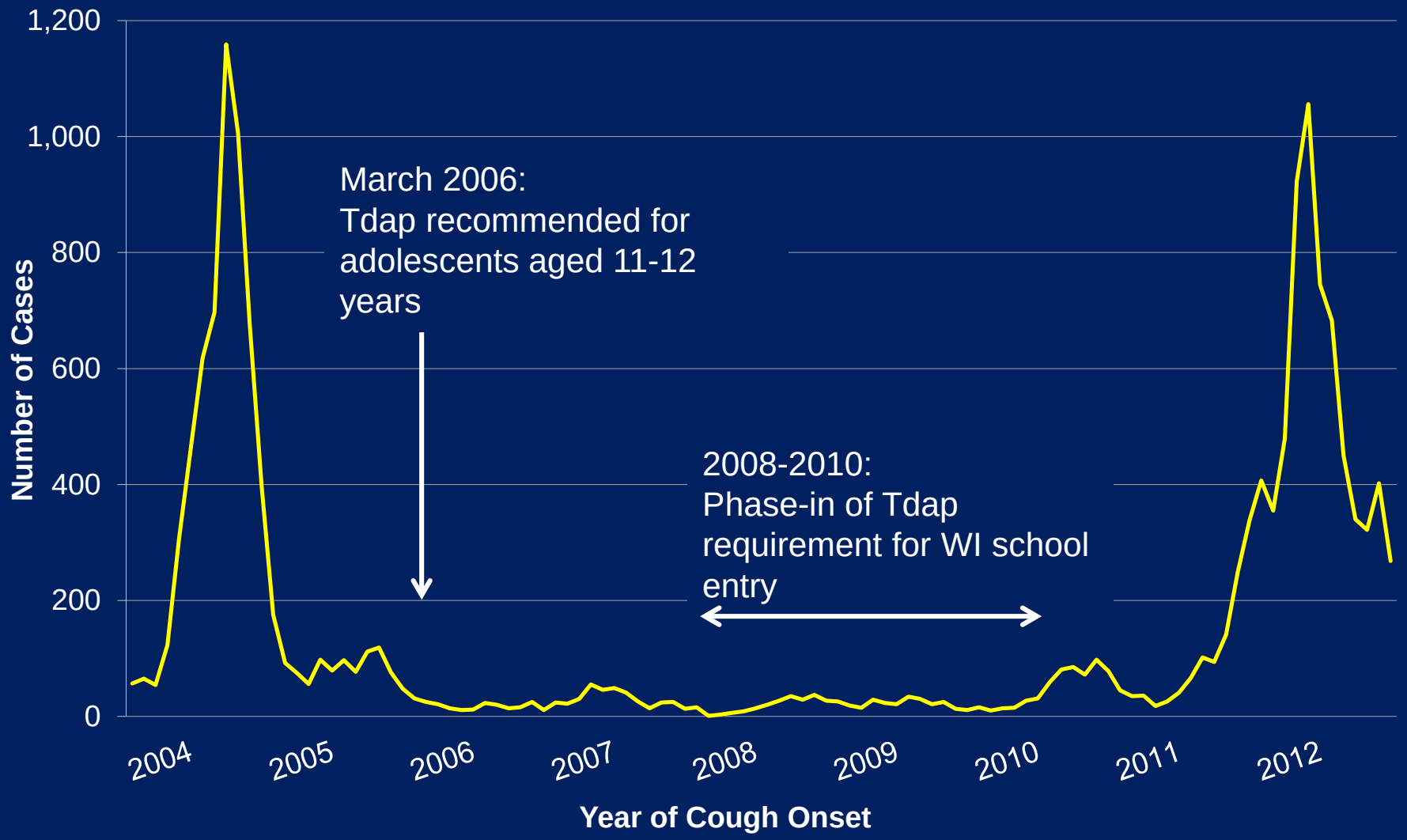
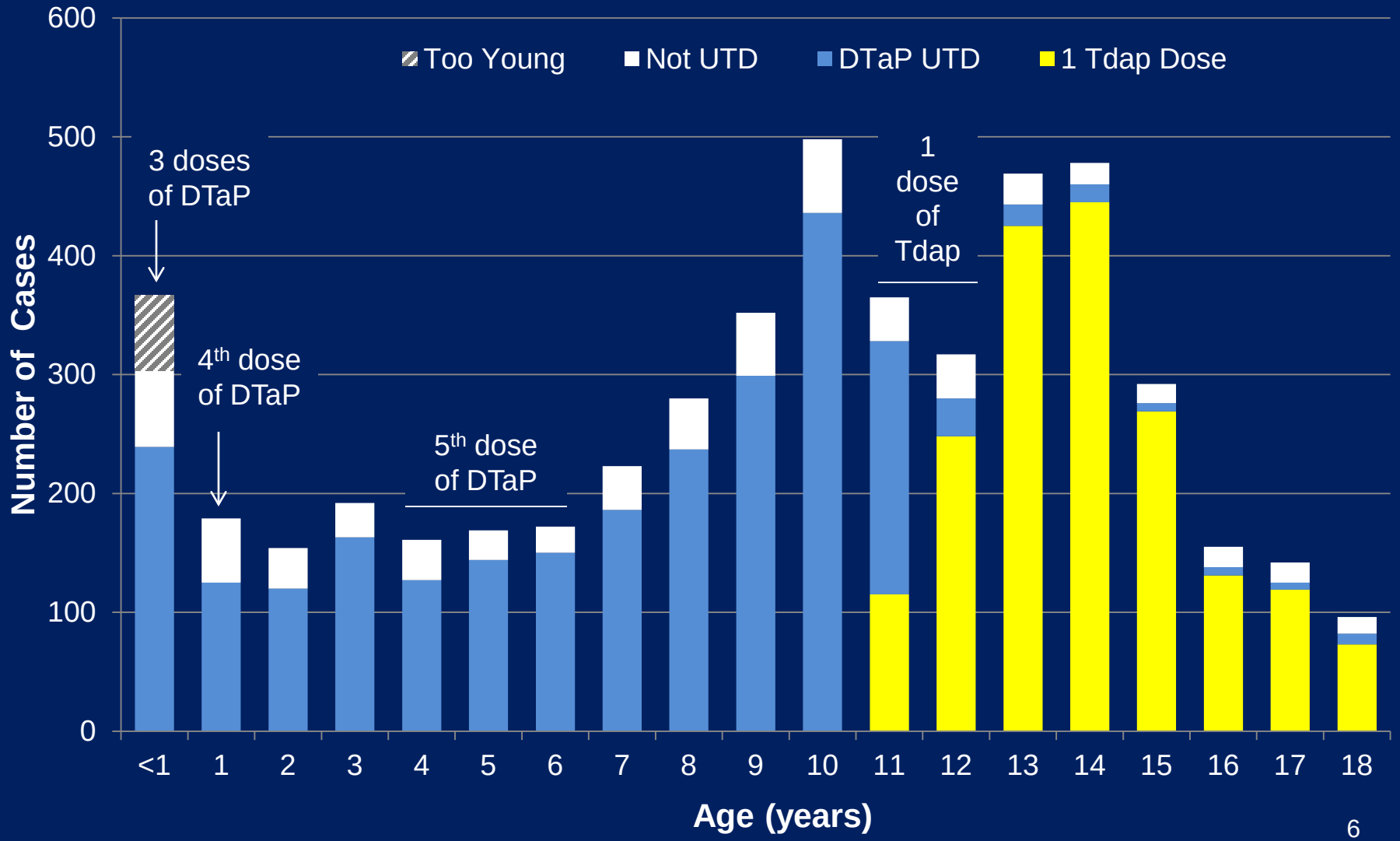
Background

Number of reported confirmed and probable cases of pertussis by month of cough onset, Wisconsin, 2004-2012



Tdap = tetanus-diptheria-acellular pertussis vaccine

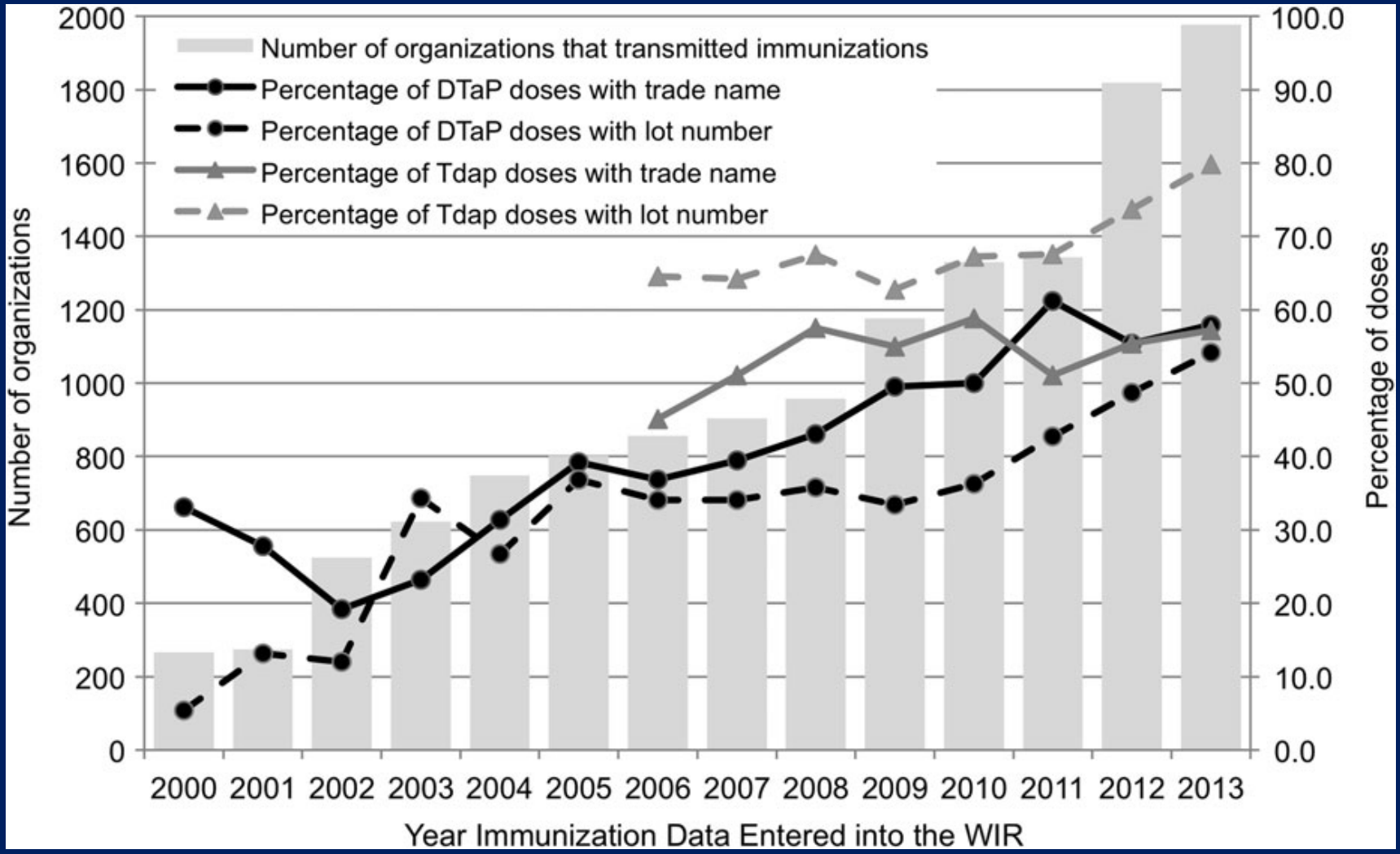
Number of confirmed and probable cases of pertussis among residents aged <19 years by age at cough onset and DTaP and Tdap vaccination status, Wisconsin, 2012



Wisconsin Immunization Registry (WIR)

- Statewide, population-based Immunization Information System (IIS), established in 1999 by the Wisconsin Division of Public Health (WDPH)
- Populated with demographic information from all birth records in Wisconsin beginning with the 1995 birth cohort
- WIR participation is not a requirement, however the WIR receives new client and immunization data from many public and private healthcare providers, HMOs, Medicaid and WIC
- Vaccine brand name and lot number data are collected, but are not required fields

Completeness of WIR data



Source: Koepke et al. Journal of Infectious Diseases

Study objectives

- Determine whether the WIR can be used to evaluate vaccine effectiveness.
- Estimate the effectiveness of Tdap for preventing pertussis among adolescents who have not received whole cell pertussis-containing vaccine (DTwP).
- Examine effectiveness by timing of Tdap receipt and by Tdap brand.

Methods

Study design

- Used WIR client and vaccination data to construct the study cohort and collect Tdap vaccination histories
- Matched reported cases of pertussis to WIR client records by first name, last name, birth date
- Calculated the incidence of pertussis among the cohort, by Tdap vaccination history

Study cohort

- Wisconsin residents
- Born during years 1998 through 2000
- Active client records in the WIR

Case definition of pertussis

- An acute cough illness meeting the CSTE clinical case definition* of pertussis
- Onset during 2012
- Reported to WDPH through the Wisconsin Electronic Disease Surveillance System (WEDSS)
- PCR or culture-confirmed *B. pertussis* infection
- In a member of the study cohort

*acute cough illness of ≥14 days duration with ≥1 of the following: paroxysmal cough, posttussive vomiting, or whoop.

Tdap history

- Collected only from the WIR
- Tdap receipt defined as having received Tdap or DTaP on or after 10th birthday and before cough onset (if a pertussis case) or before the end of 2012

Tdap brand collection and validation

- Collected from WIR only
  - Trade name field
  - Assigned based on first letter of lot number (“A” for Boostrix; “C” or “U” for Adacel)
  - If DTaP dose, brand considered “DTaP”

- Validation of brand name
  - When both trade name and lot number available, they were compared to identify discordancies
  - If conflict, lot number used to assign brand name

Adjustment of cohort size (MOGE)

- WIR clients who move out of WI are not regularly inactivated as WI residents.
- As a result, the number of WIR clients in the cohort was 21% larger than the population estimate.
- Adjustment: We excluded a sample of clients that never received Tdap and were not matched to a pertussis case so that the size of each WIR birth cohort was equal to the population estimate.

Calculation of vaccine effectiveness (VE)

- Incidence rates of pertussis were calculated by:
  - Tdap receipt (Yes/No)
  - Tdap brand received (Adacel/Boostrix)
  - Tdap receipt year (2008-2012)
- Incidence rate ratios (IRR) of pertussis were calculated using ‘Never received Tdap’ as the reference group.
- Vaccine effectiveness (VE) was calculated:

$$VE = (1.0 - IRR) * 100\%$$

Results

Characteristics of the study cohort (N=225,130)

Characteristic	Birth Year, No. (%)		
	1998	1999	2000
Pertussis case during 2012			
No	74 168 (99.5)	74 252 (99.6)	75 770 (99.7)
Yes	404 (0.5)	282 (0.4)	254 (0.3)
Total	74 572 (100.0)	74 534 (100.0)	76 024 (100.0)
Tdap receipt			
No	6253 (8.4)	7111 (9.5)	11 807 (15.5)
Yes	68 319 (91.6)	67 423 (90.5)	64 217 (84.5)
Total	74 572 (100.0)	74 534 (100.0)	76 024 (100.0)
Tdap brand[b]			
Adacel	26 805 (39.2)	25 423 (37.7)	25 999 (40.5)
Boostrix	25 839 (37.8)	28 051 (41.6)	28 016 (43.6)
DTaP	490 (0.7)	433 (0.6)	335 (0.5)
Unspecified	15 185 (22.2)	13 516 (20.0)	9867 (15.4)
Total	68 319 (100.0)	67 423 (100.0)	64 217 (100.0)

Source: Koepke et al. JID, 2014.

Validation of Tdap brand name

- 198,891 (89%) of the study cohort received Tdap
- Among Tdap recipients:
  - 53% had trade name and lot number
  - 17% had lot number only
  - 10% had trade name only
  - 20% had no trade name or lot number
- <0.18% (185/105,829) with trade name and lot number conflicted

Pertussis cases reported

- 959 cases reported
  - 959 PCR+ (3 culture+)
- 940 (98%) matched to client records in the WIR.
- Among cases that received Tdap, median time from Tdap receipt to cough onset:
  - 1.9 years (interquartile range: 1.4 – 2.6 years).

Tdap VE, by receipt year

Year of Tdap Receipt[a]	Cases, No.	Cohort Size, Subjects, No.	Adjusted[b] IRR (95% CI)	Adjusted[b] Estimated VE, % (95% CI)
No Tdap received	201	25 171	Reference	Reference
Any Tdap brand				
2012	12	27 948	0.25 (.14–0.45)	75.3 (55.2–86.5)
2011	173	65 909	0.32 (.26–.39)	68.2 (60.9–74.1)
2010	293	64 013	0.66 (.54–.80)	34.5 (19.9–46.4)
2009/2008	261	42 089	0.88 (.70–1.11)	11.9 (–11.1 to 30.1)

Source: Koepke et al. JID, 2014.

Tdap VE, by receipt year and brand

Year of Tdap Receipt[a]	Cases, No.	Cohort Size, Subjects, No.	Adjusted[b] IRR (95% CI)	Adjusted[b] Estimated VE, % (95% CI)
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By known Tdap brand[d,e]				
Adacel				
2012	8	12 262	0.38 (.19–.79)	61.8 (21.5–81.4)
2011	91	27 128	0.41 (.32–.52)	59.4 (47.9–68.4)
2010	134	22 903	0.86 (.68–1.09)	14.0 (–9.4 to 32.4)
2009/2008	112	15 934	1.02 (.77–1.34)	–1.8 (–34.0 to 22.7)
Boostrix				
2012	2	12 592	0.09 (.02–.38)	90.7 (62.4–97.7)
2011	46	27 180	0.20 (.15–.28)	79.6 (71.8–85.2)
2010	86	26 496	0.47 (.36–.61)	53.4 (39.2–64.3)
2009/2008	75	15 638	0.70 (.52–.94)	30.5 (6.2–48.5)

Source: Koepke et al. JID, 2014.

Sensitivity analyses

- Imputed Tdap brand name for those with unspecified Tdap brand
- Used a broader case definition of pertussis
- Compared risk of pertussis among Tdap recipients only, controlling for geographic region of residence
- Controlled for confounding using propensity score analysis

Discussion

Summary

- Tdap VE decreased with increasing time since receipt among recipients of both Tdap brands.
- Estimates of decline in Tdap VE are consistent with those noted during Washington state's case-control study.
- Differences in effectiveness by brand were noted. Possible explanations:
  - Difference in product formulations
  - Uncontrolled confounding factors or other bias in our data

Limitations

- Because of the MOGE adjustment, we were able to adjust VE estimates only for birth year.
- The completeness and accuracy of the WIR has not been validated for this age range.
- WIR did not have full DTaP brand histories for the cohort members.

Conclusions

- Our results provide evidence of waning immunity among recipients of both brands of Tdap.
- Our analysis suggests that Boostrix may be more effective than Adacel in preventing pertussis disease. However, our findings should be verified in additional studies that include childhood DTaP history.
- IISs, when complete and population-based, can be an efficient and useful source of vaccination data for analyses of vaccine effectiveness.

Thank you

Composition* of Tdap, by Brand

Product	PT	FHA	PERT	FIM
Boostrix	8	8	2.5	--
Adacel	2.5	5	3	5

*mcg per dose
PT = pertussis toxin
FHA = filamentous hemagglutinin
PERT = pertactin
FIM = fimbriae types 2 and 3

Source: CDC. The Pink Book: Epidemiology and Prevention of Vaccine Preventable Diseases.