

Tdap Revaccination:

Antibody Persistence and Second Tdap Safety and Immunogenicity

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WG Review and Considerations: Tdap Revaccination of the General Population

- ❑ Epidemiology of pertussis and state of vaccination program**
- ❑ Current Tdap policy and objectives**
- ❑ Tdap vaccine attributes**
 - Effectiveness/duration of protection
 - Antibody persistence
 - Revaccination
 - Safety
 - Immunogenicity
- ❑ Programmatic feasibility and acceptability**
- ❑ Decision and cost-effectiveness analysis for a second dose of Tdap**

Overview

- ❑ **Published studies**
- ❑ **Safety of second Tdap**
 - **5- and 10-years after first Tdap**
- ❑ **Immune response to Tdap**
 - **Diphtheria & tetanus**
 - **Antibody persistence over time after receipt of first Tdap**
 - **Response to second Tdap**
 - **Pertussis**
 - **Antibody persistence over time after receipt of first Tdap**
 - **Response to second Tdap**
- ❑ **WG conclusions**

PUBLISHED STUDIES

Tdap Antibody Persistence Published Studies

Country	Vaccine	Post-Tdap (yrs)	Subjects (n)		Mean age (yrs) (range)	
			Tdap	Control*	Tdap	Control*
U.S.	Boostrix	3	937	449	44.8 (21-67)	45.3 (22-67)
Canada	Adacel	1 3 5 10	¶	¶	¶	¶
Finland	Boostrix	3 5 10	264 267 75	30 36 7	14.6 (14.0-15.9) 16.6 (15.8 – 17.9) 21.1 ± 0.31	same as Tdap
Australia	Boostrix	1-3 5 10	310 240 153	77 64 35	39.8 (20-69) 45.2 (25-74) 50.3 ± 9.74	41.2 (22-57) 47.0 (28-62) same as Tdap

* Control vaccines: US – Adacel; Finland and Australia – Td + aP

¶ Summary of 3 studies: Study 1 - 11 – 54 yrs (3 lots of Tdap); Study 2 –11-13 yrs (Tdap + Hep B); Study 3 – 19-60 yrs (Td vs. Tdap)

Tdap Revaccination - Published Clinical Trials

5 years after first Tdap

Country	Product	Previously received (n)	N	Mean age (yrs)	Author
Germany	Boostrix (Tdap-IPV)	Tdap-IPV Tdap + IPV	415	11.4 ± 0.94* (range: 9 to 13)	Knuf <i>et al</i> (2010)
Canada & US	Adacel	Tdap	545	31.7 (range: 15 to 69)	Halperin <i>et al</i> (2011)

* Received first Tdap-IPV at age 4-8 years (replaced 5th DTaP dose)

10 years after first Tdap

Country	Product	Previously received (n)	N	Mean age (yrs)	Author
Finland	Boostrix	Tdap (75) DT + ap (7)	82	21.1 ± 0.31	Mertsola <i>et al</i> (2010)
Australia	Boostrix	Tdap (153) DT + ap (35)	164	50.3 ± 9.74	Booy <i>et al</i> (2010)
Canada	Adacel	Tdap Tdap-IPV	342	31.2 (range: 21 to 70)	Halperin <i>et al</i> (2012)

Tdap Revaccination U.S. Clinical Trials

- ❑ **Sanofi Pasteur – Adacel in adults administered 9-11 years after previous Tdap**
 - Study completed and presented to WG (2013)
- ❑ **GSK study of Boostrix in young adults administered 10 years after previous Tdap boosting**
 - Study started in 1Q 2013 and report in 2014

Tdap revaccination 5- and 10-years after first Tdap

SAFETY

Summary of Most Commonly Reported Adverse Events After Receipt of a Second Tdap 5 or 10 Years After First Tdap

Injection site (1 – 14 days)

	5 years after first Tdap ¹	10 years after first Tdap ²
Pain	73.2% – 87.6%	69.5% – 93.8%
Erythema	28.6% – 48.1%	23.1% – >50%
Swelling	25.6% – 40.2% ³	20.5% – >50% ⁴

¹ Tdap n=539; Tdap –IPV n=351; ² Tdap n=525; ³ 2 large injection site swellings; ⁴ 3 large injections site swellings

Systemic (4 – 7 days)

	5 years after first Tdap ¹	10 years after first Tdap ²
Myalgia	61.0% ⁴	60.1% ⁵
Headache	53.2% ⁴	9.1% – 40.6%
Malaise ³	38.2% ⁴	11.6 – 44.4%

¹ Tdap n=539; Tdap –IPV n=351; ² Tdap n=525; ³ Reported malaise or fatigue; ⁴ Halperin 2011; ⁵ Halperin 2012

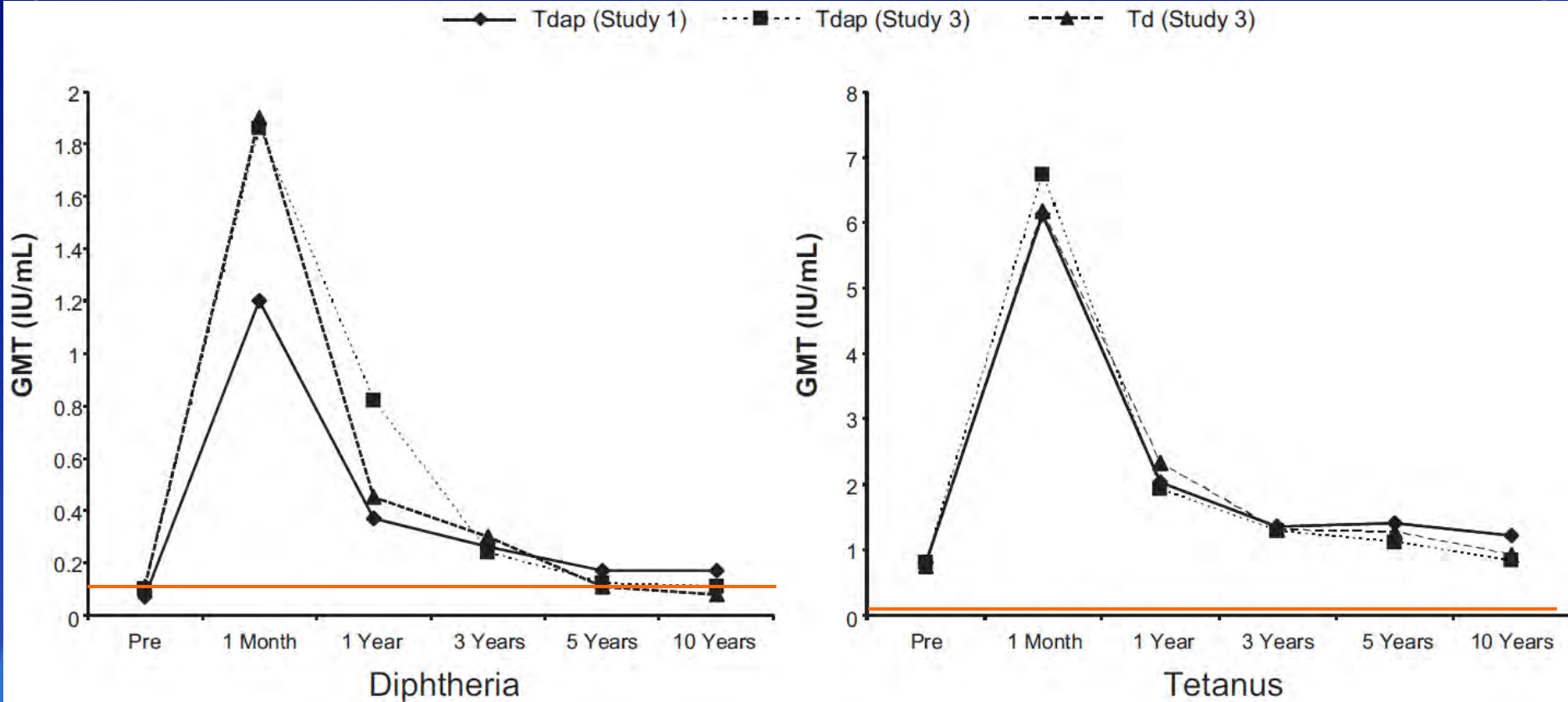
Few serious adverse events reported, not related to Tdap

Antibody persistence over time after receipt of Tdap;
Response to second Tdap

IMMUNE RESPONSE TO Tdap

Diphtheria and Tetanus: Antibody GMCs up to 10 Years After Td and Tdap (Adacel)

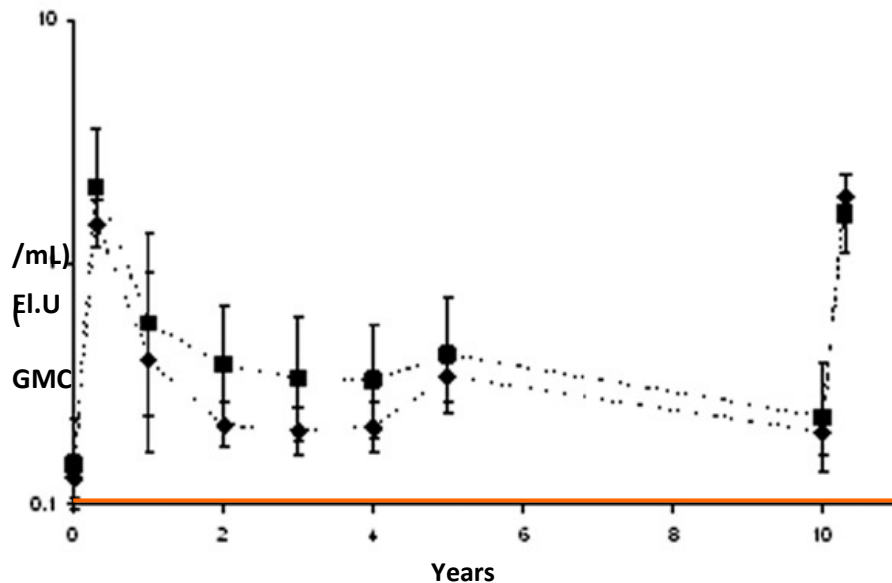
Adults (n=644)



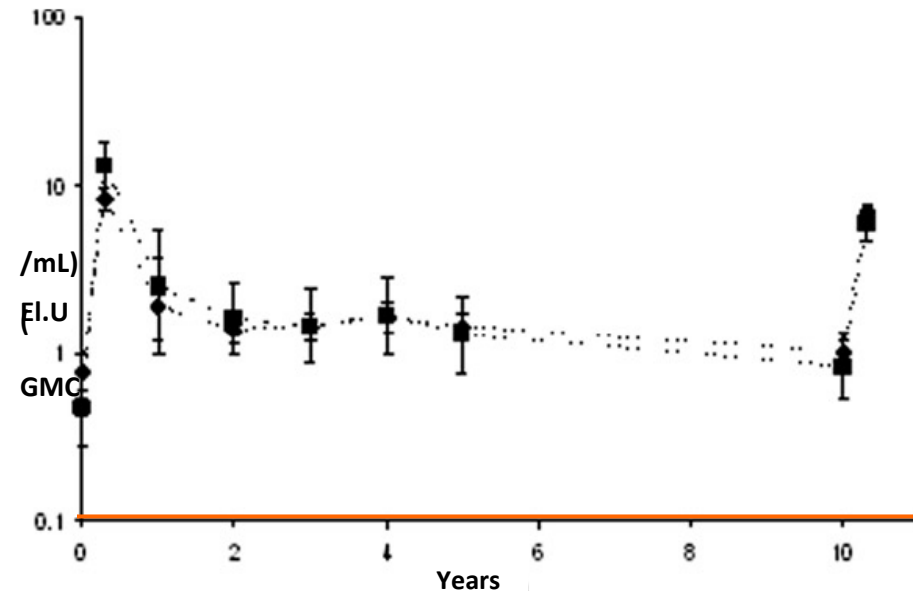
— = 0.10 IU/mL; seroprotection ≥ 0.10 IU/mL

Diphtheria and Tetanus: Antibody GMCs over 10 Years Before and After First Tdap and 1 Month After Second Tdap (Boostrix)

Adults (n=164)



Diphtheria

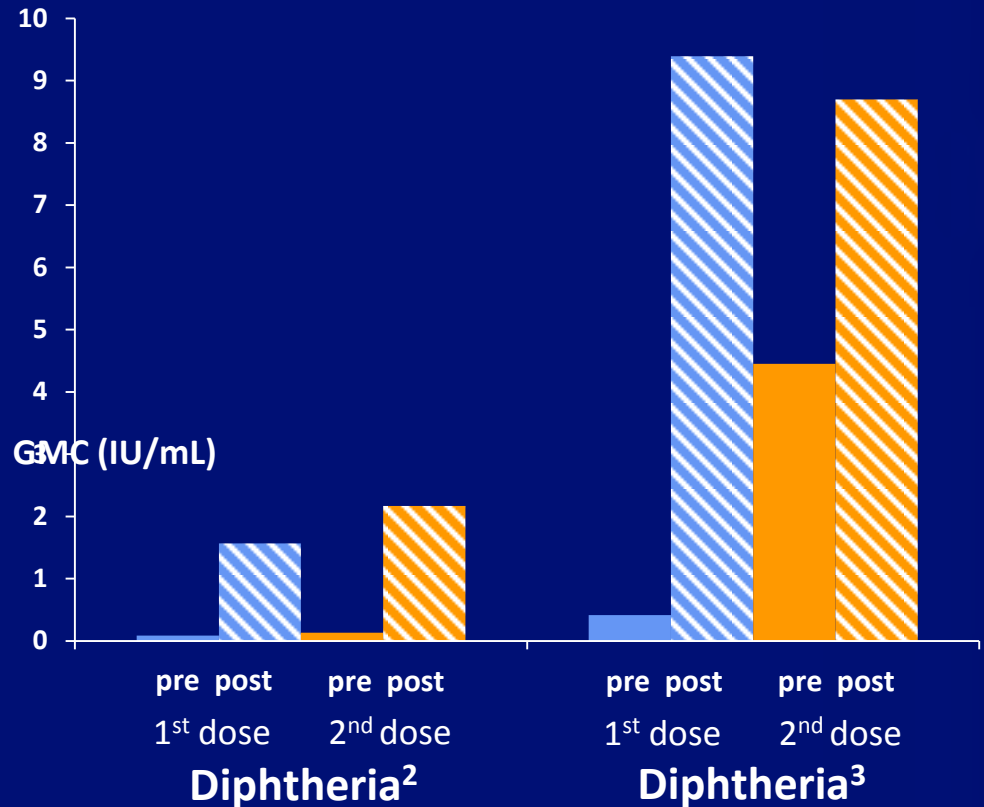
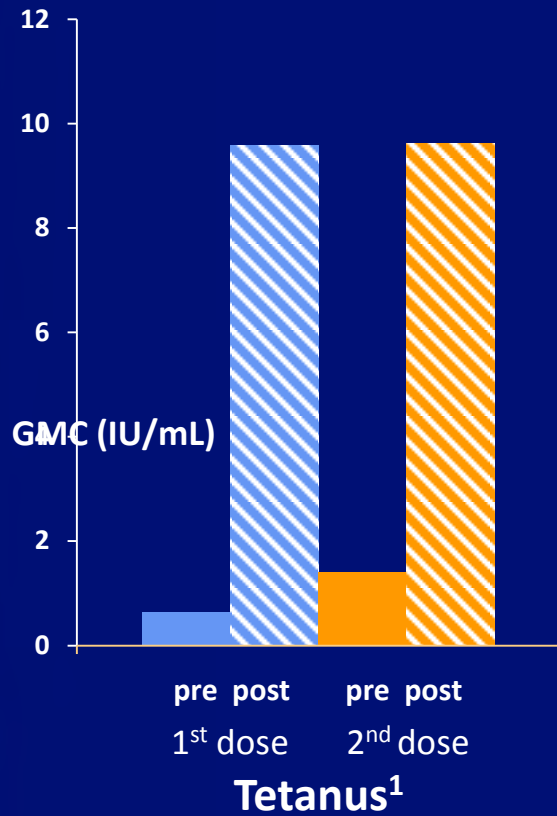


Tetanus

— = 0.10 IU/mL; seroprotection ≥ 0.10 IU/mL

Footnote: diamonds = Tdap group; squares = Td + aP group; Error bars = 95% CIs.

Tetanus and Diphtheria GMC Concentration Before and After First and Second Tdap (Adacel) After 5-year Interval



¹ Tetanus: 1st dose n=445-451, 2nd dose n=451

² Diphtheria: n=379

³ Diphtheria: n=64; received quadrivalent meningococcal vaccine (MCV4) between 1st and 2nd Tdap.

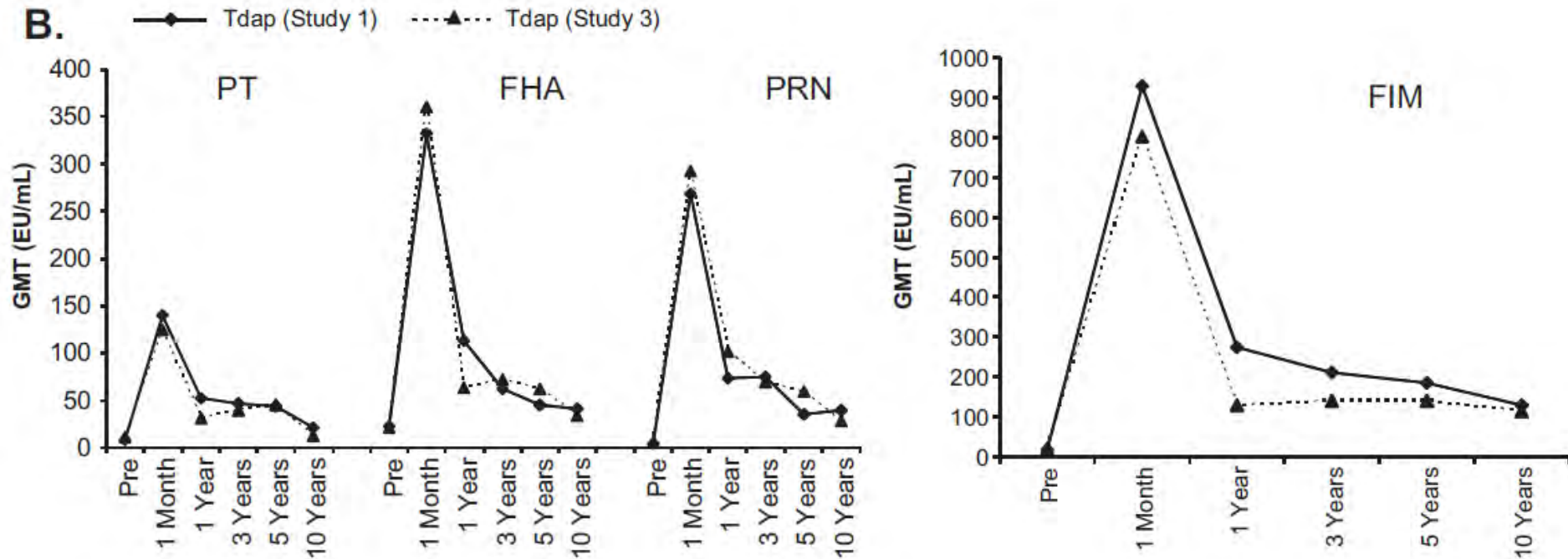
Tetanus and Diphtheria

Summary: Persistence of antibodies post-Tdap and response to second Tdap

- ❑ Robust antibody response and persistence comparable to Td**
- ❑ Although antibodies wane, levels protective at 10 years**
- ❑ Robust response to second Tdap at 5 and 10 years**

Pertussis Antigens GMC up to 10 Years After Tdap (Adacel)

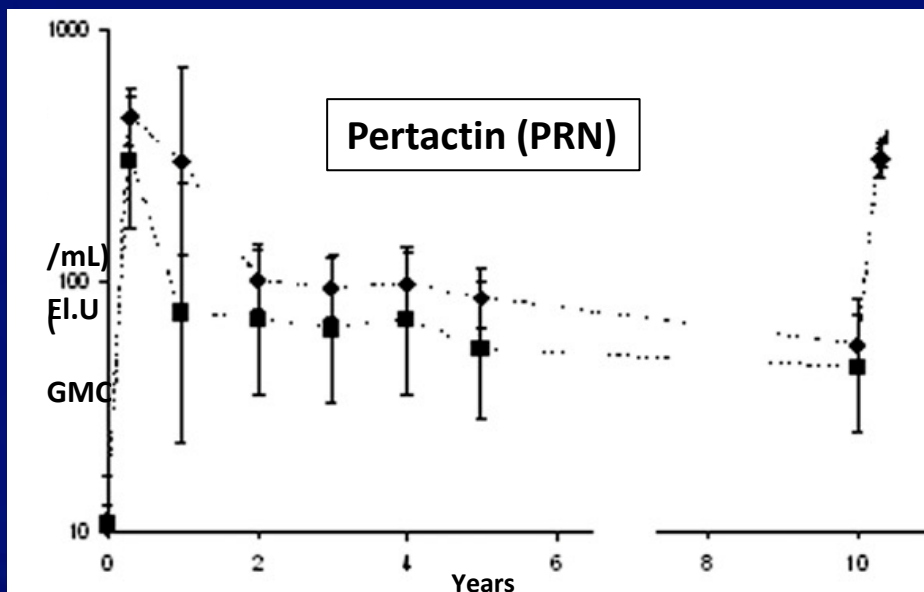
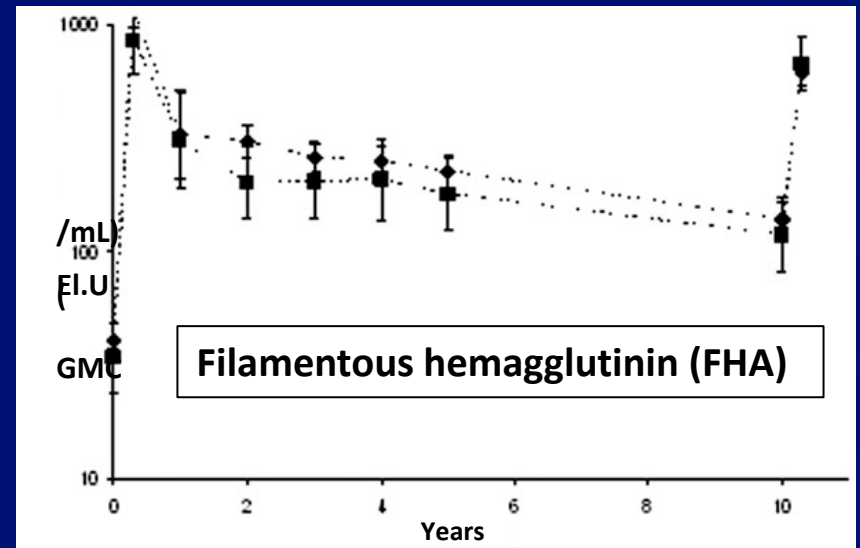
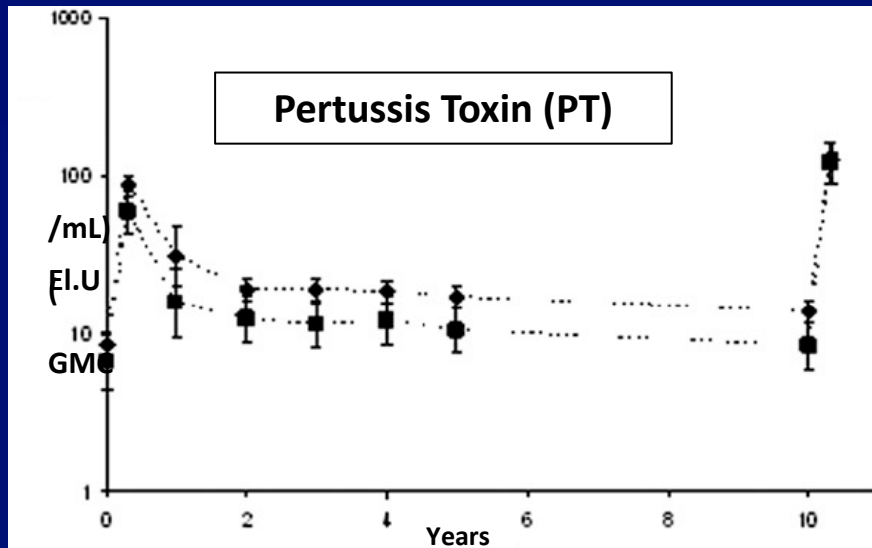
Adults (n=644)



PT: pertussis toxin; FHA: filamentous hemagglutinin; PRN: pertactin; FIM: fimbriae types 2&3

Tomovici A, et al. Humoral immunity 10 years after booster immunization with an adolescent and adult formulation combined tetanus, diphtheria, and 5-component acellular pertussis vaccine. *Vaccine*. 2012 Mar 30;30(16):2647-53.

Pertussis: Antibody GMCs Over 10 Years Before and After First Tdap and 1 Month After Second Tdap (Boostrix) Adults (n=164)

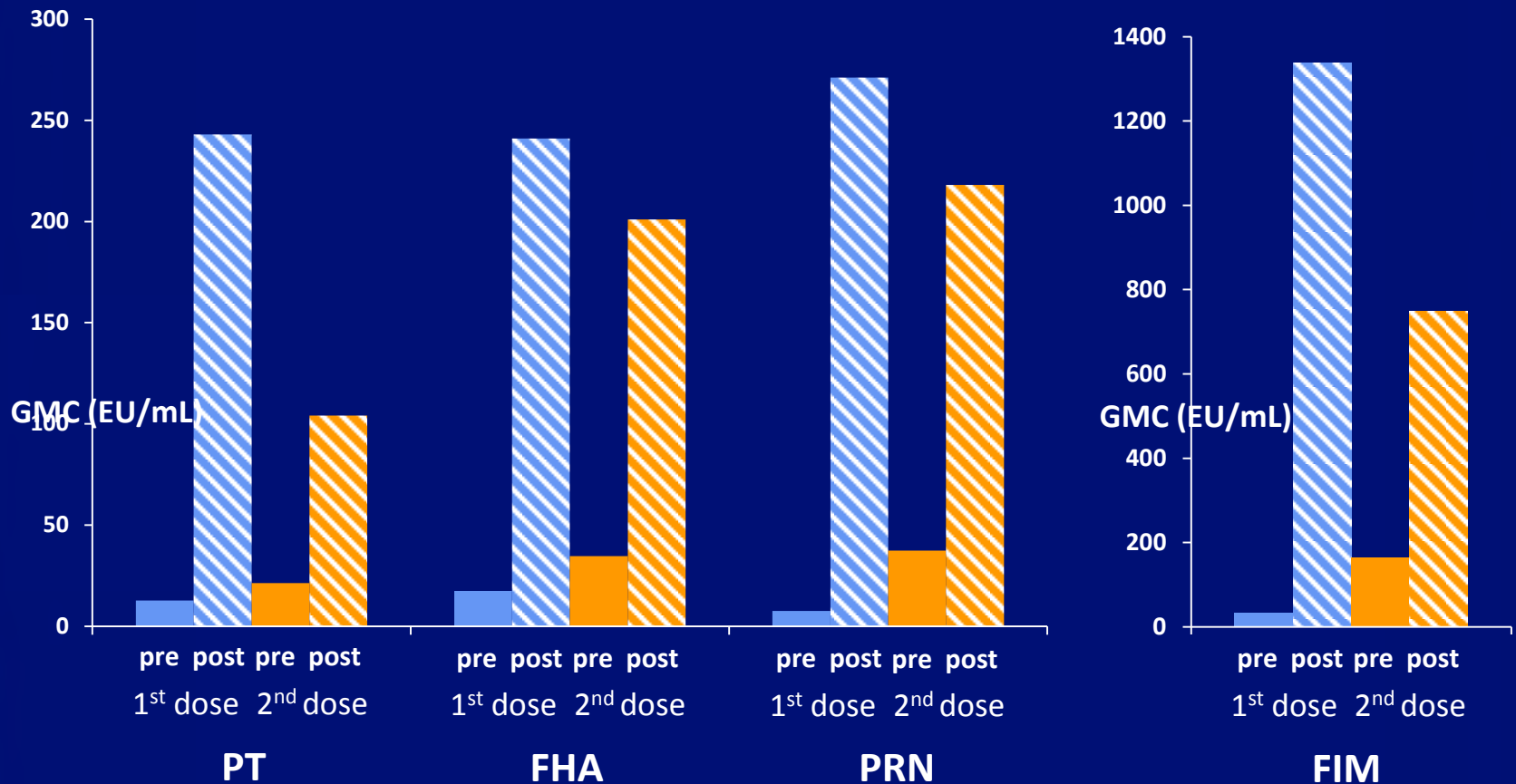


Diamonds = Tdap group

Squares = Td + ap group

Error bars = 95% CIs

Pertussis GMC Concentration Before and After First and Second Tdap (Adacel) After 5-year Interval



1st dose n=381-451
2nd dose n=425-451

PT: pertussis toxin; FHA: filamentous hemagglutinin;
PRN: pertactin; FIM: fimbriae types 2&3

Pertussis

Summary: Persistence of Antibodies Post-Tdap and Response to Second Tdap

□ Persistence of antibodies

- Rapid decline in first 1-2 years, slower decline over 10 years
- Antibody levels generally higher than pre-vaccination, but after 10 years close to pre-vaccination
- Antibody contributes to protection, but no defined level(s) of antibody correlates absolutely with protection

□ Second Tdap

- Antibody response similar to first Tdap in cohorts boosted after 5 or 10 years and naïve group receiving first Tdap

WG Conclusions

- ❑ **Second Tdap is safe and immunogenic at 5 and 10 year interval**
- ❑ **Tdap vaccine effectiveness 75% within first year, but substantial waning in 2-4 years**
- ❑ **Vaccine attributes will inform the decision and cost effectiveness analysis for a second Tdap**