Safety and immunogenicity of Boostrix in adults aged 65 years and older

Jennifer L. Liang
ACIP Pertussis Vaccine Working Group

Advisory Committee for Immunization Practices
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Composition of vaccines containing tetanus toxoid, diphtheria toxoid, and acellular pertussis antigens and approved age for persons aged 10 years and older

Trade name	Manufacturer	Pertussis antigens (µg)				Diphtheria toxoids (Lf)	Tetanus toxoids (Lf)	Approved age (years)
		PT	FHA	PRN	FIM			
ADACEL	sanofi pasteur	2.5	5	3	5	2	5	11 – 64
BOOSTRIX	GlaxoSmithKline Biologicals (GSK)	8	8	2.5	-	2.5	5	10 and older

PT- Pertussis toxin; FHA - filamentous haemagglutinin; PRN - pertactin; FIM - fimbriae

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Studies of Boostrix in subjects 65+yoa

- 2 clinical studies provide data
  - Study 011 – Randomized, observer blind, multicenter study comparing Boostrix to US-licensed Td vaccine (Decavac®, Sanofi-Pasteur)
    - 887 subjects 65+yoa received Boostrix in this study
    - Pivotal study in support of 65+ indication
    - All study objectives discussed with and agreed to by CBER prior to study initiation
  - Study 008 – Randomized, open label study of Boostrix coadministered with influenza vaccine in subjects 19+yoa
    - Primary analysis cohort 19-64yoa
    - In addition 217 subjects 65+yoa received Boostrix
- Total of 1104 subjects 65+yoa received Boostrix

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Study 011 - Enrollment

- 1332 subjects enrolled (887 Boostrix, 445 Td)
- Mean age 71.7+5.4y; age range 65-93yoa
  - Approximately 25% 75+yoa
- 53.7% female
- 95% White-Caucasian/European heritage
- No apparent differences in subject characteristics between vaccine groups

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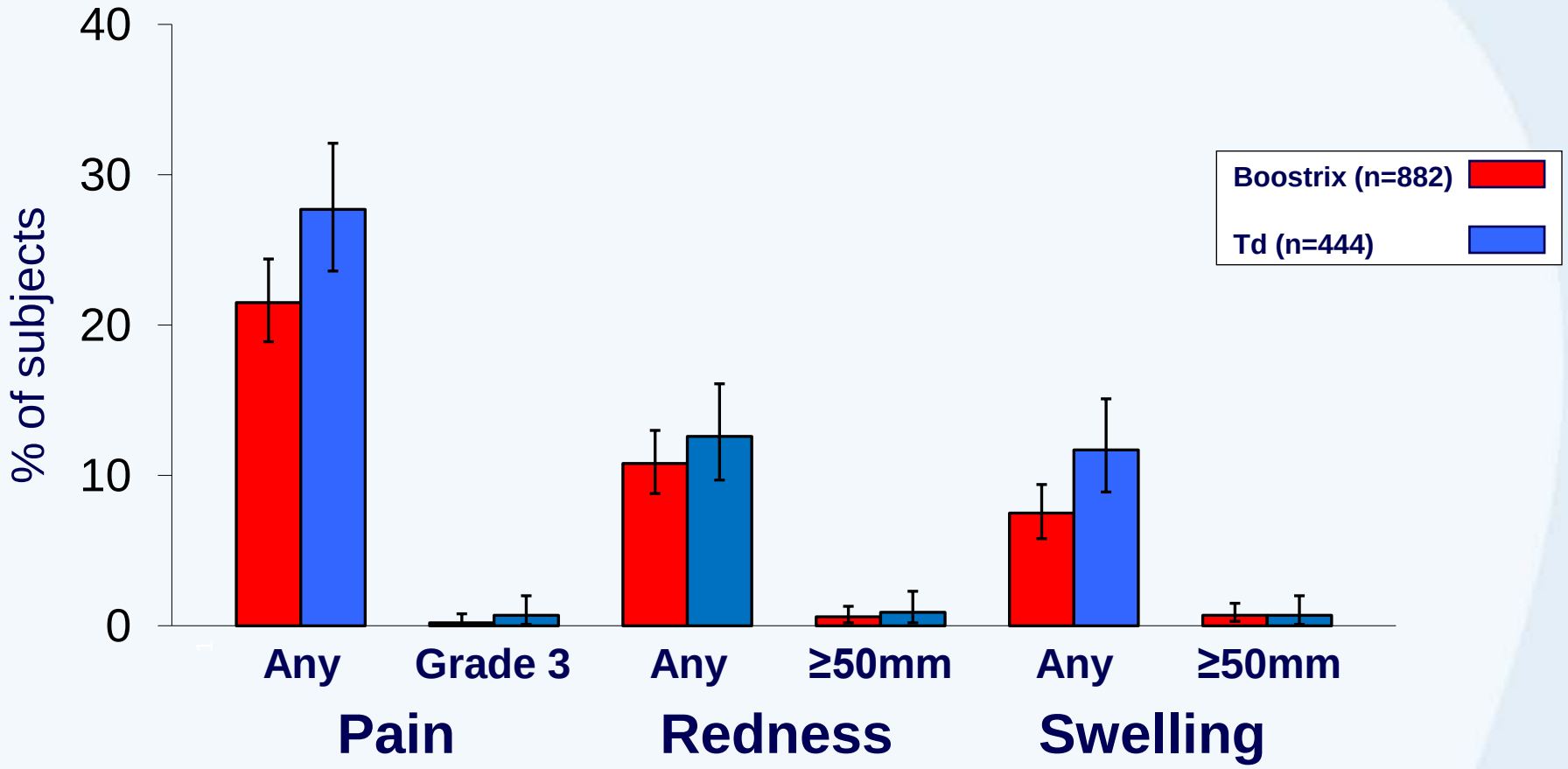
Study 011 - Solicited local symptoms within 4 days of vaccination



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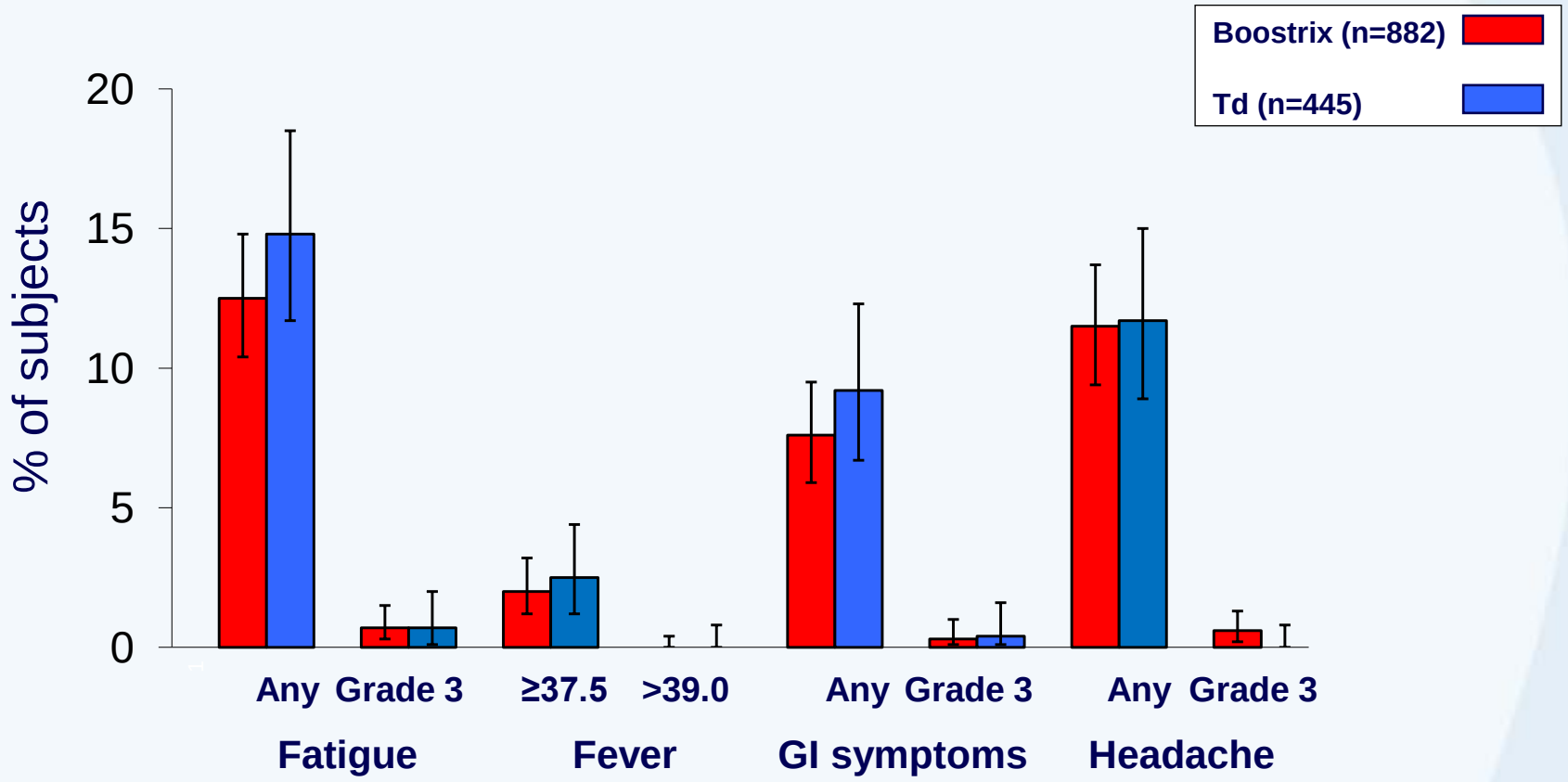
Study 011 - Solicited general symptoms within 4 days of vaccination



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Study 011 - Unsolicited AEs and SAEs

- Unsolicited AEs within 31 days of vaccination reported by 152 Boostrix recipients (17.1%), 64 Td recipients (14.4%)
  - Grade 3 US AEs reported by 13 Boostrix recipients (1.5%), 11 Td recipients (2.5%)
- SAEs within 31 days of vaccination reported by 6 Boostrix recipients (0.7%), 4 Td recipients (0.9%)
- SAEs over entire study period (6 months) reported by 37 Boostrix recipients (4.2%),10 Td recipients (2.2%)
  - 5 fatalities: 4 in Boostrix group (2 CVA, 2 MI), 1 in Td group (non-small cell lung cancer)
- No SAEs were considered by study investigators to be related to vaccination

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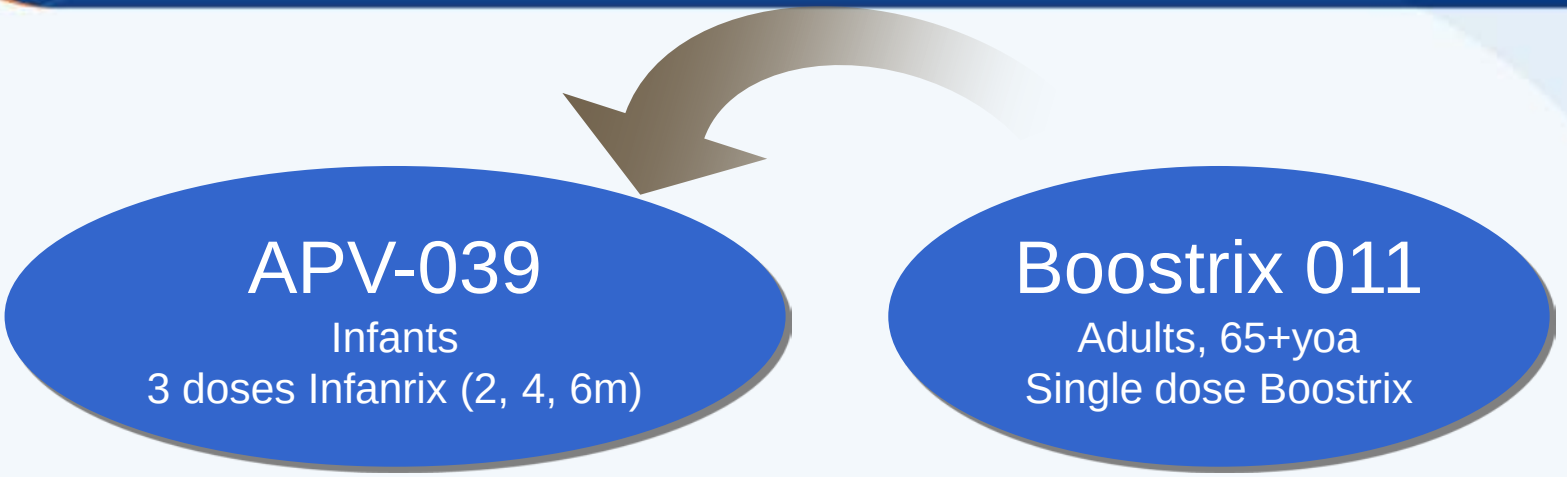
“Immunobridging” for pertussis efficacy



Efficacy determined
Pertussis immunogenicity determined

Efficacy not determined
Pertussis immunogenicity determined

Pertussis antibody GMCs 1 month post vaccination (EL.U/mL)

	APV-039 (Infants, 3 doses Infanrix)	Boostrix 011 (65+, 1 dose Boostrix)
Anti-PT	45.7	48.9
Anti-FHA	83.6	689.1
Anti-PRN	112.3	104.7
Efficacy	89%	--

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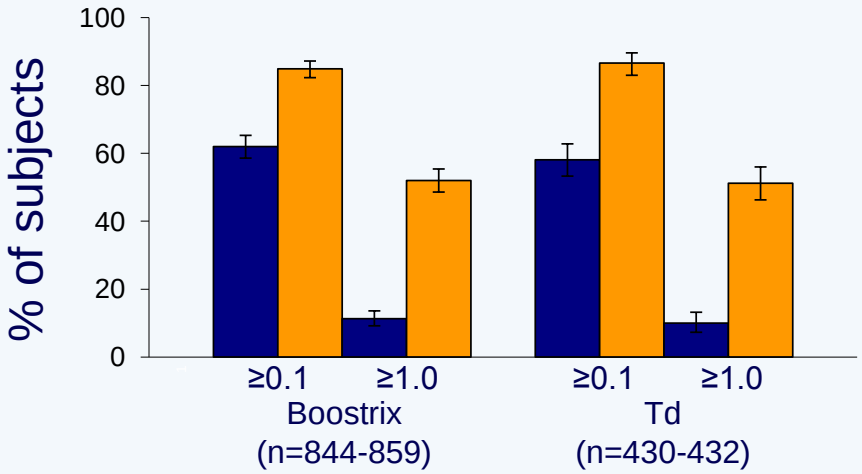
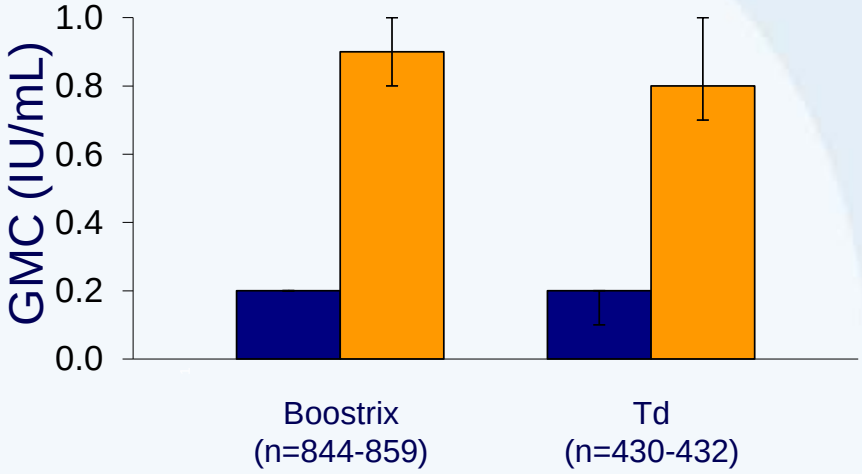
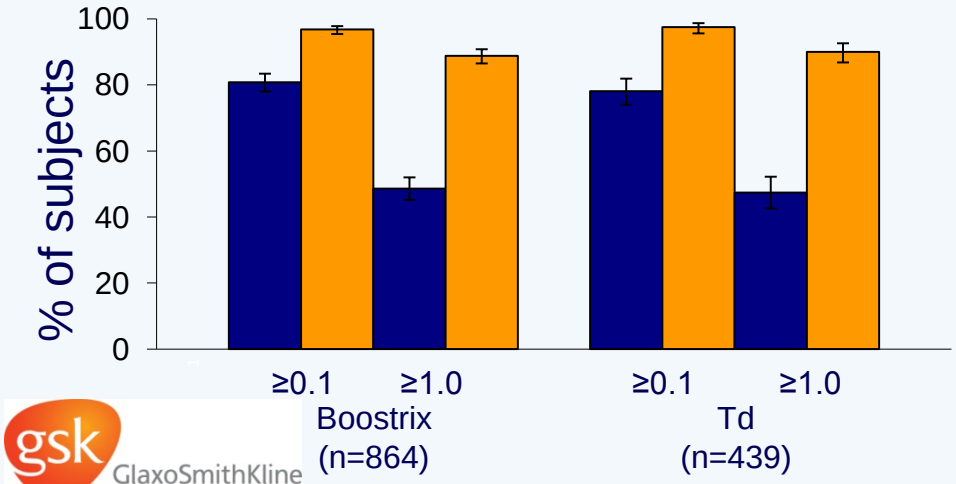
Study 011 - Increase in antibody concentrations after vaccination – Diphtheria and Tetanus

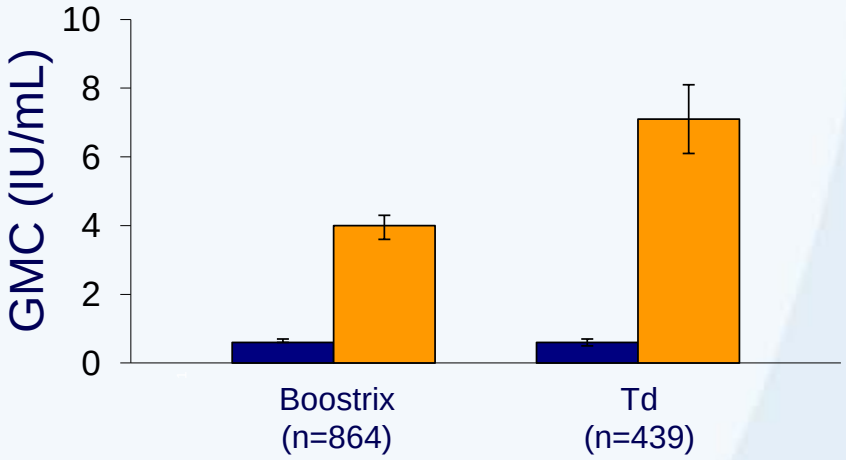
Diphtheria





Tetanus





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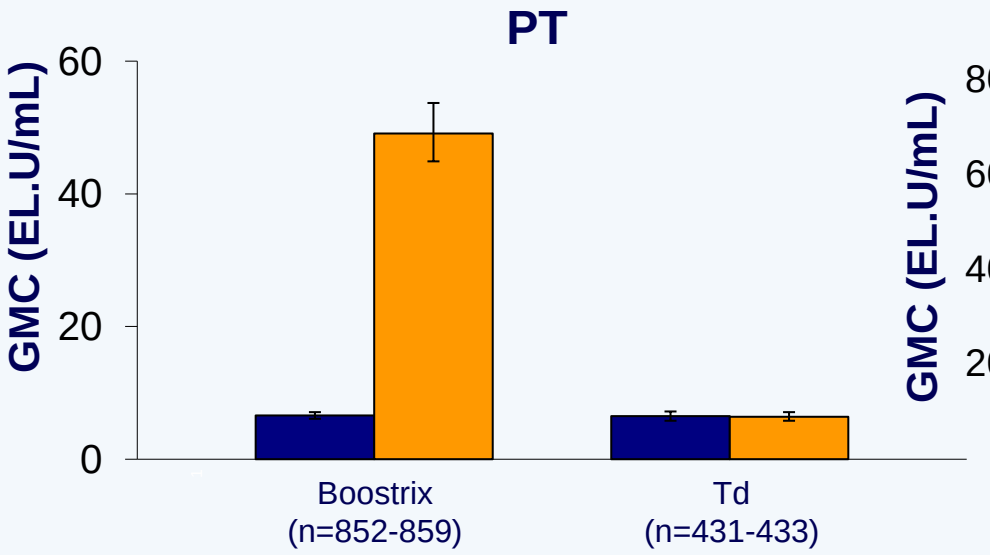
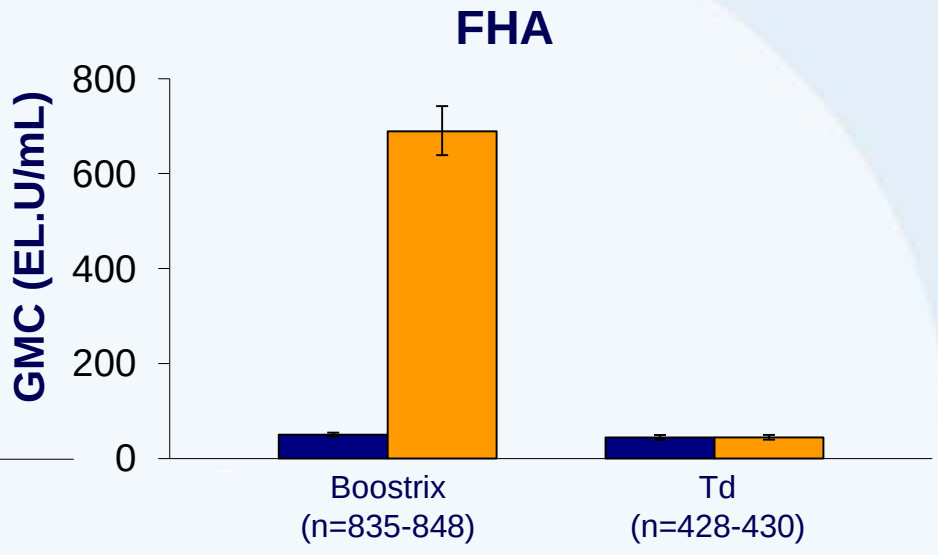
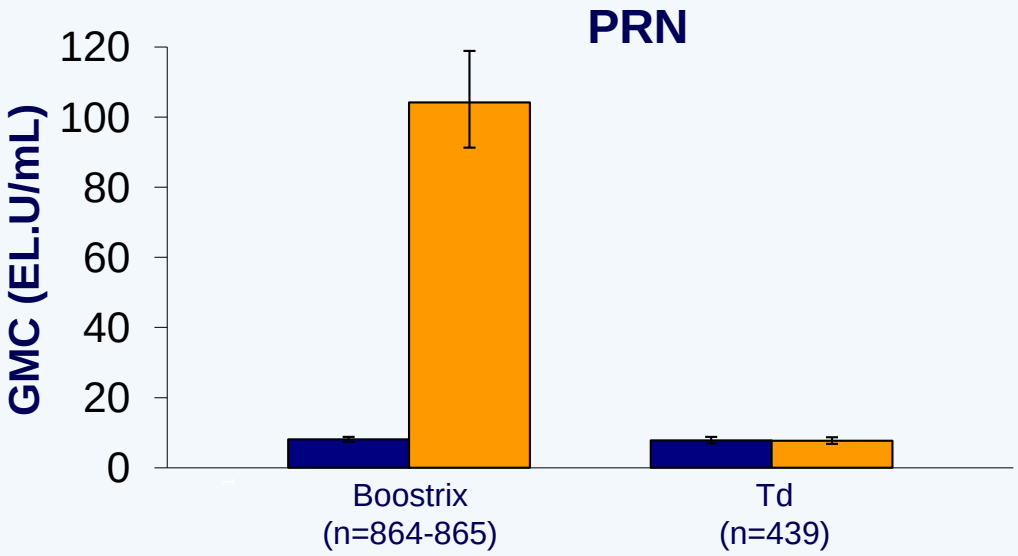
Study 011 - Increase in antibody concentrations after vaccination – Pertussis







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Safety of Tdap in adults 65 years of age and older in the Vaccine Adverse Event Reporting System (VAERS), 2005-2010

- **243 (2.2%) reports in adults 65+ years given Tdap vaccine (11,022 reports for all ages)**
  - 232 (95.5%) were non-serious reports
    - The most frequent adverse events (AEs) after Tdap were local reactions which comprised 41% of all reactions
  - 11 serious reports, included 2 deaths
    - Review of serious reports did not find any concerning patterns that could suggest a safety concern

- **Data suggest safety profile of Tdap vaccine in 65+ adults is similar to that of Td vaccine**

Moro PL, et al. Adverse events after Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccine administered to adults 65 years of age and older reported to the Vaccine Adverse Event Reporting System (VAERS), 2005–2010. Vaccine 29 (2011) 9404–9408.

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WG conclusions
Safety and immunogenicity of Boostrix for adults aged 65 years and older

- Boostrix is safe and immunogenic
- Older adults mount immune response, likely provide protection

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GSK SLIDES

Study 008 – Boostrix coadministered with influenza vaccine in subjects 65+yoa

- Randomized, open label study of Boostrix coadministered with influenza vaccine in subjects 19+yoa
  - Included a cohort of 221 subjects 65+yoa to provide proof of concept data for this age group
- Subjects received Boostrix coadministered with Fluarix (n=112) or Boostrix given 1 month after Fluarix (n=105)
- In both groups, Boostrix vaccination led to
  - Increases in antibody GMCs for all vaccine antigens
  - Increases in percentages of subjects with seroprotective levels of D and T antibodies
- Local and general reactogenicity similar between groups

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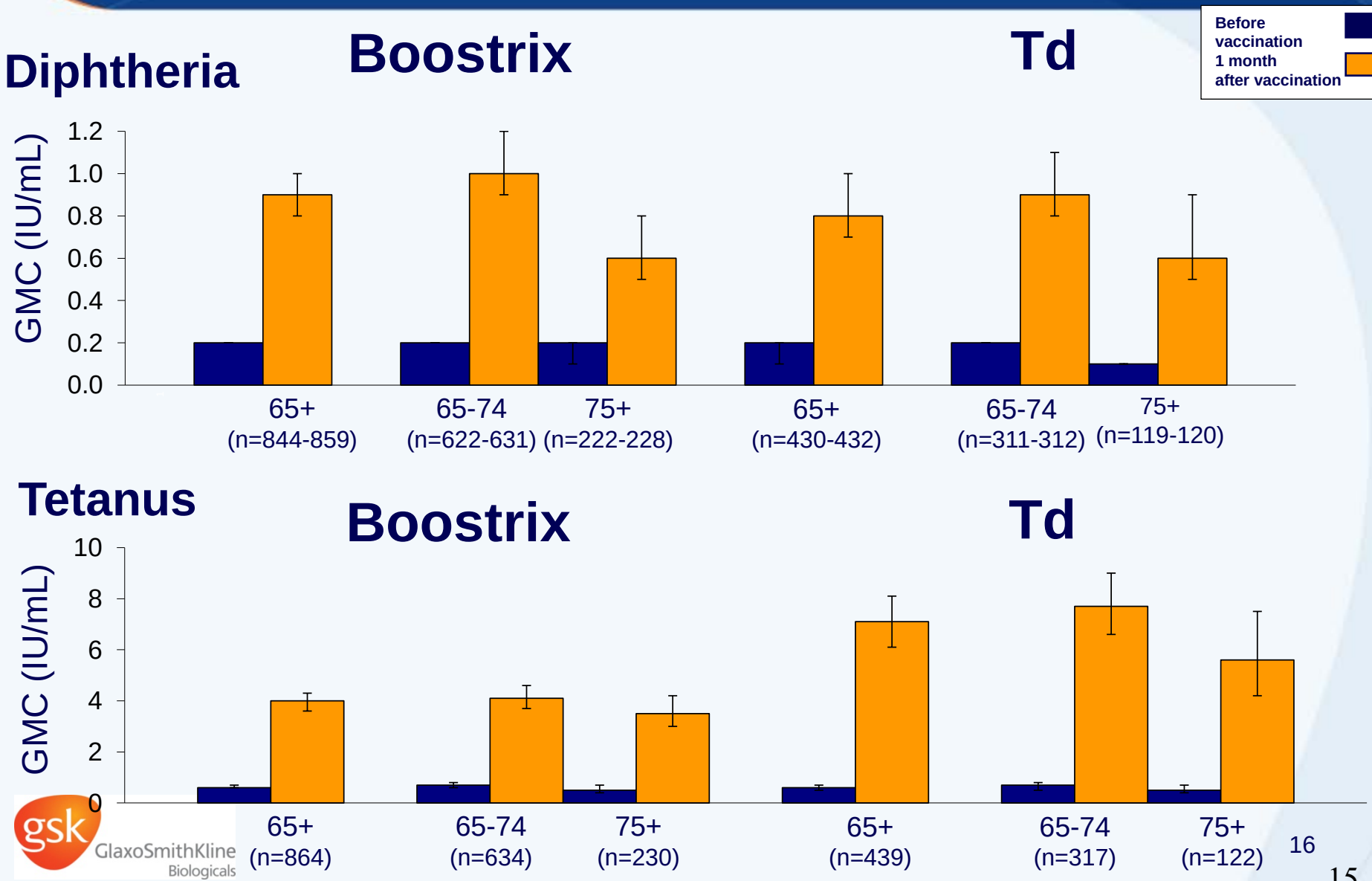
Study 011 – Responses to vaccination according to subject ages – Diphtheria and Tetanus



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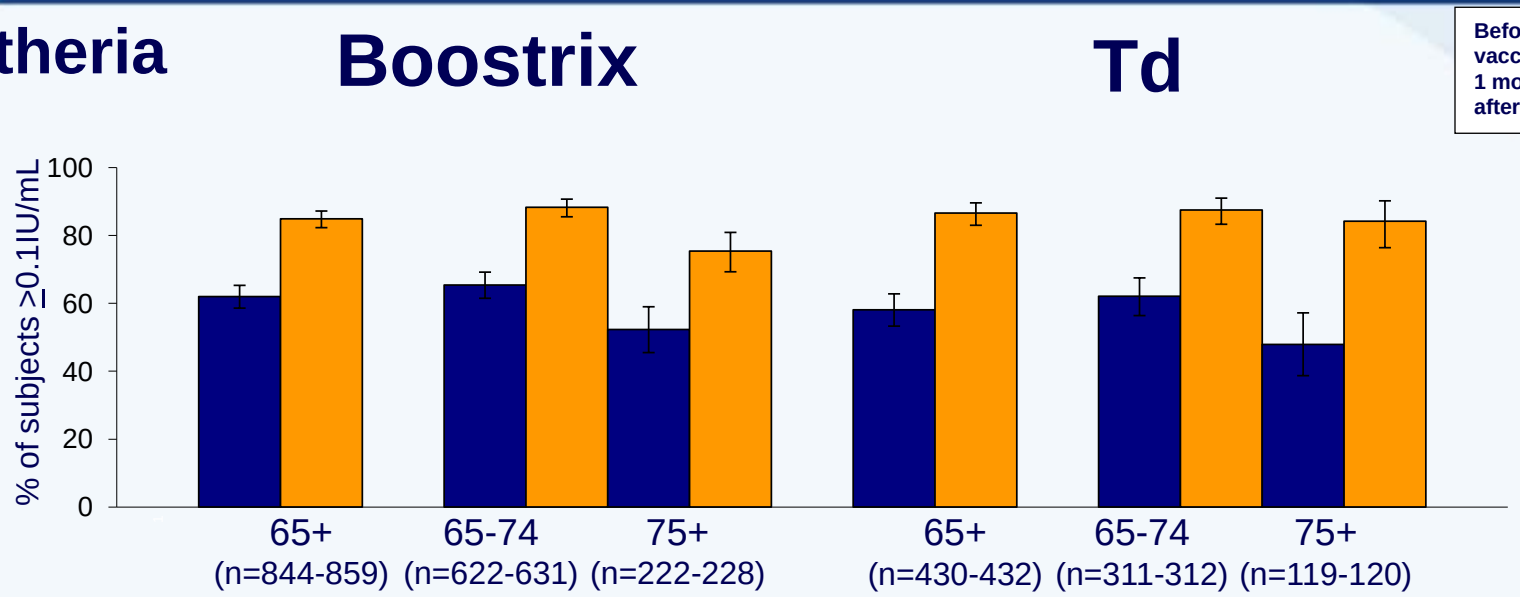
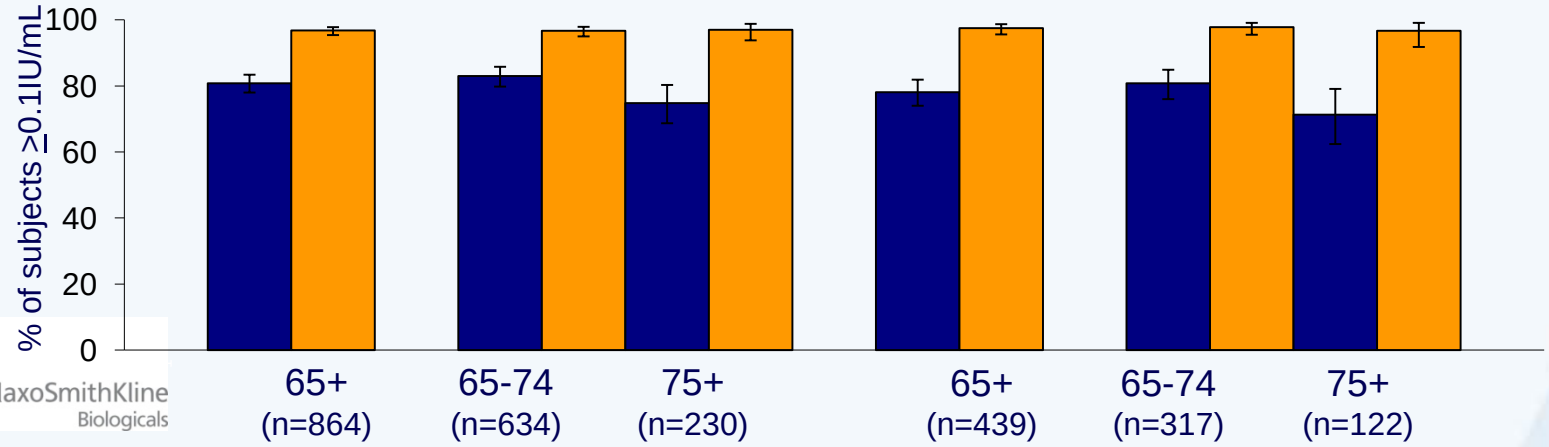
Study 011 – Seroprotection rates for diphtheria and tetanus according to subject ages

Diphtheria



Tetanus



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Study 011 – Assessing non-inferiority of Boostrix to comparators

Endpoint	Measure	Value	95% CI (LL, UL)	Non-inferior?
% Anti-D ≥0.1	LL of 95%CI for difference (Boostrix-Td) ≥-10%	-1.71%	(-5.59, 2.48)	Yes
%Anti-D≥1.0	Not defined	0.88	(-4.88, 6.65)	ND
%Anti-T≥0.1	LL of 95%CI for difference (Boostrix-Td) ≥-10%	-0.74	(-2.54, 1.41)	Yes
%Anti-T≥1.0	LL of 95%CI for difference (Boostrix-Td) ≥-10%	-1.20	(-4.59, 2.50)	Yes
Anti-PT GMC	LL of 95%CI for ratio (Boostrix/Infanrix) ≥0.67	1.07	(1.00, 1.15)	Yes
Anti-FHA GMC	LL of 95%CI for ratio (Boostrix/Infanrix) ≥0.67	8.24	(7.45, 9.12)	Yes
Anti-PRN GMC	LL of 95%CI for ratio (Boostrix/Infanrix) ≥0.67	0.93	(0.79, 1.10)	Yes

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