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Tdpa(-IPV) vaccines:

*Interchangeable use of pertussis
antigen-containing vaccines independent
of age indication*

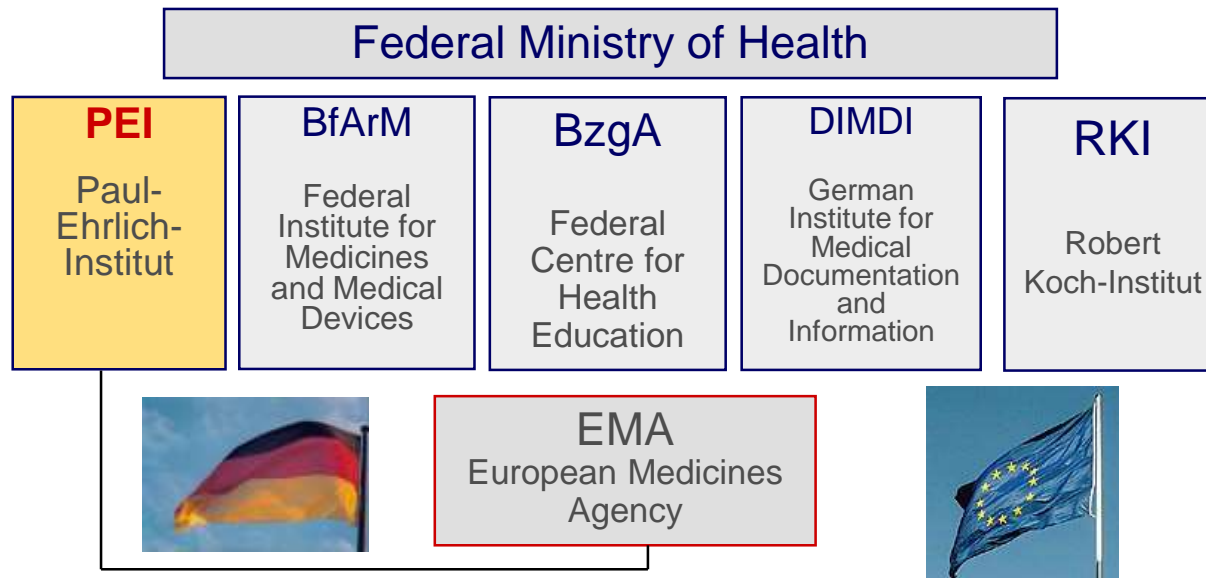
A systematic review and meta-analysis
of available data

No conflict of interest,
no funding source

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Microbiological Vaccines
ECCMID
25.04.2017

Paul-Ehrlich-Institute

- Licensing authority in Germany for biological human and animal medicinal products since 1972
 - Vaccines, Monoclonal Antibodies, Sera, Allergens, Blood products, ATMPs (e.g. Tissue engineered Products)



- Official batch release testing for Vaccines in Germany (OMCL-Network)
- WHO collaborating centre for Blood Products and Vaccines



The right vaccine for the right age

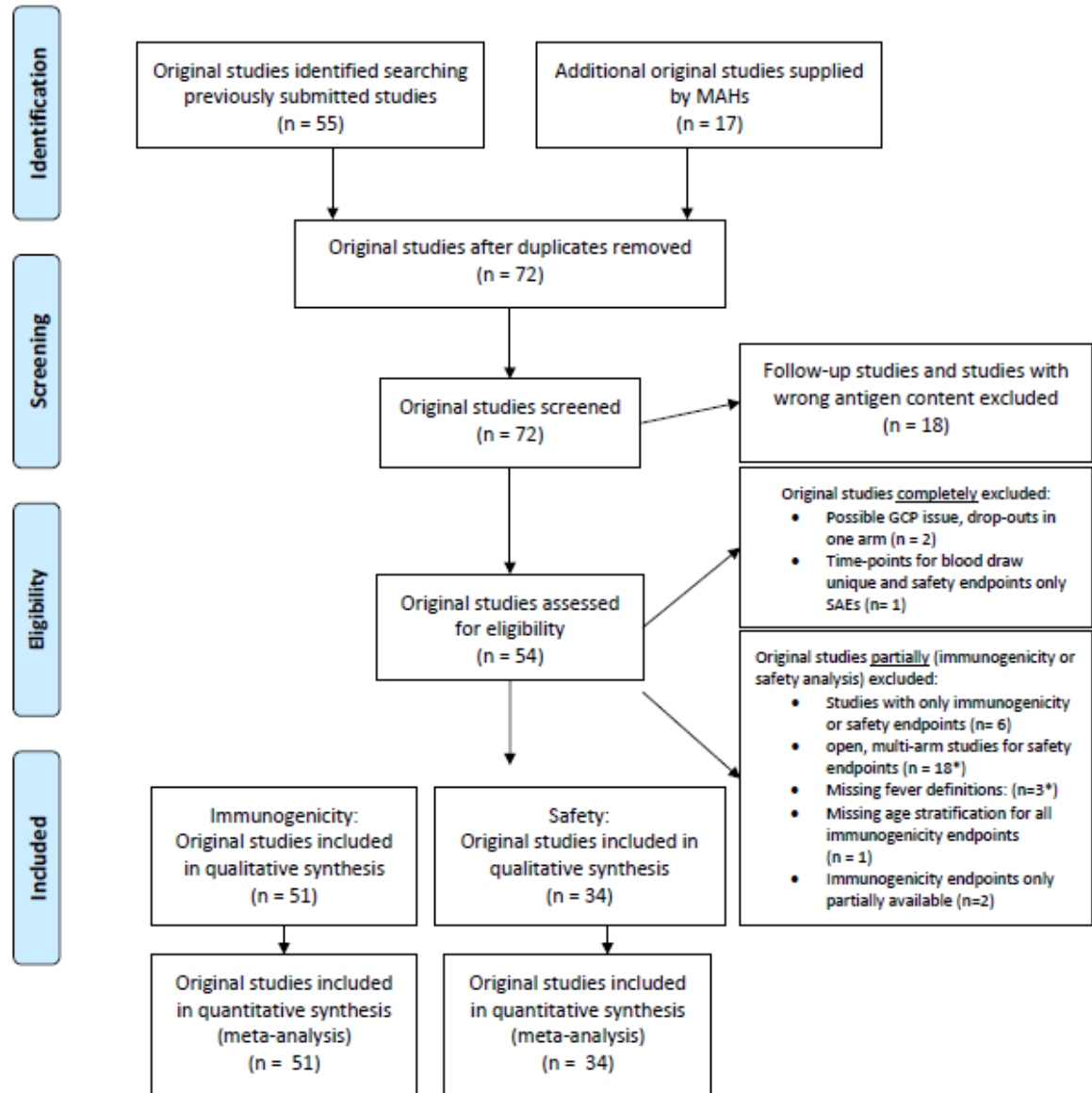
- For Infants and Toddlers higher antigen content necessary to achieve reliable immune response
- For children (>3y) and older individuals lower antigen content sufficient to “remind” immune system

	Vaccine	Diphtheria	Tetanus	PT	FHA	PRN	FIM 2/3	IPV	Age	Licensed for unvaccinated (2015)
Content unit		LF	LF	µg	µg	µg	µg	D		
TdaP	Boostrix	2.5	5	8	8	2.5	-	-	≥ 4y	>40y
TdaP-IPV	Boostrix Polio	2.5	5	8	8	2.5	-	80	≥ 4y	>40y
TdaP	Covaxis	2	5	2.5	2.5	3	5	-	≥ 4y	Excluded
TdaP-IPV	Repevax	2	5	2.5	2.5	3	5	80	≥ 3y	Adolescents
TdaP	TdaP-Immun	2	5	20	-	-	-	-	≥ 4y	≥ 4y

What to do with late vaccinees, unvaccinated and not completely primary vaccinated (or poorly documented) that fall into these “indication gaps”?

Methods

- Data supplied during regular procedures (licensure, variations)
 - Request to MAHs for electronic versions of all studies
- Use of GRADE and PRISMA
- Global studies
- Immunogenicity and safety one month post one dose



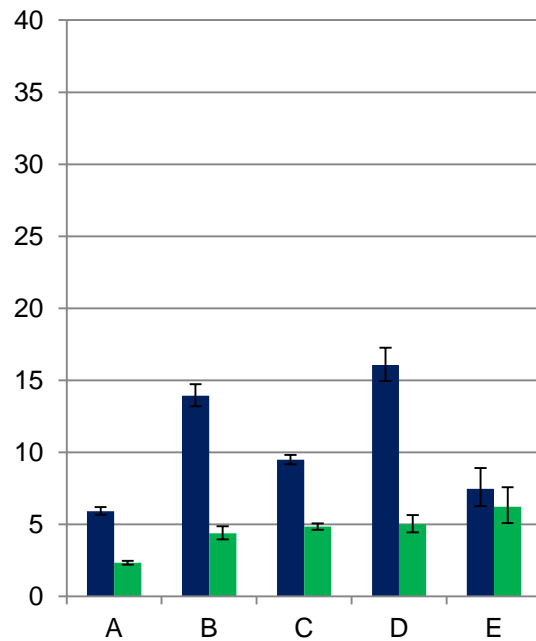


Results

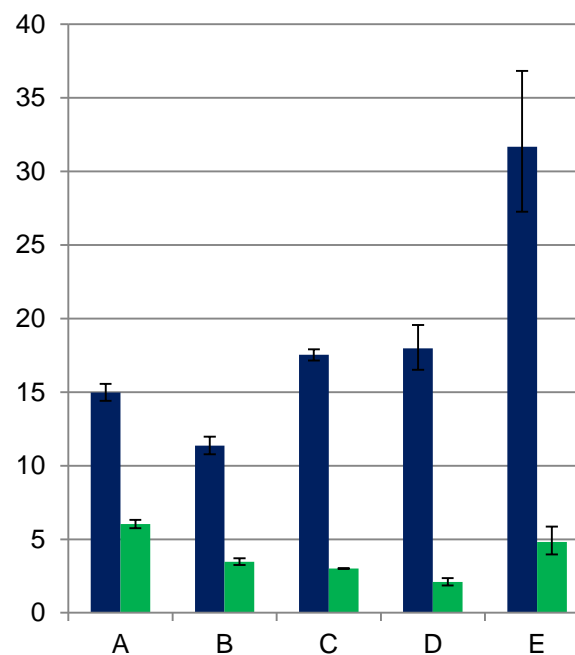
Tetanus, Diphtheria Titres

■ Tetanus ■ Diphtheria

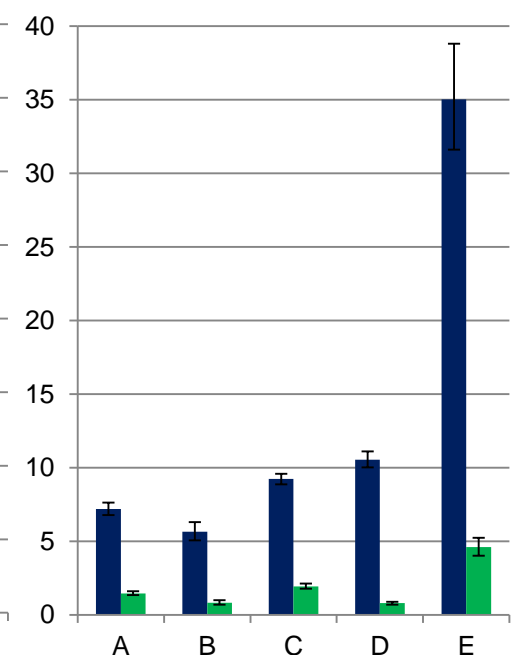
Children



Adolescents



Adults



Same antigen contents in all vaccines for Tetanus and Diphtheria



Results

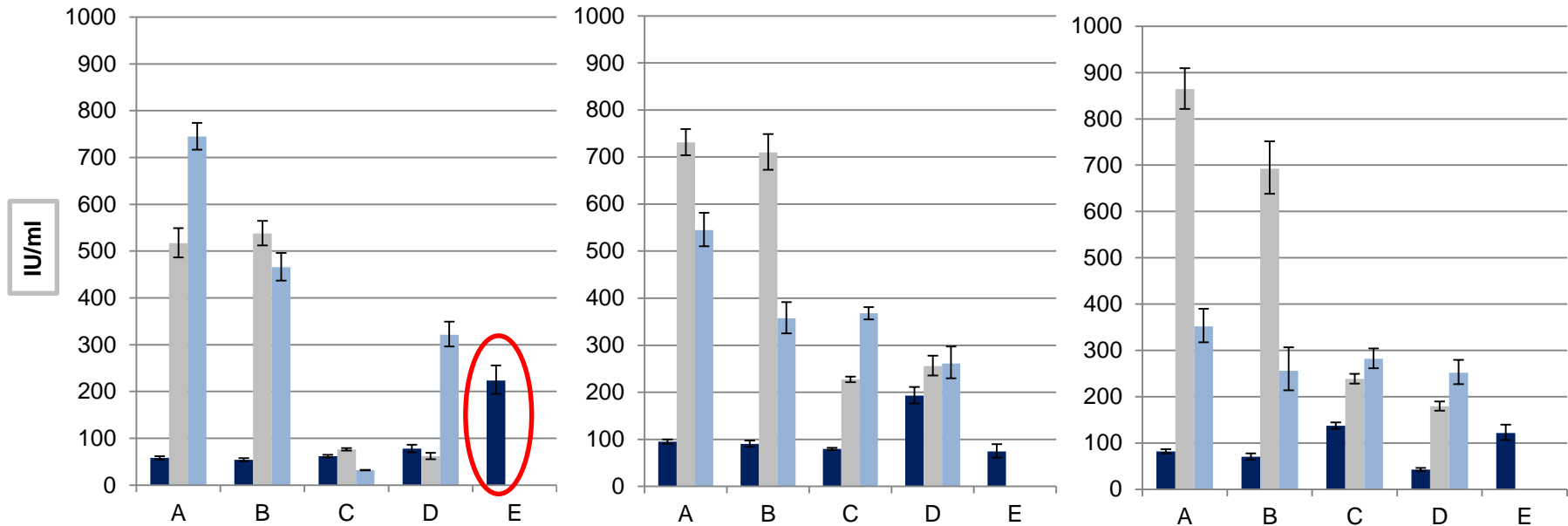
PT, FHA, PRN

■ PT ■ FHA ■ PRN

Children

Adolescents

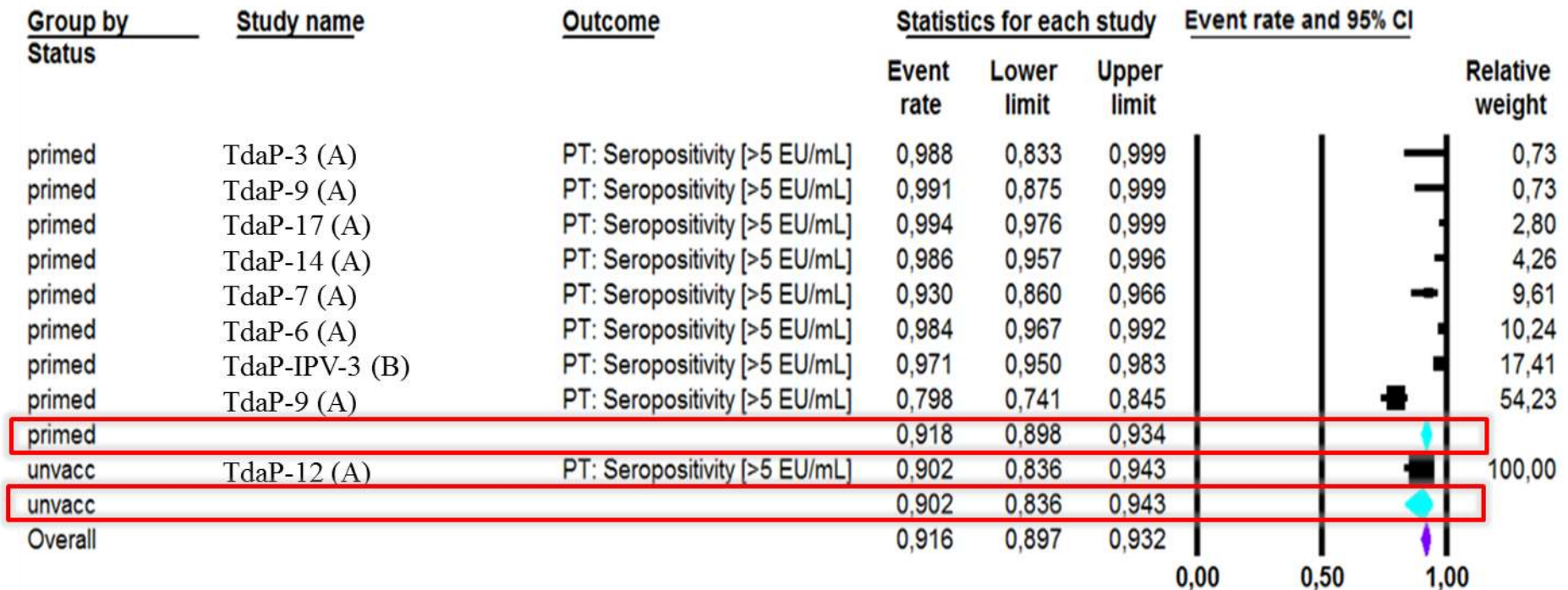
Adults



- Effect of 4-fold higher antigen content of TdaP-Immun (E) only seen in children
- Effect of higher FHA content of Boostrix/-Polio seen in all ages
- Age related ascension of anti-FHA-titres

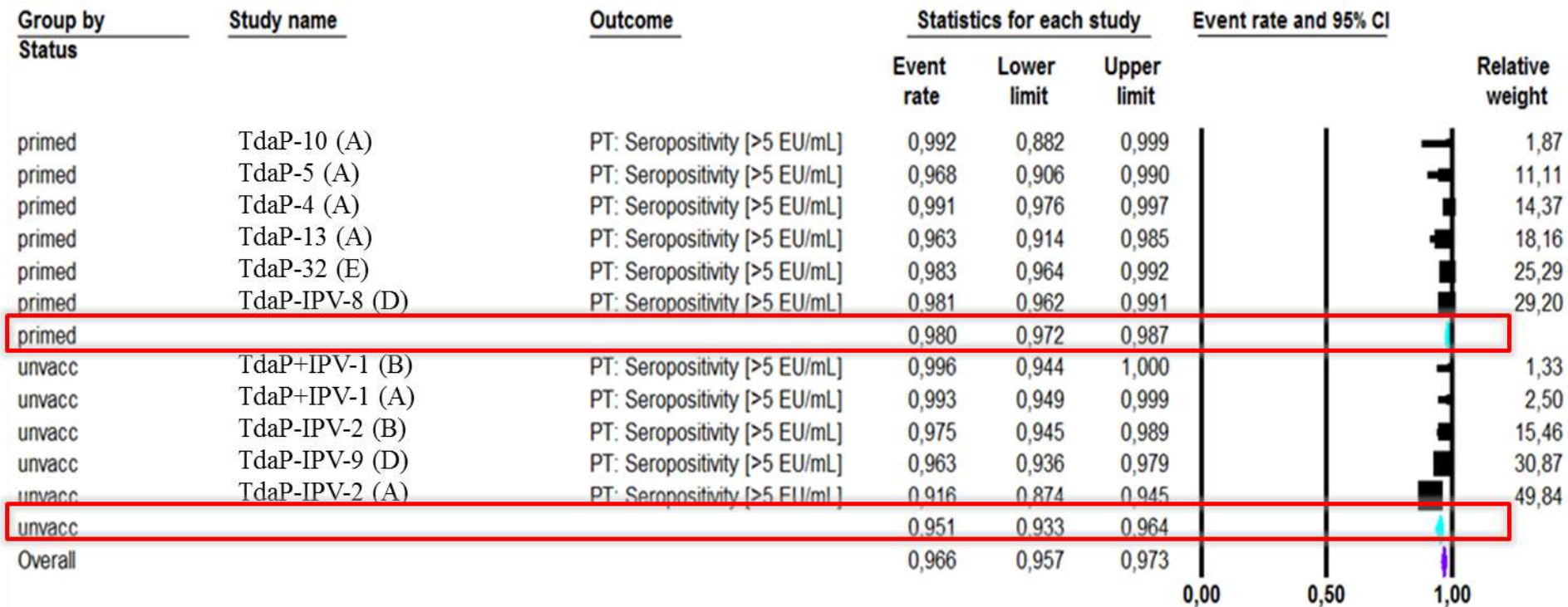


Unvaccinated vs. primed by vaccination Adolescents



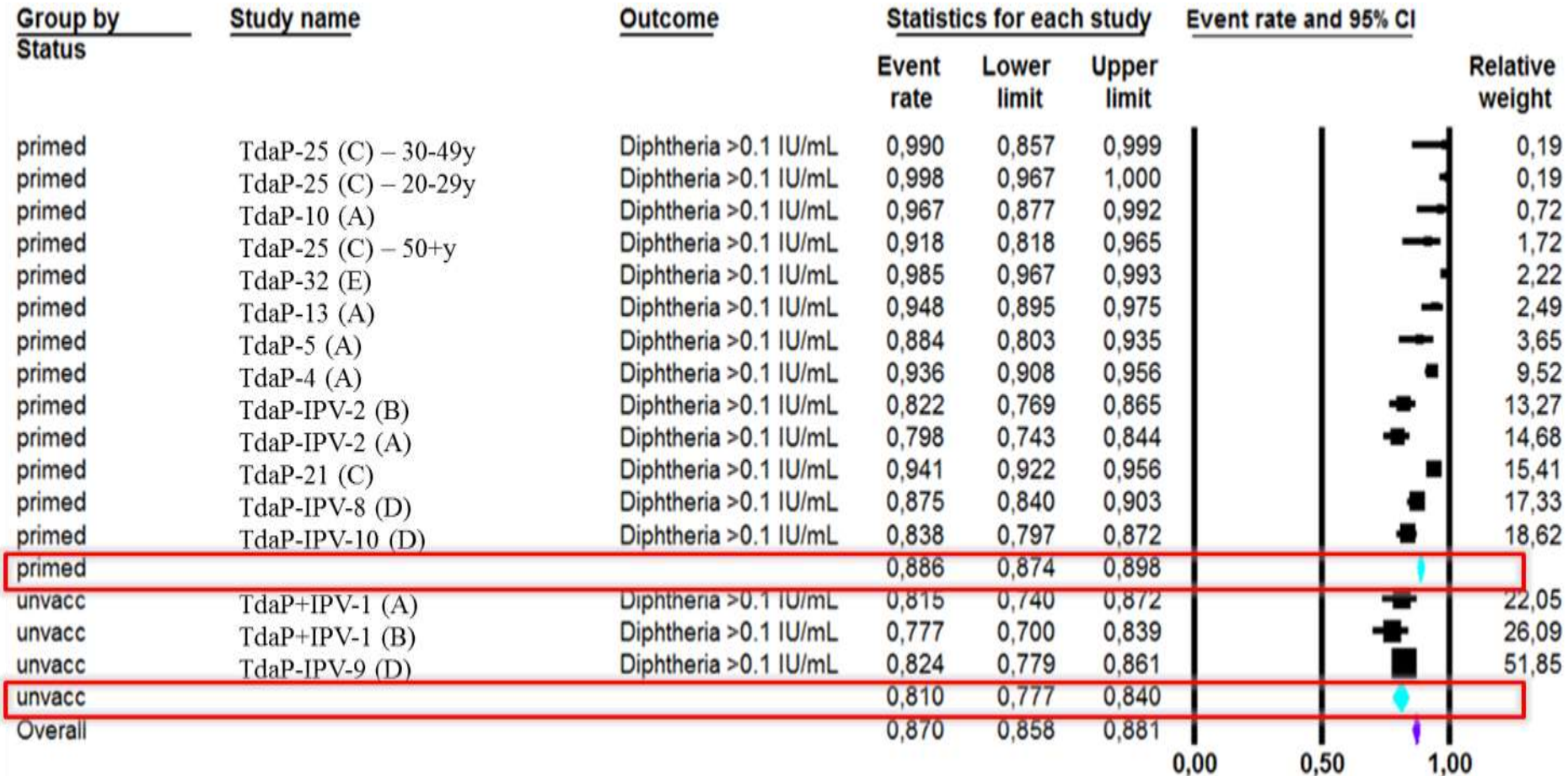


Unvaccinated vs. primed by vaccination Adults





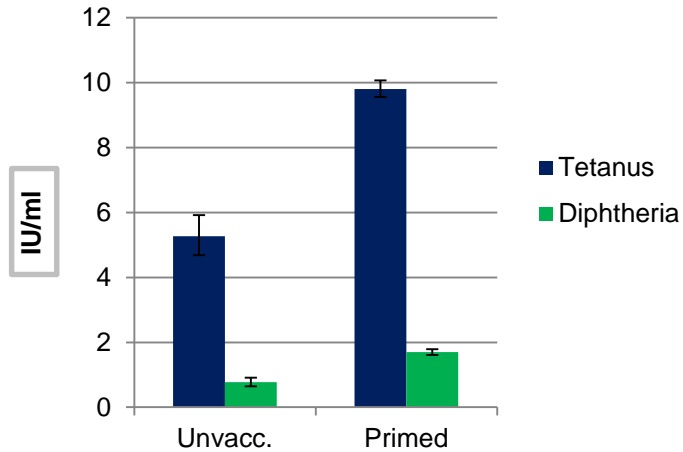
Unvaccinated vs. primed by vaccination





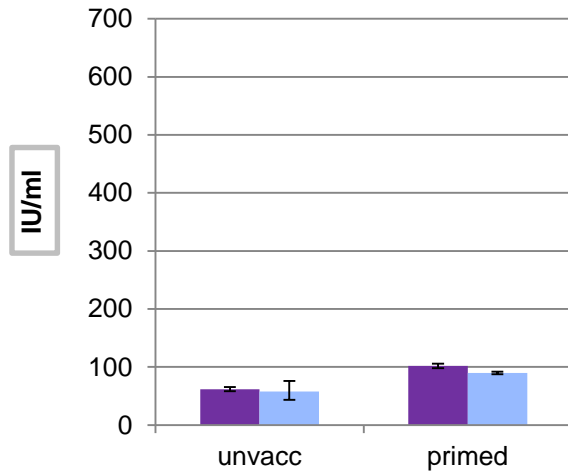
Unvaccinated vs. primed by vaccination - Titres

Adults

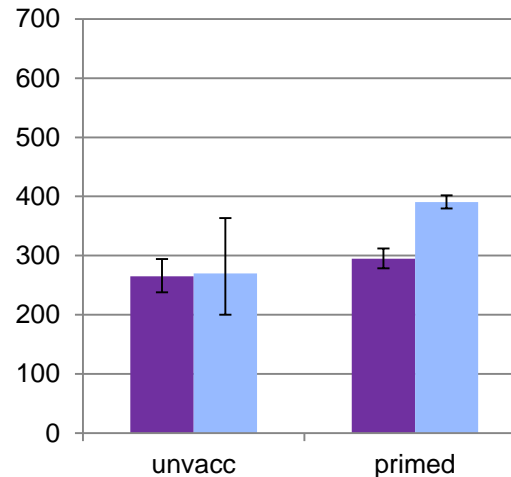


- Higher titres in primed but all above threshold of 0.1 IU/ml for T and D
- Similar titres after one dose for anti-FHA and anti-PRN regardless of priming
- Higher anti-PT titres in primed

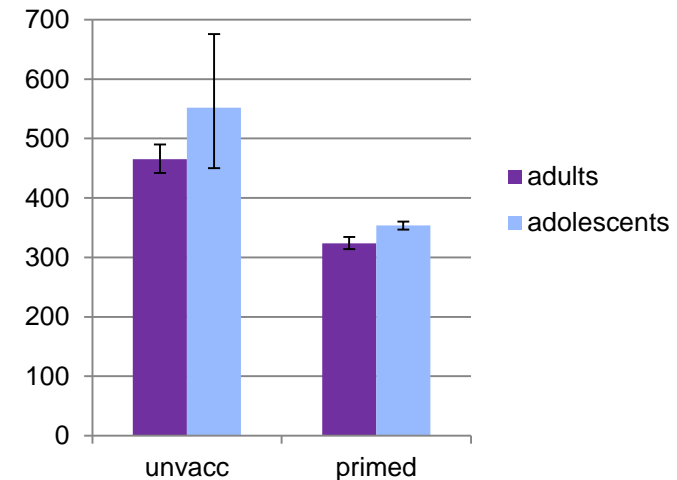
PT



PRN



FHA





Conclusions... so far

- Highly different number of studies per age for the different aspects of analysis
- Heterogeneity:
 - High even among studies using same vaccine
- Safety results show no differences between the vaccines in the different age groups
- Wide range of countries involved: no ethnicity related difference in immunogenicity or safety seen
- No scientific reason against interchangeability irrespective of age and vaccination status



Thank you

Isabelle Bekeredjian-Ding

Doris Oberle

Peter Volkers

Our colleagues from the sections microbiological vaccines,
microbiological safety, biostatistics and inspections



Open Positions for Microbiologists !

Please, contact us at microbiology@PEI.de or talk to me after the talk!