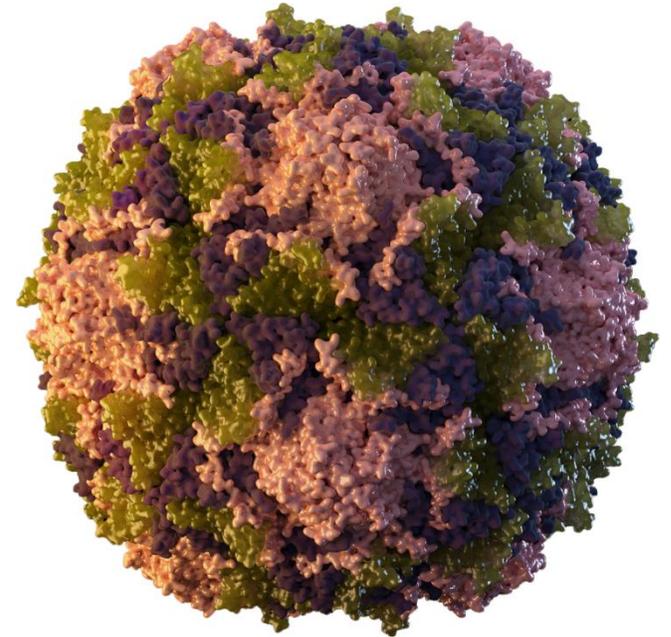


Clinical Considerations for Children who Received Fractional Dose Inactivated Polio Vaccine (fIPV) in Other Countries



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ACIP Meeting

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Background

- Wild poliovirus type 2 eradicated in 2015
- Global switch and withdrawal of Sabin type 2 virus from OPV in April 2016:
 - Replaced all trivalent OPV (tOPV; types 1, 2, and 3) with bivalent OPV (bOPV; types 1 and 3)
 - ≥1 dose IPV recommended as part of routine immunization in all countries using bOPV
- Based on clinical trial data and limited IPV availability, WHO supports use of **2 fractional doses of IPV (1/5 full dose IPV) given intradermally** in place of single full IPV dose (intramuscular)

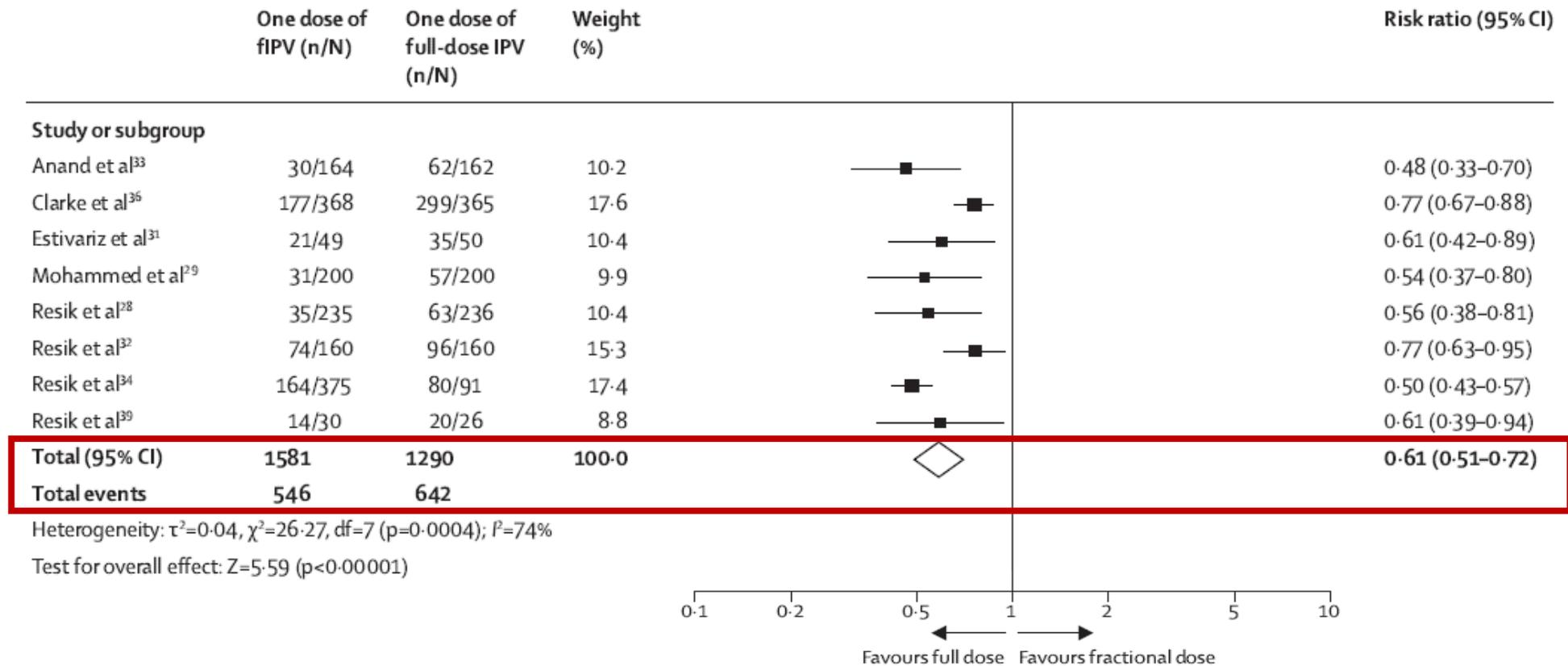
WHO. World Epidemiological Record 2016;91:561–82.

WHO. World Epidemiological Record 2021;96:613–32.

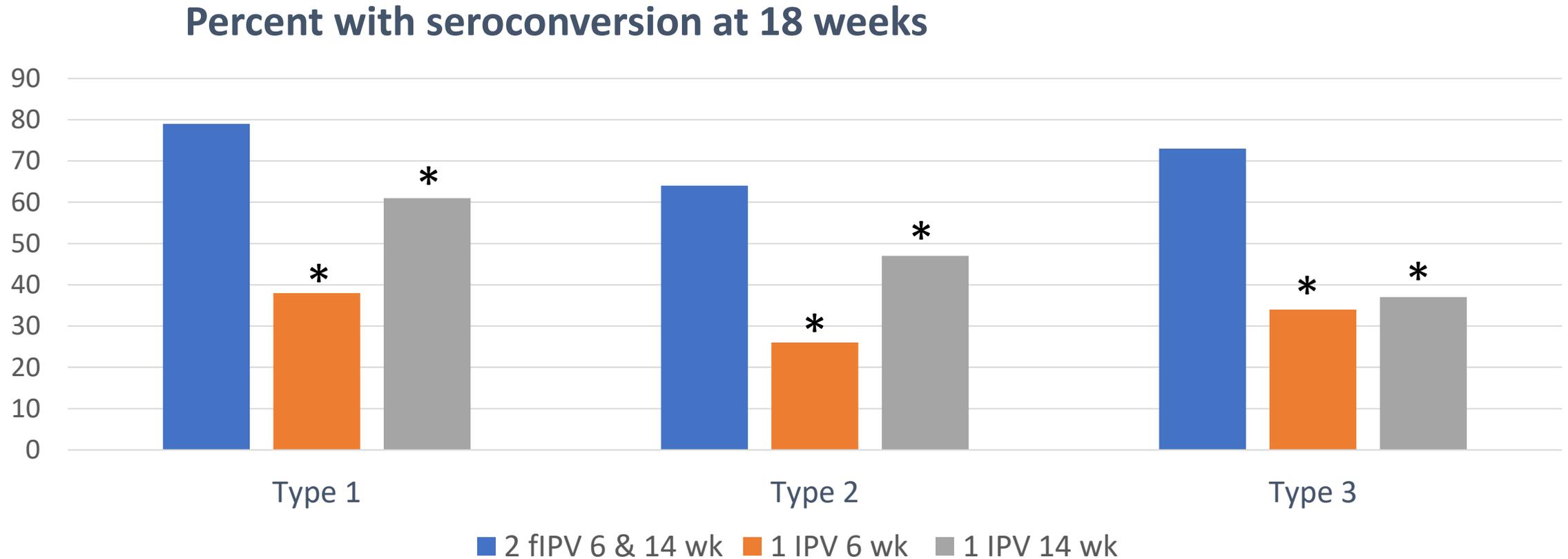
[https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/poliomyelitis-\(polio\)](https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/poliomyelitis-(polio))

ONE fractional IPV (fIPV) dose is LESS immunogenic than one full IPV dose

Meta-analysis of percent that seroconverted for poliovirus type 2 (Mashunye 2021)



TWO fractional IPV (fIPV) doses are MORE immunogenic than one full IPV dose



* $P < 0.01$ versus 2 fIPV doses

Current Use of fIPV in Routine Immunization Globally

- 6 countries (~20% of global birth cohort) use 2 fIPV doses + ≥ 3 bOPV doses in routine childhood immunization schedule
 - Bangladesh, Cuba, Ecuador, India, Nepal, Sri Lanka

Example polio vaccination schedule (India):

	Birth	6 weeks	10 weeks	14 weeks	16–24 months	Total doses
bOPV	X	X	X	X	X	5 bOPV
fIPV		X		X		2 fIPV

Current US Guidance

- Recommended polio vaccination
 - 4 total IPV doses, administered at 2, 4, 6–18 months, and 4–6 years OR
 - 3 total IPV doses if 3rd dose administered after 4th birthday and ≥6 months after 2nd dose
- For vaccines administered outside of US
 - Only tOPV or IPV doses considered valid for US vaccination schedule

Example polio vaccination schedule (India):

	Birth	6 weeks	10 weeks	14 weeks	16–24 months	Total doses
bOPV	X	X	X	X	X	5 bOPV
fIPV		X		X		2 fIPV

- Current US guidance:
- None of these doses considered valid in US
 - Needs 3–4 full IPV doses in US

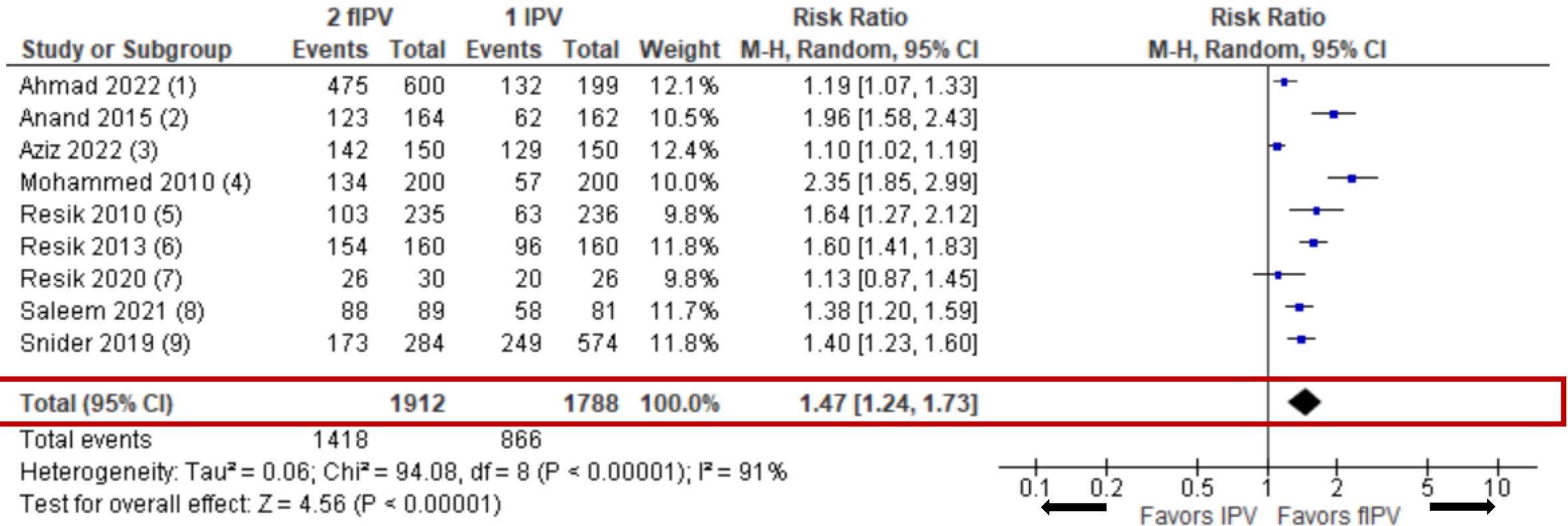
Question for Work Group:

Should 2 fractional IPV doses administered outside of the United States be counted as either 1 or 2 doses towards the US vaccination schedule?

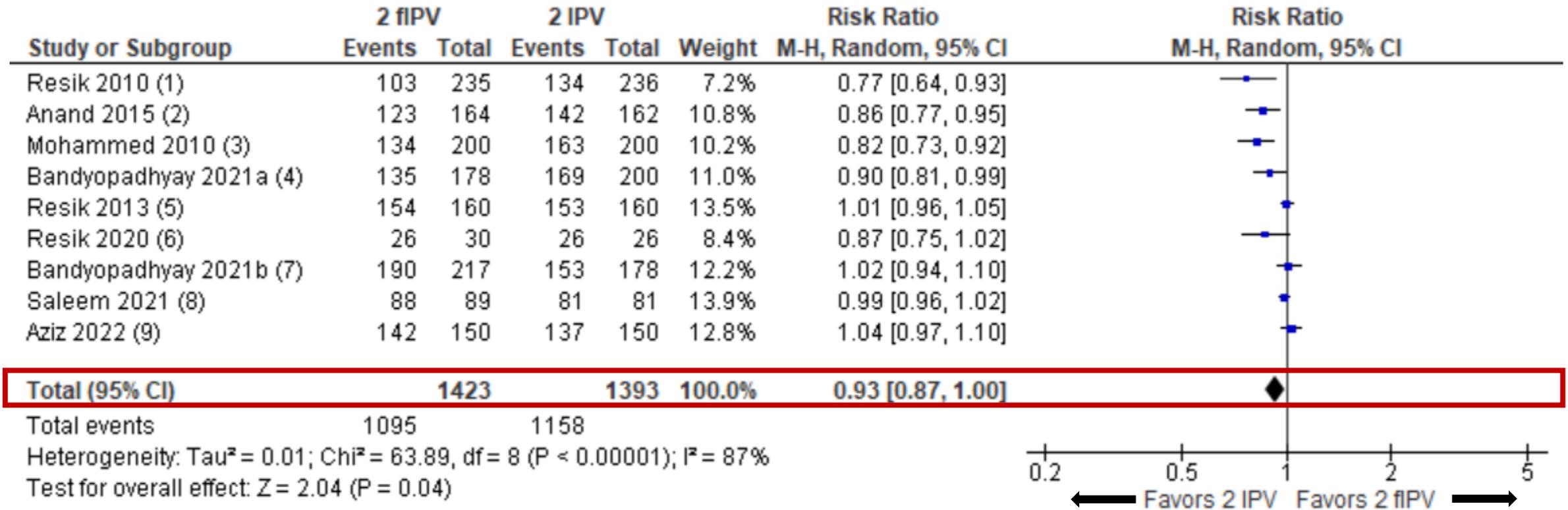
Methods: Updated Meta-Analysis

- Previous meta-analysis published in 2021 (Mashunye et al)
- Literature review using same search terms; searched Medline, Embase, Cochrane Library, Scopus, and ClinicalTrials.gov
 - Randomized clinical trials
 - Compared 2 fIPV doses to either 1 or 2 IPV doses
 - Published between January 1, 2019 and June 30, 2023
- Outcomes
 - Seroconversion for poliovirus type 2
 - Change from seronegative (titer <1:8) to seropositive (titer ≥1:8) OR
 - ≥4-fold increase in antibody titer over expected decline in maternal antibodies
 - Changes in geometric mean titers

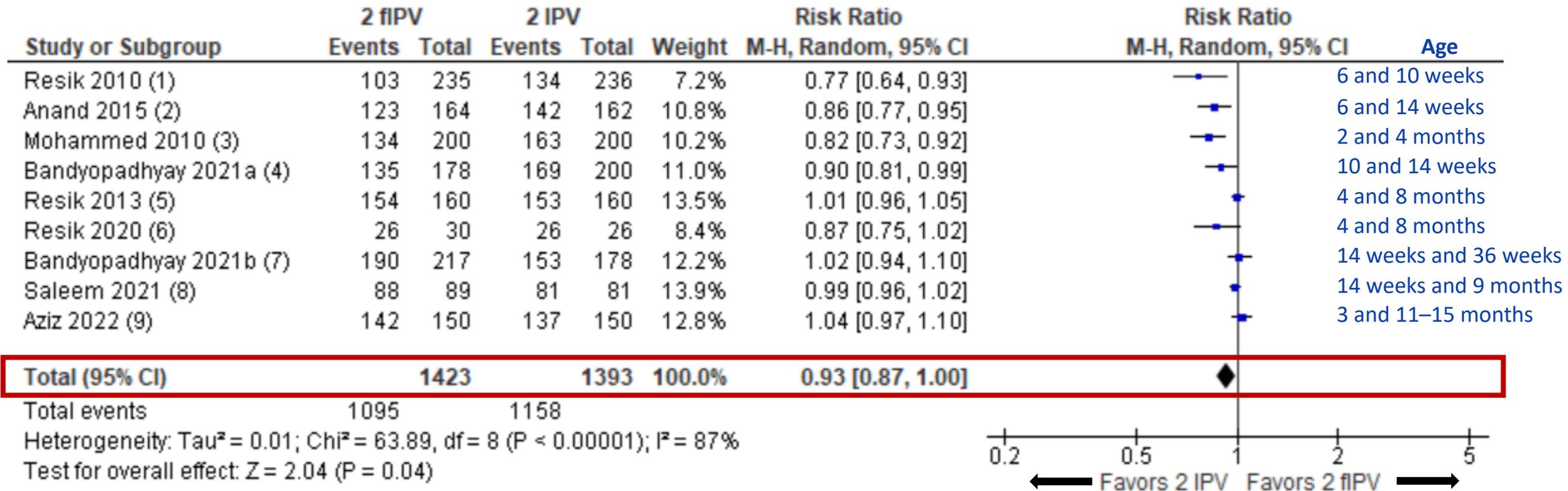
Seroconversion: 2 fIPV Doses vs. 1 IPV Dose



Seroconversion: 2 fIPV Doses vs. 2 IPV Doses

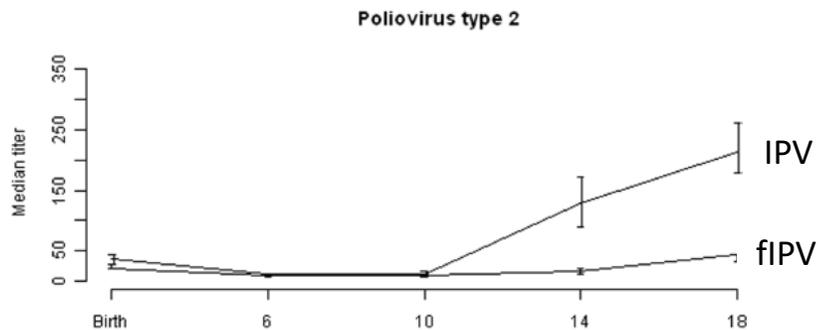


Seroconversion: 2 fIPV doses are less favorable vs. 2 IPV doses when given at younger age

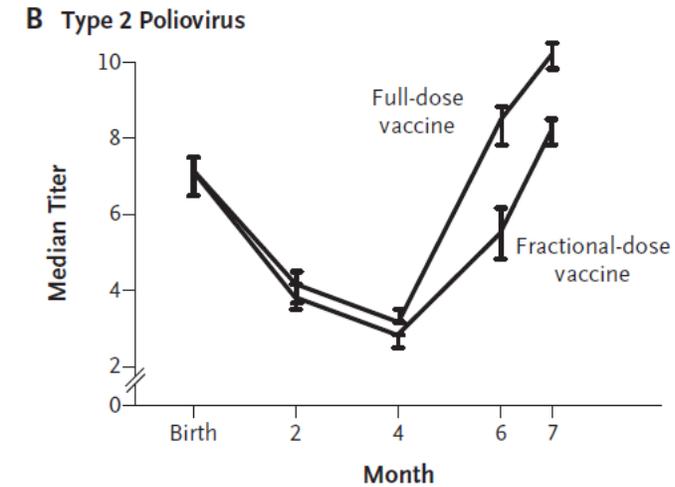


Median Antibody Titers Lower After 2 fIPV vs. 2 IPV Doses

Resik 2010 (3 doses at 6, 10, and 14 weeks)

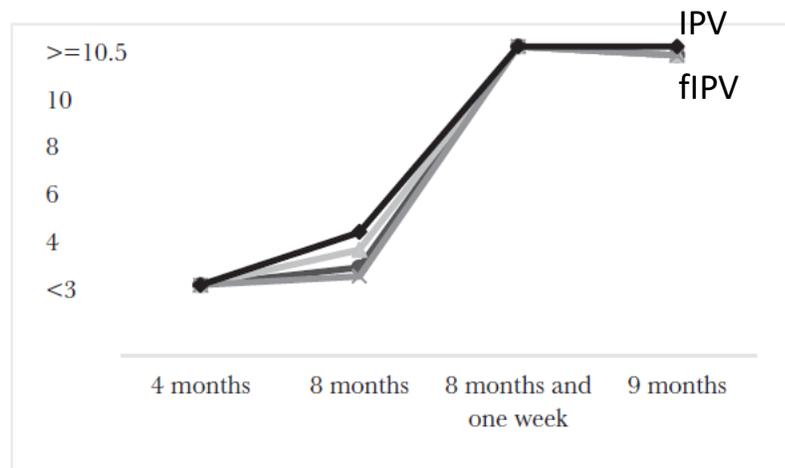


Mohammed 2010 (3 doses at 2, 4, and 6 months)



Resik 2020 (2 doses at 4 and 8 months)

Type 2

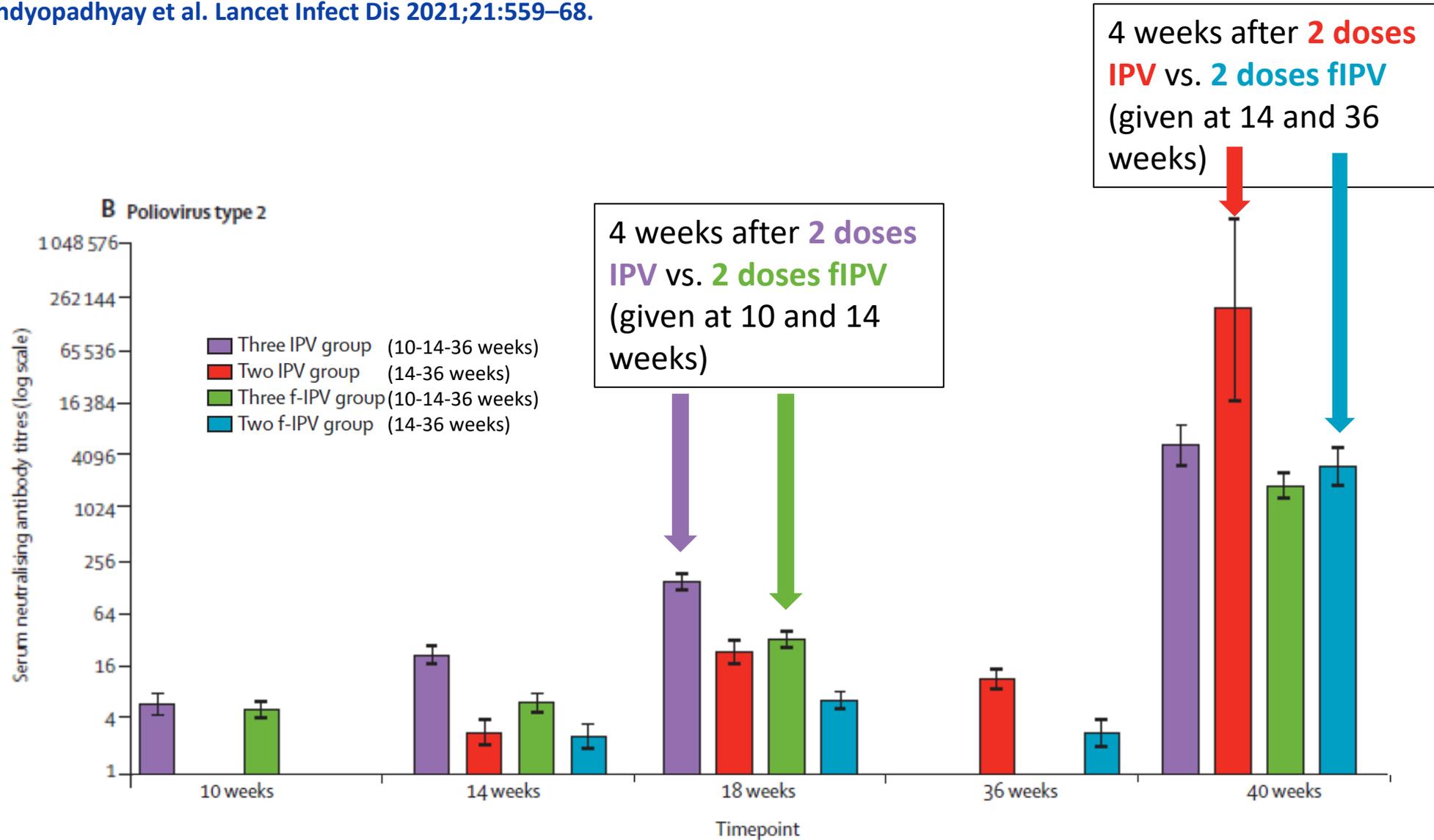


Resik 2013 and Aziz 2022: Median titer (95% CI) after 2 doses

	Age	fIPV	IPV
Resik 2013	4 and 8 months	898 (713-≥1448)	≥1448 (≥1448-≥1448)
Aziz 2022	9-13 and 11-15 months	455 (362-724)	≥1448 (1152-≥1448)

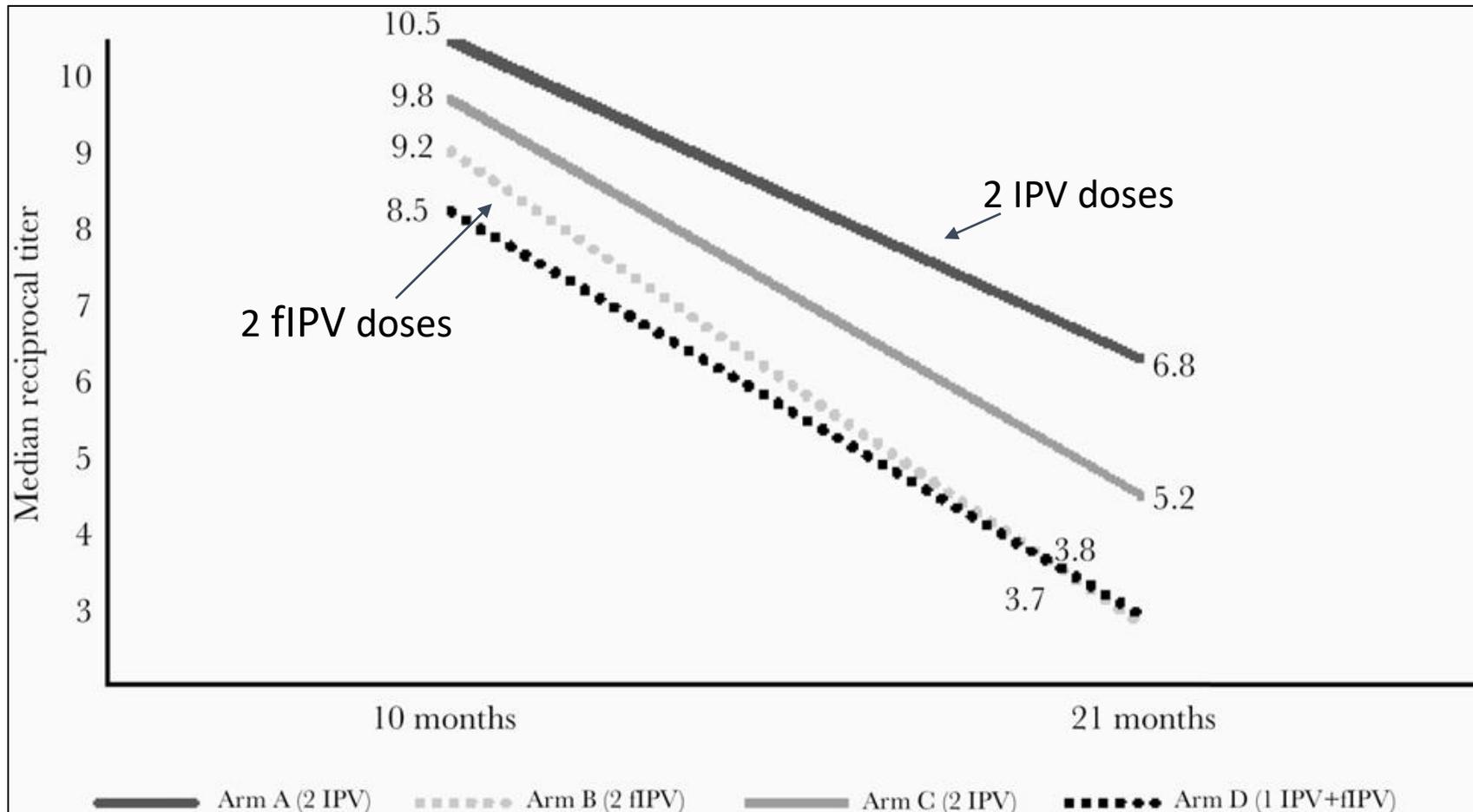
Geometric Mean Titers: 2 fIPV vs. 2 IPV Doses

Bandyopadhyay et al. Lancet Infect Dis 2021;21:559–68.



Persistence of Poliovirus Type 2 Antibodies Following 2 fIPV or 2 IPV Doses

Saleem et al. JID 2021; 223(7)1214



- As immunization series with fIPV reach lower final titers, seronegativity expected to be reached earlier

Summary

- WHO supports the use of 2 fIPV doses in place of 1 IPV dose as an IPV conservation strategy
- 2 fIPV doses associated with **higher** rates of seroconversion vs. **1** IPV dose
- 2 fIPV doses associated with **slightly lower** rates of seroconversion vs. **2** IPV doses
 - Especially when administered at 6 and 14 weeks; rates of seroconversion approach equivalency at older ages of administration
- Peak antibody titers are **lower** after 2 fIPV doses vs. **2** IPV doses

Proposed CDC Clinical Considerations

- For persons who received fractional (1/5 full dose) IPV administered intradermally outside of the United States, 2 fractional doses of IPV (fIPV) should be considered valid and counted as 1 full intramuscular dose of IPV towards the US vaccination schedule.
- If a person received only 1 dose of fIPV, this dose should not be considered valid or counted towards the US vaccination schedule.

Questions and Discussion

Polio Work Group Members

- ACIP voting members

- Oliver Brooks (Chair)
- Lynn Bahta
- Sybil Cineas

- Liaisons

- Lynn Fisher, American Academy of Family Physicians
- Chandy C. John, American Academy of Pediatrics
- Sandra Fryhofer, American Medical Association
- Kathy Kudish, Association of Immunization Managers
- Marcus Plescia, Association of State and Territorial Health Officials
- Paul R. Cieslak, Council of State and Territorial Epidemiologists
- Christine Hahn, Council of State and Territorial Epidemiologists
- Tina Q. Tan, Infectious Diseases Society of America
- Adenike Shoyinka, Infectious Diseases Society of America
- Mary Wilson, International Society of Travel Medicine
- Jaqueline Lawler, National Association of County and City Health Officials
- Kathy Edwards, Pediatric Infectious Diseases Society
- Joseline Zafack, Public Health Agency of Canada*

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*In the event of a Work Group poll, CDC, FDA, and Public Health Agency of Canada members are not included.