Table I: Addition of a second inactivated poliovirus vaccine (IPV) dose to routine immunization with bivalent oral poliovirus vaccine (bOPV)

Population : Immunocompetent children

Question necessary for recommendation development: Should a second dose of IPV be implemented alongside bOPV + 1 dose IPV in RI? Are there significant enhancements in type 2 poliovirus immunogenicity when adding an additional dose of IPV?				
			Rating	Adjustment to rating
Quality Assessment	No of studies/starting rating		5 RCTs[1]	4
	Factors decreasing confidence	Limitation in study design	Serious[2]	-1
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None detected	0
	Factors increasing confidence	Strength of association	Not applicable	0
		Dose-response	Not applicable	0
		Mitigated bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**3**
Summary of Findings	**Statement on quality of evidence**			Evidence supports a moderate level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome
	Conclusion			A second dose of IPV in bOPV-using countries significantly closes the type 2 immunity gap as well as increasing type 1 and 3 immunity.

Intervention : 2 doses IPV + bOPV

Comparison : 1 dose of IPV + bOPV

Outcome : Immunogenicity against type 2 poliovirus

[1] Five RCTs evaluated the effect of a second dose of IPV in a bOPV+IPV schedule. *Sutter et al (2015)* conducted an open label, randomised controlled trial in India enrolling 900 newborn infants. In bOPV + 2IPV group the seroconversion after 18 weeks was 99.4%, (96.5–100) for type 1, 78.1% (70.7–84.3) for type 2 and 98.7% (95.4–99.8) for type 3. *Qui et al (2017)* conducted a randomized controlled non-inferiority clinical trial including 504 infants in the study. 30 days after the last inoculation, seroprotection in 2IPV + bOPV receiving arm was 85(98.84, 93.69–99.97) for type 1, 85(98.84, 93.69–99.97) for type 2 and 86(100.0, 95.80–100.0) for type 3. *Asturias et al (2016)* performed an open label randomized controlled trial in Latin American infants assessing humoral (ie, seroconversion) and intestinal immunity (i.e., viral shedding) of a bOPV + 2IPV schedule. After a bOPV–two IPV schedule, seroconversion rates reached 100% (98·0–100) to type 1, 100% (98·0–100; p<0.0001 vs bOPV only) to type 2, and 99·5% (97·1–99·9) to type 3. *Tagbo et al (2021)* conducted a randomized controlled clinical trial in Nigerian children assessing gains in immunity with an addition of a second dose of IPV to a bOPV/IPV schedule. Seroconversion rates for type 1, 2 and 3 were 98.9% (95% confidence interval [CI], 96.7–99.8), 72.0% (95% CI, 66.2–77.3) and 98.1% (95% CI, 88.2–94.8) with one IPV dose compared to 89.6% (95% CI, 85.4–93.0), 95.9% (95% CI, 92.8–

97.9) and 98.5% (95% CI, 96.3–99.6) with two doses. Note the significant increase in type 2 seroconversion with 2 IPV doses. *O'Ryan et al (2015)* performed a randomized, controlled, open-label, non-inferiority study assessing IPV administration in a sequential schedule with bOPV. In an IPV-IPV-bOPV schedule, type 1 seroconversion was 100% (97.9–100.0), type 3 was 100% (97.9–100.0) and type 2 96.0% (92.0–98.0).

[2] An open label design was conducted in all studies since the vaccine delivery could not be masked (oral vs injectable). Only *Asturias et al (2016)* had blinded investigators.

References

1. Sutter RW, Bahl S, Deshpande JM, Verma H, Ahmad M, Venugopal P, Rao JV, Agarkhedkar S, Lalwani SK, Kunwar A, Sethi R, Takane M, Mohanty L, Chatterjee, John TJ, Jafari H and Aylward RB. Immunogenicity of a new routine vaccination schedule for global poliomyelitis prevention: an open-label, randomised controlled trial. Lancet. 2015; Sept 18; 386(10011):2413-21.
2. Qiu J, Yang Y, Huang L, Wang L, Jiang Z, Gong J, Wang W, Wang H, Guo S, Li C, Wei S, Mo Z and Xia J. Immunogenicity and safety evaluation of bivalent types 1 and 3 oral poliovirus vaccine by comparing different poliomyelitis vaccination schedules in China: A randomized controlled non-inferiority clinical trial. Hum Vaccin Immunother. 2017; Jun 3;13(6):1-10.
3. Asturias EJ, Bandyopadhyay AS, Self S, Rivera L, Saez-Llorens X, Lopez E, Melgar M, Gaensbauer JT, Weldon WC, Oberste MS, Borate BR, Gast C, Clemens R, Orenstein W, O'Ryan G M, Jimeno J, Costa Clemens SA, Ward J, Rüttimann R, and the Latin American IPV001BMG Study Group. Humoral and intestinal immunity induced by new schedules of bivalent oral poliovirus vaccine and one or two doses of inactivated poliovirus vaccine in Latin American infants: an open-label randomised controlled trial. Lancet. 2016 Jul 9;388(10040):158-69.
4. Tagbo BN, Verma H, Mahmud, Ernest K, Nnani RO, Chukwubike C, Craig KT, Hamisu A, Weldon WC, Oberste SM, Jeyaseelan V, Braka F, Mkanda P, Esangbedo D, Olowi A, Nwaze E and Sutter RW. Randomized Controlled Clinical Trial of Bivalent Oral Poliovirus Vaccine and Inactivated Poliovirus Vaccine in Nigerian Children. J Infect Dis. 2020; Nov 24;jiaa726.
5. O'Ryan M, Bandyopadhyay AS, Villena R, Espinoza M, Novoa J, Weldon WC, Oberste MS, Self S, Borate BR, Asturias EJ, Clemens R, Orenstein W, Jimeno J, Ruttimann R, Costa Clemens SA and Chilean IPV/bOPV Study Group. Inactivated poliovirus vaccine given alone or in a sequential schedule with bivalent oral poliovirus vaccine in Chilean infants: a randomised, controlled open-label, phase 4, non-inferiority study. Lancet: Infectious Diseases. 2015; 15(11):1273-1282.