Table II: IPV-only vaccination schedule

Population : Immunocompetent children (pre-OPV cessation)
Intervention : IPV-only schedule

Question necessary for recommendation development: How does the immunogenicity (humoral and mucosal) of an IPV-only schedule compare to a bOPV/IPV schedule? What is the preferred IPV-only schedule?				
			Rating	Adjustment to rating
Quality Assessment	No of studies/starting rating		24+ 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	Applicable[3]	+1
		Dose-response	Not applicable	0
		Mitigated bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			Evidence supports a high degree of confidence that the true effect lies close to that of the estimate of effect on health outcome.
	Conclusion			High scientific evidence that IPV-only schedules are at least as immunogenic (humoral immunity) as otherwise comparable IPV/OPV schedules but confers a lower degree of mucosal immunity.

Comparison : bOPV + IPV schedule
Outcome : Immunogenicity to poliovirus type 1, 2 and 3

[1] Tang et al (2018) performed a systematic review and meta-analysis of the immunogenicity of sequential OPV/IPV vs IPV-only schedules including 6 articles (Asturias et al 2007, Faden et al 1990, Liu et al 2013, Zhang et al 2014, Lu et al 2015, O'Ryan et al 2015). Seroconversion rates for types 1, 2 and 3 after three doses were close or up to 100% with no statistical difference between groups. However, the GMTs of seroconversion reached higher levels in sequential schedules than in IPV-only schedules. Thus, sequential schedules could induce a stronger immunogenicity. Macklin et al (2019) conducted a systematic review and network meta-analysis to produce comparative estimates of humoral and intestinal mucosal immunity associated with different routine immunisation schedules (i.e., IPV-only); 17 studies were included for assessment of humoral immunity and eight studies for intestinal immunity (some study overlaps with Tang et al 2018). There was no significant difference between the seroconversion achieved by two doses of full-dose IPV and intradermal fIPV (RR 0.88, 95% CrI 0.74–1.02). Adding a third dose to the schedule gave no significant increase in seroconversion (full-dose: RR 0·96 (0.81–1.15); fIPV: RR 1.01 (0.85–1.20)). There was no significant difference between three doses of any alternative IPV formulation with Salk IPV, fIPV

(0·92, 0·83–1·0), sIPV (1·01, 0·93–1·10), or IPV-Al (0·96, 0·83–1·11). The addition of an IPV to bivalent OPV schedules did not significantly increase intestinal immunity (0·33, 0·18–0·61), compared with trivalent OPVs alone. Confirming that IPV-only schedules would provide inadequate intestinal immunity and do not prevent viral shedding following a challenge dose, but they might reduce the quantity and duration of shedding; IPV can boost mucosal immunity in OPV primed schedules in a serotype-specific manner. Brickley et al (2018) analysed the intestinal immunity conferred by an IPV/OPV vs IPV-only schedule through a randomized, controlled trial. The study reported type 2-specific viral shedding in 37% of infants in the IPV/OPV schedule compared to 26% in an IPV-only schedule. These results underscore the concept that mucosal and systemic immune responses to polio are separate in their induction, functionality, and potential impacts on transmission and, specifically, provide evidence that primary vaccine regimens lacking homologous live vaccine components are likely to induce only modest, type-specific intestinal immunity. The meta-analysis presented in the August SAGE WG analysed different IPV-only schedules. 2 IPV doses (full/fractional) starting at 14 weeks with an interval of at least 4 months provide high sero-protection against all three polio types. 3 IPV full doses (Salk/Sabin) provide high seroprotection when starting from 8 weeks of age with benefit of early protection. 3 IVP full doses (Salk/Sabin) using «early schedule» starting at 6 weeks of age (6,10, 14 weeks) showed lesser immunogenicity. 3 fIPV doses in «early schedule» (6, 10, 14 weeks) do not provide equivalent/high seroconversion as compared to 2 fIPV starting at 14 weeks of age with longer interval between the doses. Affordable fIPV scheule options with benefits of early protection and higher immunity being investigated: 10,14,36 weeks fIPV data available; 6,14,36 weeks fIPV data being generated. Moreover, fIPV IM study in Cuba showed equivalence to fIPV ID

[2] Faden et al 1990 and Lu et al 2015 had poor follow-up rates (<90%). Masking was not possible in participants and physicians because of the oral vs injectable nature of OPV and IPV, respectively.

[3] As aforementioned, all studies included in the meta-analysis (Tang et al 2018) demonstrated near 100% seroconversion rates after 3 doses of IPV, indicating non-inferior humoral immunity. However, it must also be considered the poor mucosal immunity IPV-only schedules confer (Brickley et al 2018).

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