

Table. Checklist of pre-specified criteria to compare studies with IPD and with only AD

Checklist			Case study	
Item	Description	Explanation	Findings case study	Judgement case study
Data availability	Proportion of events unavailable for primary outcome if only IPD are included	Number of trials or overall sample size often misleading, since not all trials have primary outcome data available. Number of events more informative.	Proportion of events unavailable for primary outcome (infant mortality) if only IPD are included: 11.9%	?
Statistical methods	Statistical methods used to derive AD sufficiently comparable to IPD	E.g. controlling for same covariates/ confounders, linear or logistical regression methods	Similar statistics for main analysis (logistic regression), but no adjustment for multiple births and covariates in AD. Complex analyses (e.g. subgroup analyses) not possible with AD.	?
Baseline characteristics	Differences between key baseline characteristics IPD vs AD	Identify whether IPD and AD studies assessed comparable populations	Systematic differences between gestational age, birthweight (infants in IPD trials were lower birthweight and lower gestational age) and sex (more females in AD trials)	✗
Study characteristics	Differences between key study characteristics	Systematic differences between the types of studies providing data (e.g. study year, size)	AD studies slightly smaller and older, but differences too small for exclusion of AD	✓
Effect size	Differences in effect size for 2-3 key pre-specified outcomes (meta-regression, visual inspection of forest plots & contour-enhanced funnel plots)	Major differences in effect sizes may point toward bias or different underlying populations	Systematic differences for 2 out of 3 outcomes, much larger effect sizes in AD studies 1) Mortality: no difference between IPD and AD, interaction p = .79 2) Intraventricular Haemorrhage: OR _{IPD} (95%CI) = .97 (.83-1.14); OR _{AD} (95%CI) = .51 (.34-.76); interaction p < .001. 3) Blood transfusion: OR _{IPD} (95%CI) = .86 (.80-.93); OR _{AD} (95%CI) = .35 (0.18-0.69); interaction p = .01	✗
Risk of bias	Differences in risk of bias IPD vs AD	Assess and compare risk of bias for primary outcome, applying standard risk of bias tool (e.g. Cochrane ROB 2 for RCTs)	Risk of bias lower for IPD studies across all domains Overall risk of bias for mortality high for 86% of AD studies versus 29% of IPD studies	✗
Trustworthiness	Differences in trustworthiness assessments IPD vs AD	Perform integrity checks to compare trustworthiness of included studies	More trustworthiness issues for AD studies (e.g. implausible results, lack of ethics approval), many additional checks not possible without IPD	✗
Overall decision	Do concerns about AD outweigh data availability concerns?	Overall assessment across categories, and severity of concerns	Concerns in most categories, some are severe. Decision: Exclude AD from primary analysis	✗

Note: AD = aggregate data, IPD = individual participant data, RCT = randomised controlled trial, OR = Odds Ratio, CI = Confidence Interval ✓ = no concerns with AD, ? = some concerns with AD, ✗ = major concerns with AD