Reflections on evidence synthesis methods within child health

Aim(s)	Method	Reflections on the methods application within child health
To determine the relative effectiveness and ranking of health interventions in children and young people.	**Bayesian network meta-analysis** (NMA) (1) using aggregate data from randomised control trials (RCTs) in children **and young people**.	**Bayesian NMA** is an **invaluable tool** within child health, reducing the need for additional clinician trials in children through the estimation of indirect treatment effects. **Informative prior distributions** can be specified for the treatment effect and between-study heterogeneity where evidence is particularly sparse.
To determine whether integrating adult clinical trial data improves the precision of relative effect estimates in children and young people.	**Bayesian information-sharing model** incorporating aggregate data in adults for health interventions present in a network of treatments in children. Methods should **account for differences** in relative treatment effect between children and adults (2).	Incorporation of **adult evidence** often requires **considerable resources** and may only be beneficial where there are **sufficient similarities** (or predictable/ consistent differences) in treatment effect between populations. Comparison between treatment effect estimates reported in the primary literature for different populations is recommended.
To determine whether joint synthesis of outcomes can improve the precision of treatment effects for poorly reported outcomes in children and young people.	**Multivariate meta-analysis** (3)/ NMA using individual participant data (IPD) from RCTs in children and young people.	The **benefits of multivariate synthesis depend** upon there being **sufficient correlation** between outcomes of interest. The likely strength of correlation should be carefully considered prior to IPD collection.
To determine whether patient-level characteristics (personal and/or treatment-related) alter the relative treatment effect in children and young people.	**IPD network meta-regression** using data acquired from RCTs in children and young people. OR **Multi-level network meta-regression** (ML-NMR) (4) using IPD and aggregate data.	**IPD network meta-regression** is a **valuable tool** in child health, given that it is often difficult to establish interaction effects within individual paediatric clinical trials (due to small sample sizes). The analyses may help to **personalise care** in an often-heterogeneous population.

Public involvement

N.B Within evidence synthesis in child health, children and their families should be involved in projects to identify patient-important outcomes (which may be different for children of different ages). These outcomes can be prioritised for extraction as aggregate data and collection as IPD, helping to both improve the usefulness of the evidence synthesis and help to identify evidence gaps where present, as well as guide recommendations for future primary research. Patient support charities can help to facilitate connections with children and families and may also help to advertise involvement activities, e.g. through their social media outletsMethodological.

Key references for methods

1) Dias, S., Ades, T., Welton, N. J., Jansen, J., & Sutton, A. J. (2018). *Network Meta-Analysis for Decision-Making*. Wiley.

2) Walker R, Phillips B, Dias S (2023) Comparison of Bayesian methods for incorporating adult clinical trial data to improve certainty of treatment effect estimates in children. PLOS ONE 18(6): e0281791.

3) Riley, R. D., Price, M. J., Jackson, D., Wardle, M., Gueyffier, F., Wang, J., Staessen, J. A., and White, I. R. (2015) Multivariate meta-analysis using individual participant data. *Res. Syn. Meth.*, 6: 157–174.

4) Phillippo DM, Dias S, Ades AE, Belger M, Brnabic A, Schacht A, Saure D, Kadziola Z, Welton NJ. Multilevel network meta-regression for population-adjusted treatment comparisons. J R Stat Soc Ser A Stat Soc. 2020 Jun;183(3):1189-1210.