Can Adult Evidence Improve Our Understanding Of Treatment Effect In Children?

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Background

Data on treatment effect **in children** is often **lacking** compared to that in adults, in part, due to a lower disease incidence in children.

Incorporating **adult evidence** into evidence syntheses that inform child health policy, may be useful, as it may **improve our understanding** of how treatments work in children. However, this approach may also be **risky** as children may respond differently to treatments compared to adults.

Research aims

This concept was explored using data from randomised control trials (RCTs) evaluating **anti-sickness medications** in **patients receiving chemotherapy**.

The main aim was to determine whether the inclusion of adult evidence could improve the precision of treatment effect estimates in children and/or change conclusions about which treatment are most effective.

Methods

Firstly, a Bayesian **network meta-analysis (NMA)** comparing anti-sickness medicines recommended for use in children, was conducted using data from **child RCTs** only. These analyses were conducted using BUGS software.

Adult evidence was then **incorporated** into these analyses. The NMA model was modified to **simultaneously combine child and adult data**, whilst estimating differences in relative treatment effect between the two populations.

Models assuming all studies estimate the same effect (fixed-effect), were **compared** to models assuming study effects are exchangeable or similar (random effects).

Outcomes of '**complete response**' i.e. no vomiting or use of rescue medication, were assessed in the acute (0-24hrs post chemotherapy) and delayed (24hrs-5 days post chemotherapy) phase.

The ability of the analyses to **improve** our understanding of **how well treatments work in children** was assessed.

Results

Sixteen studies were included in the analyses, four (1118 patients) in children and twelve (8034 patients) in adults. In the NMA's of child data, the fixed effects models mainly were preferred. Differences in relative treatment effect between the two populations meant when incorporating adult evidence into the NMA of child data, random effects models were mainly preferred.

On average, **children gained greater relative benefit** from anti-sickness medicines compared to adults (when medicines were compared to the reference treatment ondansetron), as shown in the example below for complete response in the acute phase (other outcomes showed similar results).

Including adult evidence introduced (in most cases), **additional uncertainty** into the analyses, making **estimates of treatment effect** in children, **less precise**. Even for outcomes where precision was improved, our understanding of which anti-sickness medicines work in children receiving chemotherapy has not changed.

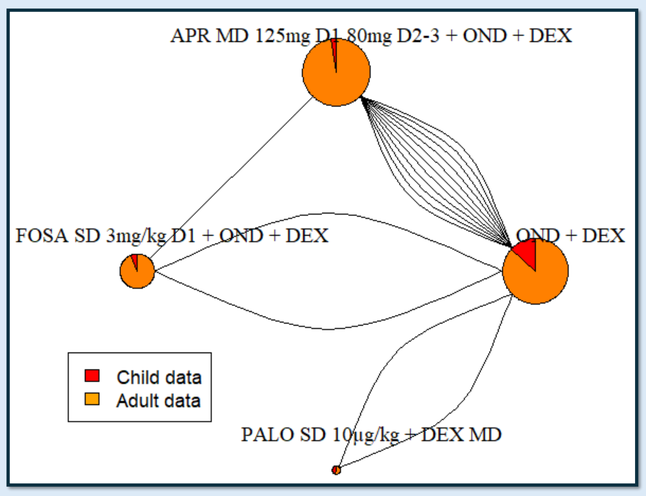

Figure 1. *Network diagram for antiemetic regimens given with dexamethasone the outcome complete response in the acute phase. The circle size is proportional to the number of patients and the number of the lines equals the number of clinical trials. All doses are indicative of dosing in children. (OND= ondansetron, APR= aprepitant, FOSA= fosaprepitant, PALO= palonosetron, DEX= dexamethasone, SD= single dose before chemotherapy, MD= multiple doses, both before and after chemotherapy).*

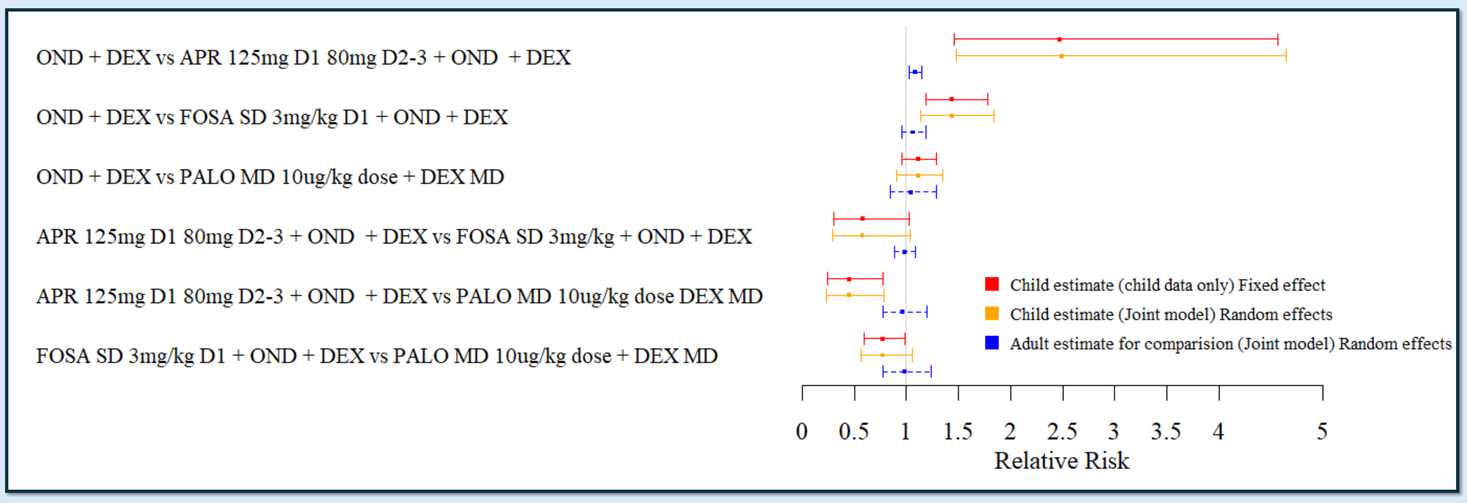

Figure 2. *Forest plot: Relative risk (RR) (95% credible interval (CrI)) in children, estimated from child data only (red), and a joint model of child and adult data (yellow). RR (95% CrI) in adults estimated from the joint model of child and adult data (blue) are shown for comparison. The outcome is complete response in the acute phase (0-24 hours after chemotherapy administration) (studies comparing antiemetic regimens given with dexamethasone). Values of above one favour the second named intervention. (OND= ondansetron, APR= aprepitant, FOSA= fosaprepitant, PALO= palonosetron, DEX= dexamethasone, SD= single dose before chemotherapy, MD= multiple doses, both before and after chemotherapy). N.B antiemetic regimens given with and without dexamethasone were analysed in separate networks due to differences in the emetogenicity of chemotherapy received by the underlaying population.*

Conclusion

Adult evidence should not be assumed generalisable to children, and methods of synthesising child and adult data should account for differences in treatment effect which may be present. For the inclusion of adult evidence to be beneficial, there may need to be sufficient similarities in treatment effect between the child and adult populations. It may therefore be advisable to compare relative treatment effects in primary studies, between child and adult populations, before deciding whether to include adult evidence in syntheses of child data.

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