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Children with complex congenital heart disease and new meta-analyses

Darlene Huisenga[1,2], Sacha la Bastide-Van Gemert[3], Andrew Van Bergen[4], Jane Sweeney[5], Mijna Hadders-Algra[2]

1 Advocate Children's Hospital – Pediatric Rehabilitation and Development, Oak Lawn, IL, USA. **2** University of Groningen, University Medical Center Groningen – Developmental Neurology, Groningen; **3** University of Groningen, University Medical Center Groningen – Epidemiology, Groningen, the Netherlands. **4** Advocate Children's Hospital – Heart Institute Division of Pediatric Cardiac Critical Care, Oak Lawn, IL; **5** Rocky Mountain University of Health Professionals – Pediatric Science Doctoral Program, Provo, UT, USA.

Correspondence to: m.hadders-algra@umcg.nl

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EDITOR–We thank Ilardi et al.[1] for their critical comments on our systematic review.[2] They raise important points. First, they stress the importance of avoiding overlap between studies in meta-analyses. We fully agree. As noted in our review, the Western Canadian Registry (WCR) contributed largely. Most likely, WCR studies sometimes overlapped to some extent (e.g. partial overlap in surgery period or diagnoses). The extent of overlap was, however, often not clear. For our meta-analysis this meant we had to balance between being unnecessarily strict by omitting all studies with any potential overlap and allowing some overlap therewith using all potential information available ('not throwing out the baby with the bathwater'). We used the latter strategy. In addition, as we share with the authors the interest in the effect of age, we had included longitudinal studies if the data were collected at least 3 years apart. Application of a statistically strict approach where we avoided any potential overlap yielded the following results (Fig. 1).

The new meta-analyses of the Bayley Psychomotor and Mental Developmental Indices (psychomotor developmental index [PDI] and mental developmental index [MDI]) resulted in similar findings as the published ones. The estimated mean PDI was 78.29 (95% CI 74.28–82.29), with a significant difference between children with single (1V) and two ventricle (2V) physiology (76.78 [70.49–83.08], 87.40 [82.94–91.86], p=0.003). The effects of surgery period (p=0.01) and age were similar to those reported before. The estimated mean MDI was 84.92 (95% CI 81.54–88.30) with no statistically significant difference between children with 1V and 2V complex congenital heart disease (CCHD). The effects of surgery period (p<0.001) and age (p=0.01) were similar to the published ones.

The new meta-analyses of the IQ data revealed IQ scores comparable to those published before, with estimated mean IQ scores: full-scale IQ 95.80 (95% CI 93.52–98.07), verbal IQ 96.16 (95% CI 92.33–99.99), and performance IQ 96.09 (95% CI 92.92–99.25). The difference in full-scale IQ of children with 1V and 2V CCHD showed a similar trend as reported before, but was now borderline statistically significant (92.00 [88.04–95.95], 97.04 [92.51–

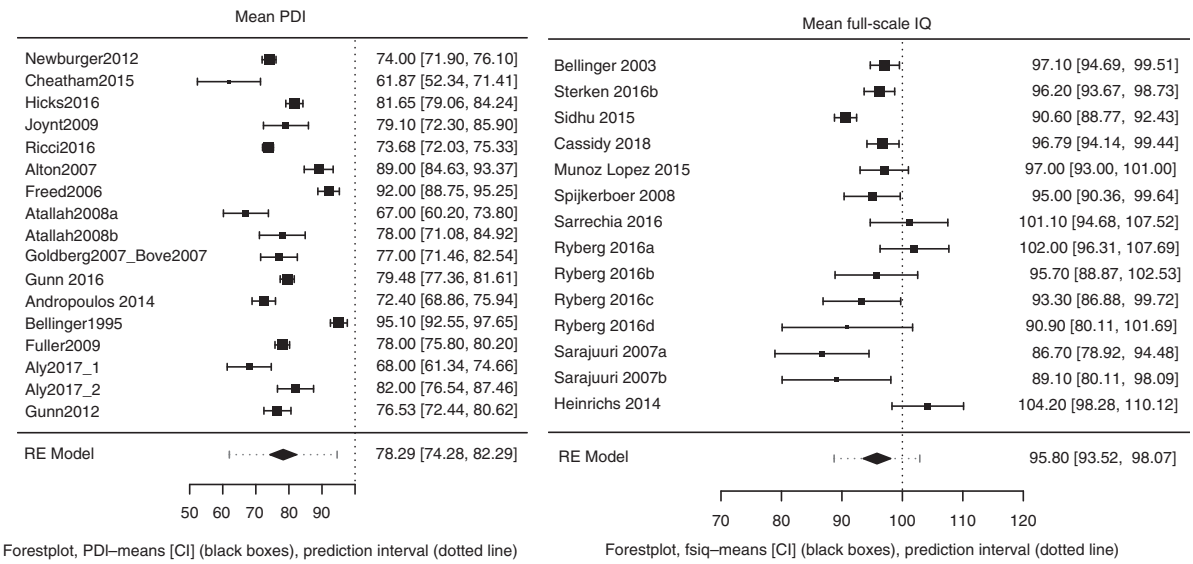

Figure 1: Forest plots of the new meta-analyses of Bayley psychomotor developmental index (PDI) and full-scale IQ scores.

101.56], p=0.07). Similar effects occurred for verbal IQ and performance IQ. The age effect reported for verbal IQ (p=0.08) was no longer significant, the age effect for performance IQ could no longer be reliably calculated.

Second, Ilardi et al. commented that our remark 'children with 2V CCHD gradually outgrow their initial developmental impairment' contradicts decades of research indicating high-risk infants often grow into developmental impairments when they get older. Again, we fully agree; the concept of growing into a deficit is well-known. However, the notion of growing out of an initial impairment is equally true.[3,4] Some children present in early life with neurodevelopmental impairment due to perinatal and neonatal illness. But when they recuperate from illness their young brain with its high neuroplasticity may recover. Our systematic review data suggest this may occur in children with 2V CCHD: their Bayley scores at early age were about 10 points below the mean, whereas IQ scores at older age were close to the mean (full-scale IQ 97). Our data suggest that the picture may be somewhat different for children with 1V CCHD: their Bayley scores were ≥15 points below the mean, and their IQ scores about 8 points. The latter means, in terms of general performance, that some children with 1V CCHD improve, whereas a substantial proportion of these children continue to show neurodevelopmental impairment. The latter may not only manifest in lower IQ but also in other neurocognitive impairments (as the systematic review suggested). We did not intend to negate any prior research, but rather the contrary. Therefore, we advocate long-term prospective studies, as knowledge on which children with CCHD are most at risk is still scarce.

REFERENCES

1. Ilardi D, Wolfe KR, Sanz JH, Cassidy AR. Meta-analysis in congenital heart disease: a question of sampling and interpretation. *Dev Med Child Neurol* 2020 Sep 10. https://doi.org/10.1111/dmcn.14668. Online ahead of print.
2. Huisenga D, La Bastide-Van Gemert S, Van Bergen A, Sweeney J, Hadders-Algra M. Developmental outcomes after early surgery for complex congenital heart disease: a systematic review and meta-analysis. *Dev Med Child Neurol* 2020 Mar 9. https://doi.org/10.1111/dmcn.14512. Online ahead of print.
3. Hadders-Algra M. Two distinct forms of minor neurological dysfunction: perspectives emerging from a review of data of the Groningen Perinatal Project. *Dev Med Child Neurol* 2002; **44**: 561–71.
4. Hadders-Algra M. Early diagnosis and early intervention in cerebral palsy. *Front Neurol* 2014; **5**: 185.