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Fertility treatments, maternal intelligence, and child cognition

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More than three decades of research and clinical experience with fertility treatments have led to an ever-growing number of children conceived using these technologies, but recent advances in embryology and epigenetics have raised concerns regarding possible disruption to embryologic development. Although fertility treatments are associated with increased perinatal morbidity risks, most studies examining cognitive outcomes have found no differences between children conceived with fertility treatments and those spontaneously conceived (Bay et al.), *Fertil Steril* 2013;100(3):844–53). However, previous studies have not considered important potentially confounding parental factors. Access to fertility treatments has been associated with higher parental intelligence, education, age, and socioeconomic status, which are associated with more optimal offspring cognitive development, while subfertility may be related to heritable issues associated with poorer cognitive outcomes.

In this prospective study examining potential effects of fertility treatments on 5-year cognitive function, the authors addressed these confounding issues by separately examining children born to subfertile parents (time to pregnancy >12 months) and those conceived with fertility treatments, compared with spontaneously conceived controls, and by adjusting for

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The authors have no conflicts of interest to disclose.

maternal intelligence and education in regression models with and without these covariates. *No between-group differences* were seen in child IQ, attention, or executive function. Together, maternal IQ and education accounted for 15% of the variability in child IQ, whereas the remaining variables (fertility treatment; maternal age, BMI, alcohol consumption, smoking; child sex and age; examiner) jointly explained only 5%. Furthermore, the model *without* maternal intelligence/education yielded a fertility treatment-related 5-point IQ deficit that may explain similar findings in previous studies that failed to adjust for maternal IQ/education. Confounding effects of maternal intelligence have been similarly important in other scientific models of effects on child IQ, e.g., breastfeeding (Jacobson et al., *Pediatrics*1999;103:e71). This study confirms that adjusting for parental intelligence should be the norm when examining child IQ as an outcome. Another elegant feature is inclusion of a range of child cognitive outcomes: IQ, attention, and executive function.

Confidence in the conclusions of this study is bolstered by examining the reported confidence intervals. When comparing children of parents with subfertility to children spontaneously conceived by parents without subfertility, the authors reported mean differences for IQ, executive function, and two of the three attention measures that were close to zero with narrow confidence intervals that notably did not overlap with values that would be clinically significant. Similar near-zero group difference estimates and narrow confidence intervals were seen for attention and executive function in children conceived with fertility treatments compared with controls. Although the confidence intervals for differences in IQ for the latter comparison were somewhat wider, any true difference in IQ is likely to be exceedingly small and not clinically meaningful. Thus, this prospective study with adjustment for maternal intelligence and education provides elegant and convincing evidence that subfertility is not associated with deficits in child cognitive function and the most convincing evidence to date that fertility treatments are not associated with cognitive impairment—findings of great importance to the growing number of families and medical providers using fertility treatments.

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