

### **Fertility treatment: long-term growth and mental development of the children**

*Bjørn Bay, Thesis defended May 23 2014*

#### Abstract

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Fertility treatment has been associated with obstetrical and perinatal complications. It is, however, uncertain whether fertility treatment or parental subfertility is associated with long-term development of the children. We aimed to assess the growth and mental health of children and adolescents conceived after fertility treatment compared to spontaneously conceived controls.

First, we evaluated all previous studies comparing neurodevelopmental outcomes between children born by parents conceiving after fertility treatment and spontaneous conceived controls. The systematic review clarified methodological limitations in the existing literature on the long-term development of children conceived after medical assisted reproduction. Although several studies had been published, large, well-controlled studies with long-term follow-up and thorough statistical adjustments were still few.

Second, we evaluated the children's mental health by assessing the risk of mental disorders. We studied a population of 555,828 children conceived after spontaneous conception and 33,139 children conceived after fertility treatment with follow-up in 2012 when the children were 8-17 years old. The absolute risk and hazard ratio of overall and specific mental disorders were estimated while adjusting for potential confounding variables. Further, we estimated the association between subtypes of procedures, hormonal treatment, gamete types and cause of infertility on the one hand and the risk of mental disorders on the other. Children conceived after ovulation induction had a low, but significant increased risks of autism spectrum disorders, hyperkinetic disorders, conduct, emotional, or social disorders, and tic disorders. Children conceived after in vitro fertilization or intracytoplasmic sperm injection showed no increased risk, except for a small risk of tic disorders. There was no risk systematically related to any specific type of hormone drug treatment. Thus, the increased risks may rely on residual confounding such as unknown parental factors associated with infertility in the ovulation induction group.

Third, we assessed the intelligence, attention and executive functions in 1782 5-year-old singletons. Compared with children conceived after spontaneously conception, there were no differences in test scores in children conceived by subfertile parents waiting more than 12 months before conceiving naturally or children born by parents conceiving after fertility treatment.

Finally, we evaluated the growth of children born after fertility treatment or to subfertile parents. Compared to children conceived spontaneously, children born after fertility treatment or by subfertile parents had a significantly lower birth weight -an important predictor of mental development. In contrast, no differences on height, weight, or head circumference were found at the age of 5 years.

In conclusion, we found no differences on long-term growth and neurodevelopment of children conceived after fertility treatment or by subfertile parents compared with spontaneously conceived children. Children born after ovulation induction had a low, but increased risk of mental disorders in childhood or adolescence, although this risk may rely on unknown parental factors associated with infertility.