

No overall increased risk of cancer in children born after fertility treatment

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Children born after assisted reproductive technology (ART) do not appear to be at greater risk of developing cancer than other children, according to the first study to look at the long-term cancer risk in ART

children compared to those in the general population or who were naturally conceived by subfertile women.

The study of 47,690 [children](#) is published today (Monday) in *Human Reproduction*, one of the world's leading reproductive medicine journals, and is important because, until now, there has been conflicting evidence about whether or not ART children have an increased risk of [cancer](#). The children in this study were followed for a median average of 21 years, which makes it the first study to compare outcomes in these children over such a long period of time.

Lead researcher, Professor Flora van Leeuwen, Head of the Department of Epidemiology in The Netherlands Cancer Institute, Amsterdam (The Netherlands), said: "This study, with a median follow-up of 21 years, is especially important because it includes a comparison group of naturally conceived children born to subfertile women; these women are different from the [general population](#) and it is possible that difficulty in conceiving could be a factor that influences the risk of cancer in their offspring."

The first author of the study, Ms Mandy Spaan, a Ph.D. student in the Department of Epidemiology, said: "We found that of the 47,690 children included in the analysis, 231 developed cancer. After adjusting for factors that could confound the results such as age and the parental cause of subfertility, the overall long-term risk for cancer was neither increased in the ART-conceived children compared with naturally conceived children from subfertile women, nor when compared with the general population.

"However, cancer risk was somewhat increased, although not statistically significantly so, in children conceived after intracytoplasmic sperm injection [ICSI] or from embryos that had been frozen before being thawed and used for [fertility treatment](#). These are two types of fertility

treatments that are used more often nowadays. We also found a slightly increased, statistically insignificant risk of lymphoblastic leukaemia and melanoma. As the numbers of cancers in these groups were small, these findings may be due to chance and must be interpreted with caution."

Researchers analysed data from a large, nationwide study of subfertile women (the OMEGA study) who were treated in one of 12 Dutch fertility clinics between 1980 and 2001. They also collected data on the offspring and the information was linked to data on the incidence of cancer from The Netherlands Cancer Registry between January 1989 and November 2016. Information on the method of conception and any confounding factors, such as the cause of the parents' subfertility, the mother's age, the child's birth year, birth weight, duration of pregnancy, and whether they were single or multiple births, was also collected from the mothers' completed questionnaires and medical records.

Of the 47,690 children born alive, 24,269 were conceived by ART, 13,761 were naturally conceived and 9,660 were conceived naturally or with the help of fertility drugs, such as ovarian stimulation medication, but not by ART.

Of the 231 cases of cancer occurring among all the offspring, there were 31 cases of lymphoblastic leukaemia and 26 cases of melanoma.

Ms Spaan said: "There is no clear explanation for why there should be higher numbers of these cancers. It could be that some fertility treatments might induce heritable alterations in certain genes that increase the risk of melanoma and leukaemia; however, more research with larger numbers is needed to clarify this finding."

Prof van Leeuwen concluded: "These results provide reassuring evidence that children conceived as a result of fertility treatments do not have an increased risk of cancer after a median follow-up of 21 years. They will

enable physicians to better inform couples considering fertility treatment about its long-term safety for their children.

"However, as ever more children are born through ICSI and cryopreservation of embryos, the long-term cancer risk should be investigated in larger numbers of children born as a result of these techniques.

"We are currently expanding our study to include more than 30,000 ART-conceived children born in more recent years. It will include children born after ICSI and/or embryo cryopreservation of the embryo. We hope this will provide more evidence about the possible long-term risk of cancer for these children."

Cancer in children and [young adults](#) is rare, occurring in less than one per cent worldwide, and so a limitation of this study is that the small number of cancers makes it difficult to produce reliable results from subgroup analyses. In addition, the method of conception could not be identified in 12% of children from the information in the mothers' questionnaires and medical records. A strength of the study is its large size, the long and complete follow-up, the comparison with naturally conceived children from subfertile women as well as the general population, and the detailed information on potential confounding factors.

More information: *Human Reproduction* (2018). [DOI: 10.1093/humrep/dey394](https://doi.org/10.1093/humrep/dey394)

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