MI-CRE 2025 Annual Research Symposium and Policy Forum

Medically assisted reproduction and childhood cancers: Results from the CREATE study

Investigators: Walker, A.R.[1], Vajdic, C.M.,[1] Opdahl, S.M.[2], Chambers, G.M.[1], Venetis, C.A.[3]

Author Affiliations:

[1] UNSW Sydney, New South Wales, Australia
[2] Norwegian University of Science and Technology, Trondheim, Norway
[3] Aristotle University of Thessaloniki, Thessaloniki, Greece

Presenter's email address: adrian.walker@unsw.edu.au

Disclosure of Interests Statement: C.A.V. reports grants, personal fees (speaking fees and fees for participating in advisory boards), and travel support from Merck KGaA, Darmstadt, Germany; personal fees (speaking fees and fees for participating in advisory boards) and travel support from Merck, Sharpe and Dohme; personal fees (speaking fees and fees for participating in advisory boards) and travel support from Organon; grants, personal fees (speaking fees and fees for participating in advisory boards) and travel support from Ferring; personal fees (speaking fees) from IBSA, personal fees (speaking fees and fees for participating in advisory boards) and travel support from Gedeon-Richter; and personal fees (speaking fees) from Vianex and Sonapharm. C.A.V. is also a Board Member of the Hellenic Society of Fertility & Sterility, a Member of the Editorial Board of *Human Reproduction* and a Senior Deputy of the Coordination Committee of the Special Interest Group 'Reproductive Endocrinology' of the European Society of Human Reproduction and Embryology (ESHRE).

Is the presenter an HDR student? No

Has this research been submitted or presented elsewhere? If so where and when? No

Abstract

Background and Aims: Medically assisted reproduction (MAR), including in vitro fertilization (IVF), involves the administration of hormonal drugs to induce ovulation. Researchers have raised concerns that receiving MAR treatments may increase the likelihood of certain childhood cancers, particularly leukemia, lymphoma, retinoblastoma, neuroblastoma, and embryonal cancers. However, establishing causality between MAR conception and cancer is complex. Challenges include historically small sample sizes, short follow-up times, the rarity of childhood cancers, and study design concerns. The current study attempts to address all four issues.

Design and Methods: We formed two retrospective cohorts of around 5 million singletons (~180,000 MAR-conceived) born in Australia between 1991-2019. As well as examining the overall effect of MAR conception, we stratified by MAR type or technology (either Assisted Reproductive Technology [ART] or Ovulation Induction/Intrauterine Insemination). We further stratified ART by conception method (IVF or intracytoplasmic sperm injection) and whether the embryo was a fresh or frozen transfer. We defined 13 childhood cancers of interest; twelve International Classification of Childhood Cancers 3rd edition groups and a custom embryonal cancer group. We followed each child until cancer diagnosis, death, or 31 Dec

2019. We calculated standardised incidence ratios (SIRs) adjusted for age, sex, state and calendar year, and hazard ratios using an emulated target trial design and flexible parametric survival modelling.

Results: Compared to the general population, leukemias were elevated following ART conception (SIR: 1.32, 95%CI: 1.02-1.69) and renal tumours were elevated after IVF conception with a fresh embryo (SIR: 2.32, 95%CI: 1.02-4.67) and any ART treatment with a frozen embryo (SIR 2.52, 95%CI: 1.09-4.97). However, after adjusting for confounding factors, there was no evidence that any cancers were elevated in risk following any type of MAR conception.

Conclusions and Impact: Our findings provide reassurance that MAR conception is not related to the development of childhood cancer. Multi-country federated data analyses would help overcome statistical power limitations for the rarer childhood cancer types.