# Comparing indicators of health and development of singleton young adults conceived with and without assisted reproductive technology

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**Objective:** To compare outcomes for young adults conceived by assisted reproductive technology (ART) with non-ART–conceived young adults.
**Design:** Cohort study.
**Setting:** Not applicable.
**Participant(s):** Mothers and their offspring (aged 18–28 years) conceived by ART; mothers and their non-ART–conceived offspring, randomly selected from the same source population.
**Intervention(s):** Structured telephone interviews, one with mothers and another with their young adult offspring.
**Main Outcome Measure(s):** Maternal report on young adult offspring hospitalizations and chronic illness accumulated over the first 18 years of their lives; young adult self-report on perceived current quality of life, body mass index, pubertal development, and educational achievement.
**Result(s):** Of 1,480 eligible ART mothers, 80% were traced and contacted. Of those, 656 (55%) participated, reporting on 705 ART-conceived offspring; 269 (23%) declined participation and 262 (22%) did not respond. Of the participants, 84% consented to contact with their young adult offspring, of whom 547 (92%) participated. Random-digit dialing recruited 868 non-ART mothers and 549 offspring. Compared with non-ART young adults, the ART group had significant increases in three maternally reported outcomes: 1) hospital admissions, including those in the secondary school years; 2) atopic respiratory conditions; and 3) combined endocrine, nutritional, and metabolic disease ICD-10 category. Young adult reported outcomes were similar for both groups.
**Conclusion(s):** This study addresses gaps in knowledge of outcomes beyond adolescence for those conceived by ART. Results show few adverse outcomes in this large cohort of young adults, but additional assessment through clinical review is required to address issues unable to be examined in this study. (Fertil Steril® 2014;101:1055–63. ©2014 by American Society for Reproductive Medicine.)
**Key Words:** Assisted reproductive techniques, young adults, chronic disease, quality of life, cohort study

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Many people who were conceived with the use of assisted reproductive technologies (ART) have now reached adulthood. The safety of ART and whether it affects adult health is likely to be of interest to these families, couples contemplating treatment, clinicians, and scientists (1). It is already known that, compared with spontaneously conceived babies, ART-conceived babies are at increased risks of preterm birth, low birth weight, being small for gestational age, and perinatal mortality (2–4). These adverse birth outcomes may have long-term consequences for adult heath, as shown by many studies about developmental origins of health and disease (5–7). We hypothesized that periconception and early intrauterine exposures associated with ART, specifically the hormonal milieu created by ovarian stimulation and in vitro culture associated with ART treatment (8–10), lead to poorer physical health outcomes through epigenetic changes, influencing growth and development and higher prevalence of chronic illness compared with those conceived spontaneously (11, 12). These outcomes may manifest in young adults. The possibility that this process could be mediated by formation of an aberrant epigenetic profile around the time of fertilization is supported by findings of an increased prevalence of rare imprinting disorders, such as Beckwith-Wiedemann syndrome, in children conceived with ART (13).

The present study also tested the hypothesis that parental experiences of infertility and ART may lead to poorer well-being and quality of life in ART-conceived young adults compared with those conceived spontaneously. Although studies on the psychosocial development of ART-conceived children indicate that they are similar to spontaneously conceived children (14, 15), it is possible that differences in psychologic functioning and social adjustment might emerge as the young person matures.

To test these hypotheses, we recruited a large cohort of 18–28 year old singletons conceived by ART and a similar aged cohort conceived without use of ART in Australia and compared aspects of their health, perceived quality of life, timing of puberty, body mass index (BMI) and educational achievements through maternal and self report.

## MATERIALS AND METHODS

The protocol and full details of measurements used in this study have been published and are available elsewhere (16). Institutional Review Board approval was obtained for all aspects of the project from the Royal Women's Hospital (project 08/37), Epworth Healthcare (project 46409), and Australian Institute of Health and Welfare regarding use of the National Death Index (project 2009/2/15). Participants each gave informed consent before taking part in the study.

### Setting

When the young adults described in this study were born there were two infertility treatment services in the state of Victoria, Australia, providing care in the private and public health service sectors to infertile couples. Both services participated in this study, enabling access to the entire cohort of mothers of ART-conceived people aged $\geq$18 years in the state of Victoria.

### ART Population

Eligible women comprised those who had conceived with ART and given birth to one or more singleton offspring from January 1982 to December 1992. Mothers were excluded if they had emigrated, could not be traced, had inadequate English language skills, or their child had died. Maternal deaths were determined through record linkage to the Australian National Death Index.

Names of both parents were provided by the ART treatment service, and addresses were checked with the use of either electoral rolls or telephone directories across Australia. A letter of invitation was sent by registered mail from the ART doctor who had provided treatment $\geq$18 years earlier or a medical delegate of each service. Women were asked to respond even if they wished to decline participation. A time was scheduled with each consenting woman to complete a structured telephone interview. With maternal consent and the contact details that mothers provided, their young adult offspring also were invited to participate.

There were 1,480 eligible ART mothers who gave birth to singleton children from January 1982 to December 1992, and contact addresses were found for 80% (n = 1,187). Of those approached, 78% responded: 23% declined participation and 55% participated. Final numbers were 656 mothers reporting on 705 offspring, which included 49 sibling pairs. Of these mothers, 84% gave permission for their offspring to be contacted; 92% of those offspring agreed to participate, resulting in a total of 547 young adult participants. Over three-fourths (76%) of the mothers had in vitro fertilization, and the remainder had gamete intrafallopian transfer. Conception was with donor sperm in 47 cases (9.7%) and donor oocyte in 9 cases (1.4%).

### Non-ART Population

The comparison groups were women from the general population who had conceived spontaneously (without the use of ART) and their singleton offspring. The non-ART mothers were recruited with the use of random digit dialing from the same source population as the ART group, to identify and screen households for those with a consenting mother of a young adult aged 18–28 years. The sampling fraction in the source population for the non-ART group of mothers was 71%, with ~1,200 women being identified by telephone screening as eligible.

In total, 868 control mothers were recruited and 85% consented to their young adult offspring being contacted. During recruitment, frequency matching of non-ART young adults with those in the ART group was done according to the proportions of male and female within age strata. Eighty-four percent of offspring agreed to participate. Recruitment continued until there were approximately equal numbers of ART and non-ART young adults (n = 549).

### Interview Schedule and Outcome Measures

Mothers completed an 80-item telephone interview about their offspring over the first 18 years of life. Young adults completed a 150-item interview about their health, development, and well-being. Interviews took ~35 minutes to complete.