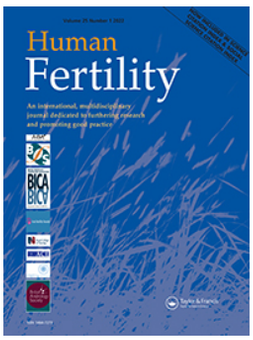

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ORIGINAL ARTICLE

Does being conceived by assisted reproductive technology influence adult quality of life?

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ABSTRACT

Numerous studies have investigated the physical health and development of children and adolescents conceived with assisted reproductive technology (ART). Less is known about the quality of life of ART-conceived adults. This study explores the contributions of being conceived with ART and psychosocial cofactors present in young adulthood to the quality of life of adults aged 22–35 years. Young adults conceived through ART or natural conception (NC) completed questionnaires which included a standardized measure of quality of life (World Health Organization Quality of Life – Brief assessment (WHOQoL-BREF)) when aged 18–28 years (T1) and again when aged 22–35 years (T2). The WHOQoL-BREF has four domains: (i) Physical, (ii) Psychological, (iii) Social relationships and (iv) Environment. A total of 193 ART-conceived and 86 NC individuals completed both questionnaires. When accounting for other cofactors in multivariable analyses, being ART-conceived was strongly associated with higher scores (better quality of life) on the Social relationships, and Environment WHOQoL-BREF domains at T2. In addition, less psychological distress, a better relationship with parents, a better financial situation, and perceptions of being about the right weight at T1 were associated with higher scores on one or more of the WHOQoL-BREF domains at T2. In conclusion, being ART-conceived can confer advantages in quality of life in adulthood, independent of psychosocial cofactors.

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ART; adults; parental relationship; psychological wellbeing; quality of life; WHOQoL-BREF

Introduction

Assisted reproductive technology (ART) refers to all interventions that include the *in vitro* handling of both human oocytes and sperm or of embryos for the purpose of reproduction (Zegers-Hochschild et al., 2017). In the more than four decades since the first birth following *in vitro* fertilization (IVF) in 1978, it is estimated that around 8 million children have been born as a result of ART (Fauser, 2019). In that time, many studies have investigated the physical health and development of children born from ART.

Reviews of studies of the perinatal outcomes after ART have found that ART conception is associated with increased risks of congenital anomalies, prematurity and low birth weight (Palomba et al., 2016), which in turn increase the risk of cerebral palsy and neurodevelopmental delay (Hart & Norman, 2013). Studies of the physical health of ART-conceived children are broadly reassuring with some residual uncertainty related to altered cardiovascular and metabolic health risks (Bergh & Wennerholm, 2020; Stormlund et al., 2019), while ART-conceived adolescents have been shown to have similar general health to that of comparison groups but with some observed physiological differences warranting further study (Roseboom, 2018; Wilson et al., 2011).

Evidence relating to the psychosocial wellbeing of ART-conceived children has also been summarized in several reviews. One such review concluded that the longer-term mental and emotional health outcomes for ART-conceived children are reassuring and comparable to those of naturally conceived (NC) children (Hart & Norman, 2013). A later review concluded that

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cognitive and behavioural outcomes and rates of autism spectrum disorders (ASD) are similar in adolescents and young adults conceived by ART or NC (Shankaran, 2014). The most recent review found that in broad terms, children born through ART have positive parent–adolescent relationships and are well-adjusted (Ilioi & Golombok, 2015). Furthermore, a recently published longitudinal study of 74 people conceived with donor sperm (approximately equal numbers of anonymous, known and open identity donors) and born to lesbian parents found that most scored in the normal ranges on psychological measures at ages 10, 17 and 25 years (Carone et al., 2021).

Less is known about the health and wellbeing of ART-conceived adults, because, in most countries, the number of ART-conceived people who have reached adulthood is still low. However, in the state of Victoria in Australia, a comparatively large number of women underwent IVF and gave birth in the early and mid-1980s (Trounson, 2018). This allowed us to initiate an investigation of the health and development of ART-conceived young adults aged 18–28 years and age-matched NC controls in 2010. This study found that the ART group had significant increases in maternally reported physical health problems (hospital admissions, atopic respiratory conditions, and the combined endocrine, nutritional, and metabolic International Classification of Diseases (ICD-10) category), but adult reported outcomes were similar for both groups (Halliday et al., 2014). In a subsequent follow-up of these cohorts, then aged 22–35 years, we found no evidence of increased vascular or cardiometabolic risk, nor of growth or respiratory problems in the ART group compared with the NC group (Halliday et al., 2019; Juonala et al., 2020).

In addition to assessing the physical health of the people in the two cohorts, we enquired about quality of life, perception of the quality of the relationship with parents, and psychological distress in the initial and follow-up studies. The World Health Organization (WHO) defines quality of life as 'individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns' (World Health Organization, 1993). In the last two decades, there has been increasing interest in quality-of-life measures as indicators of psychosocial wellbeing.

The aim of this study was to use longitudinal data from the two studies to assess the contribution of ART conception to adult (22–35 years) quality of life, considering demographic and psychosocial factors present in young adulthood (18–28 years).

Materials and methods

The initial study was approved by The Royal Women's Hospital (project 08/37) and Epworth Healthcare (project 46409). The follow-up study was approved by The Royal Children's Hospital Human Research Ethics Committee (project 33163).

Study population

All women who had given birth after IVF or gamete intrafallopian transfer (GIFT) between 1982 and 1992 in Victoria and who could be traced ($n = 1{,}187$) were invited to participate in the initial study. Mothers who had given birth after NC were recruited from the same source population as the ART group through random digit dialling (Lavrakas, 2008). Participants were asked to provide information about the health of their son or daughter and, if they agreed, to provide the researchers with the young adults' contact details so that they could be invited to provide information about their own health and wellbeing (Wilson et al., 2013). In all, 656 ART mothers and 868 NC mothers provided information on 705 and 868 offspring, respectively. Around 85% gave permission for the researchers to contact their young adult child. Of those invited to participate, 547 ART (92%) and 549 NC (84%) young adults agreed. For the follow-up study, 4–6 years later, the 540 ART and 532 NC young adults who participated in the initial study and had consented to be re-contacted for future research were invited to participate. Of these, 193 (36%) ART and 86 (16%) NC individuals agreed, and their data were included in analyses.

Materials

In the initial study (time 1, T1), the young adults completed a 150-item interview about their health, development and well-being. The follow-up study (time 2, T2) involved completing a questionnaire online and attending a 2–3-hour clinical review appointment.

The following questions relevant to psychological wellbeing were included in the T1 interview: (i) mother's age when the respondent was born; (ii) sexual orientation (heterosexual/homosexual/bisexual/not sure); (iii) family financial situation in secondary school (living comfortably/doing alright/just getting by/quite difficult/very difficult); (iv) perceptions of own weight

(about the right weight/very overweight/somewhat overweight/very underweight/somewhat underweight); (v) number of close friends (1–2/3–5/6+); (vi) frequency of vigorous exercise (never/a few times a year/monthly/2–3 times a month/weekly/2 or more times a week); and (vii) quality of the relationship with parents rated on an 11-point Likert scale (0 = really bad to 10 = absolutely perfect).

The Kessler Psychological Distress Scale (K10) was also included at T1. It has been validated as a screening instrument to identify likely cases of anxiety or depression in the community and has excellent internal consistency reliability (Cronbach's alpha = 0.93) (Kessler et al., 2002). Respondents are asked to indicate the amount of time that they experienced nervousness, agitation, psychological fatigue and depression in the past four weeks on a five-point Likert scale. Scores for the 10 items are summed, yielding a possible score of 10–50, with lower scores indicating lower levels of psychological distress.

The World Health Organization Quality of Life – Brief assessment (WHOQoL-BREF) measure of quality of life (WHOQUAL Group, 1998) was included at T1 and T2. This 26-item instrument assesses four domains of quality of life: (i) Physical (seven items relating to pain, sleep, energy levels, mobility, daily living activities, dependence on medical substances and work capacity), (ii) Psychological (six items relating to positive and negative feelings; thinking, learning, memory and concentration; self-esteem; body image; and spirituality), (iii) Social relationships (three items relating to personal relationships, social support and sexual activity) and (iv) Environment (eight items relating to freedom and physical safety and security, home environment, financial resources, accessibility and quality of social and health care, educational opportunities, leisure activity participation opportunities, physical environment and transport). WHOQoL-BREF has good discriminant validity, content validity, test–retest reliability and internal consistency (Cronbach's alpha for the four domains are: Physical Health = 0.84, Psychological = 0.77, Social relationships = 0.69 and Environment = 0.80). Items in each domain were coded, summed and scored according to prescribed methods to create raw domain scores which were transformed to 0–100 scales where higher scores indicate better quality of life (WHOQUAL Group, 1998).

Data management and statistical analysis

Data were analysed with STATA, version 15 (StataCorp LLC, College Station, TX). The outcomes of interest were the associations between factors present at T1 (mode of conception, mother's age when the respondent was born, sexual orientation, family financial situation in secondary school, perceptions of own weight, number of close friends, frequency of vigorous exercise, and quality of the relationship with parents) and the scores on the four domains of WHOQoL-BREF at T2. Univariable and multivariable analyses using linear regression were done. Covariates were included in the multivariable model if the univariable analysis resulted in a p value of <0.1. Due to the small number of participants reporting a value less than 7 on the quality of the relationship with parent 11-point Likert scale, these were combined into one group resulting in a five-point Likert scale with values ranging from 1 to 5.

The primary outcomes of interest were the four Australian WHOQoL-BREF domains. Population norms would be expected in the SC group with means and standard deviations (SDs) ranging from a mean of 72 (SD 18) for the social domain to a mean of 80 (SD 17) for the physical domain (WHOQUAL Group, 1998). Therefore, using a two-sample comparison of these means, a sample size of 193 ART and 86 SC adults will detect a moderate effect size of 0.36 as significant (social domain, alpha 0.05, power 80%) (StataCorp LLC, College Station, TX).

Results

Participants' characteristics at T1 are shown in Table 1. The unadjusted and adjusted model relationships

Table 1. Participant characteristics at T1 ($n = 279$)[a].

Characteristics	*N* (%)/mean (SD)
Age, mean (SD), years	20.9 (2.6)
Sex	
Female	170 (61%)
Male	109 (39%)
Mode of conception	
ART	193 (69%)
NC	86 (31%)
Financial status in secondary school	
Living comfortably/doing alright	230 (84%)
Just getting by/quite difficult/very difficult	45 (16%)
Sexual orientation	
Heterosexual	265 (95%)
Non-heterosexual	14 (5%)
Frequency of vigorous exercise	
Never/a few times a year	19 (7%)
Less than weekly	68 (24%)
At least once a week	191 (69%)
Perception of weight	
About the right weight	201 (72%)
Not the right weight	78 (28%)
Number of close friends	
1–2	20 (7%)
3–5	125 (45%)
6+	133 (48%)
Parental relationship score, mean (SD)	8.2 (1.3)
K10 score, mean (SD)	49.5 (10.4)
Mother's age at birth, mean (SD), years	33.2 (3.99)

[a]Numbers do not always add up to 279 because of missing data.

Table 2. Unadjusted and adjusted model relationships between factors present at T1 and the Physical, Psychological, Social relationships and Environment.

	Physical domain		Psychological domain		Social relationships domain		Environment domain	
Baseline factors	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
Group								
Non-ART	Ref							
ART	4.22 (0.3, 8.12)*	2.26 (−1.4, 6.0)$^{\times}$	4.61 (0.3, 8.9)*	3.89 (−0.0, 7.8)*	7.21 (2.2, 12.2)**	6.66 (1.8, 11.5)**	5.36 (2.0, 8.7)**	4.74 (1.5, 7.9)**
Perception of weight								
About the right weight	Ref							
Not the right weight	−7.04 (−11.1, −3.0)**	−3.13 (−7.1, 0.8)$^{\times}$	−7.88 (−12.2, −3.6)§	−5.08 (−9.2, −0.9)*	−6.78 (−12.0, −1.6)*	−2.33 (−7.3, 2.6)$^{\times}$	−4.97 (−8.4, −1.5)**	−1.88 (−5.3, 1.5)$^{\times}$
K10 score	−0.47 (−0.6, −0.3)§	−0.40 (−0.6, −0.2)§	−0.57 (−0.8, −0.4)§	−0.49 (−0.7, −0.3)§	−0.27 (−0.5, −.04)*	−0.18 (−0.40, 0.06)$^{\times}$	−0.33 (−0.5, −0.2)§	−0.25 (−0.4, −0.1)**
Mother's age at birth	0.33 (−0.1, 0.8)$^{\times}$		0.0002 (−0.5, 0.5)$^{\times}$		0.16 (−0.4, 0.8)$^{\times}$		0.44 (0.0, 0.8)*	0.25 (−0.1, 0.6)$^{\times}$
Parental relationship score	3.15 (1.8, 4.5)**	2.19 (0.9, 3.5)**	3.63 (2.1, 5.1)§	2.41 (1.0, 3.9)§	3.29 (1.5, 5.1)§	2.59 (0.9, 4.3)**	2.16 (1.0, 3.5)§	1.32 (0.1, 2.5)*
No. of close friends								
3–5	Ref							
1–2	−6.97 (−14.3, 0.3)*	−5.72 (−12.3, −0.8)*	−2.14 (−10.1, 5.8)$^{\times}$		−10.10 (−19.3, −0.9)*	−7.91 (−16.5, 0.7)$^{\times}$	−3.31 (−9.5, 2.9)$^{\times}$	
6+	1.80 (−2.0, 5.6)$^{\times}$		2.61 (−1.5, 6.7)$^{\times}$		2.66 (−2.1, 7.5)$^{\times}$		2.67 (−0.6, 5.9)*	
Financial situation								
Living comfortably /doing alright	Ref							
Just getting by/quite/very difficult	−10.26 (−15.1, −5.4)§	−7.48 (−12.1, −2.8)**	−5.8 (−11.2, −0.4)*	−2.51 (−7.6, 2.5)$^{\times}$	−4.13 (−10.6, 2.3)$^{\times}$		−6.59 (−10.8, −2.3)**	−4.39 (−8.4, −0.3)*
Sex								
Male	Ref							
Female	0.12 (−3.7, 3.9)$^{\times}$		3.15 (−0.9, 7.2)*	2.51 (−0.0, 7.8)$^{\times}$	9.70 (5.1, 14.3)§	9.57 (5.0, 14.1)§	4.32 (1.4, 7.5)**	4.34 (1.3, 7.4)**
Age	−0.72 (−1.4, −0.0)*	−0.68 (−1.3, −0.0)*	−0.09 (−0.8, 0.7)$^{\times}$		−0.92 (−1.8, −0.0)*	−0.74 (−1.6, 0.1)	−0.28, (−0.9, 0.3)$^{\times}$	
Sexuality								
Heterosexual	Ref							
Non-heterosexual	−4.42 (−13.6, 4.7)$^{\times}$		−7.97 (−17.8, 1.9)*	−5.79 (−15.0, 3.5)$^{\times}$	−12.22 (−23.8, −0.7)*	−7.80 (−19.3, 3.3)$^{\times}$	−8.81 (−16.6, −1.10)*	−5.91 (−13.5, 1.6)$^{\times}$

WHOQoL-BREF domains at T2 (p values: $^{\times}>0.1$; *0.01–0.1; **0.001 to <0.01; $^{\S}<0.001$).

between factors present at T1 and the Physical, Psychological, Social relationships and Environmental WHOQoL-BREF domains at T2 are shown in Table 2. Frequency of vigorous exercise was not included in the multivariable models because it was not associated with any of the domains in the unadjusted analysis.

In the adjusted model, being ART-conceived was associated with higher scores (better quality of life) on the Psychological, Social relationships and Environmental WHOQoL-BREF domains at T2 with p values of <0.001 for the Social relationships and Environmental domains. In addition, the Psychological domain scores were positively associated with a better relationship with parents and negatively associated with more psychological distress (K10 score) at T1, and Social relationship domain scores were positively associated with female sex (all p values <0.001). Weaker, but still significant positive associations ($p = 0.001$), with one or more of the WHOQoL-BREF domains at T2 were observed for those in a better financial situation and with a perception of being about the right weight at T1.

Discussion

To our knowledge, this is the first study to explore the contributions of being conceived with ART and psychosocial factors present in young adulthood to the quality of life of adults. In terms or the effect of ART conception on adult quality of life, findings suggest that being ART-conceived confers some advantages. Together with the previously published evidence that ART and NC groups have similar physical health in adulthood, this is reassuring for people who are ART-conceived and those who need ART to conceive.

Not surprisingly, this study found that a better relationship with parents and less psychological distress in early adulthood were strongly linked to better quality of life in later adulthood. Other studies have found that the quality of the relationship with parents in adolescence is a strong predictor of adult mental health and wellbeing (Hair et al., 2009; Morgan et al., 2012). Furthermore, a longitudinal study of more than 3,000 people in the UK who were followed from early adolescence to the age of 43 found that higher reported parental care and lower parental psychological control in adolescence were associated with greater wellbeing at ages 36 and 43 (Stafford et al., 2016). Regarding ART, it is possible that people who achieve parenthood after ART have a particularly strong desire for and commitment to parenthood and feel lucky to have had a successful outcome. This may make them more likely to adopt an authoritative parenting style which is characterized by having high expectations on children, while simultaneously providing warmth and support. Evidence suggests that the authoritative parenting style is associated with less risk taking and better psychosocial adjustment in adolescence than other parenting styles (Newman et al., 2008).

Another finding was that a better self-reported family financial situation in early adulthood was linked to better quality of life in the Physical and Environment domains of WHOQoL-BREF in later adulthood which is consistent with other studies. A meta-analysis showed that subjective socio-economic status (SES) is associated with mental health outcomes, self-rated health and general health symptoms in adolescence (Quon & McGrath, 2014). There is also evidence that adolescents in low SES families are at higher risk of developing mental health problems than their peers in higher SES families (Reiss et al., 2019).

Perceptions of not being about the right weight in young adulthood were associated with worse quality of life in the Psychological domain in adulthood. The Psychological domain of WHOQoL-BREF includes a question about body image which is known to be associated with self-esteem. People with lower self-esteem are more likely to have poor body image, regardless of age or gender (O'Dea, 2012). It is possible that the observed lower scores in the Psychological domain among people who considered themselves to be over or underweight were due to poor body image.

Based on existing evidence, we expected that sexual orientation would contribute to quality of life and that being non-heterosexual would have a negative effect on one or more of the WHOQoL-BREF domains. For example, a study based on data collected in 2012 of two nationally representative cohorts, one in the UK with almost 33,000 people aged over 16 years and one in Australia with more than 12,000 people aged over 15 years, found that people who identify as lesbian, gay and bisexual were significantly less satisfied with their lives than otherwise comparable people who identify as heterosexual (Powdthavee & Wooden, 2015). However, in this study, sexual orientation did not make a significant independent contribution to any of the quality of life domains. We speculate and hope that acceptance of sexual orientation diversity has increased over time and that being non-heterosexual has less negative impact on wellbeing in contemporary high-income Western societies than previously. However, as the absolute number of non-heterosexual participants was low, the finding may not be generalizable.

The main limitation of this study was the low participation rate in the follow-up study. The results

presented here had the potential to be biased due to low participation rates. This, however, was negated through use of multiple imputation regression analysis, published in the manuscript describing the health outcomes of this cohort at the time of the clinical follow up. That analysis demonstrated no differences in health measures with and without imputed data (Halliday et al., 2019). We therefore feel confident that the results presented in this paper are likewise free of significant bias. There are several potential reasons for the low participation. First, the logistics of travelling to the hospital for the clinical assessment which itself required 2–3 hours to be completed may have discouraged some from participating. It is also possible that interest in the study had dissipated in the years since they first participated, especially among NC individuals who may have felt that they had little to gain from participating. Lastly, when the initial study was completed, participants were informed about the findings showing very few differences in the health and development between the ART and NC groups. This may have diminished interest in contributing to the follow-up study.

In conclusion, when accounting for other factors present in young adulthood, being ART conceived appears to confer some advantages in quality of life, particularly in the Social relationships and Environment domains. In addition, and not surprisingly, this study found that, independently of mode of conception, a more positive relationship with parents, less psychological distress, and a better family financial situation contributed to better quality of life.

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Disclosure statement

The authors have no conflicts of interest to declare.

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