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ORIGINAL ARTICLE

Families with children resulting from ART: psychosocial and financial implications

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STUDY QUESTION: What are the psychosocial and financial issues experienced among families with children 2–12 years of age conceived by ART?

SUMMARY ANSWER: Our results suggest that families with children, 2–12 years of age, conceived via ART are doing well, although impacts were identified on parents of twins and higher-order multiples.

WHAT IS KNOWN ALREADY: Multiple births have been associated with higher morbidity and mortality of children, as well as financial costs to families and society.

STUDY DESIGN, SIZE, DURATION: This study was an assessment of familial response to birth of singletons, twins and higher order multiples at child's ages of 2–12.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Semi-structured interviews and surveys were conducted with mothers ($n = 348$) and fathers ($n = 338$) of singletons, twins and higher-order multiple gestations who received fertility services.

MAIN RESULTS AND THE ROLE OF CHANCE: No significant differences were observed between the groups in domains of primary caregiving or parental separation/divorce. Impacts were identified on parent's ability to maintain employment. The revised 15-item scores of the Impact on Family Scale were significantly lower, reflecting more negative impacts, among families with twins (beta = −2.6, 95% confidence interval (CI), −4.7, −0.5, $P = 0.014$) and multiples (beta = −7.4, 95% CI, −10.4, −4.5, $P < 0.001$) than among families with singletons. Similarly, the Parenting Stress Index total scores were significantly lower among families with twins and multiples, indicating greater levels of stress, when compared to those with singletons. In addition, the Beck Depression Inventory total score were significantly higher for twins and multiples, and the Child Behaviour Checklist for ages 1.5–5 total problem score was significantly higher for twins when compared to singletons.

LIMITATIONS, REASONS FOR CAUTION: The study was limited to families who received fertility treatment and constitutes a population that was well educated and had higher incomes. Additionally, interview data was self-reported.

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Key words: assisted reproductive technology / ART / psychosocial implications of ART / financial implications of ART

WHAT DOES THIS MEAN FOR PATIENTS?

This study looks at the money issues and way people think and feel in families who have had children (aged 2–12) by assisted reproductive technologies.

They looked at families who had a single child, twins and other multiple births who received infertility services at centres which are a part of the Cooperative Multicenter Reproductive Medicine Network funded by the National Institutes of Health. Families were interviewed about their family, health and financial experiences. Parents also answered questions looking at stress levels, impact on family, depression, marital satisfaction and the children's behaviour.

The authors did not find any real differences between the family groups in primary caregiving, friends or families to assist with caregiving or parental separation or divorce since the children's birth. Among the family groups, differences between the families who had a single child, twins and other multiple births were found regarding the mothers' employment, parenting stress, impact on the family, depression and child behaviour. The findings suggest the families are doing well, but compared to families with single children, families with twins or other multiple births had more family impacts.

The authors hope that this information will improve information available to families when they have to make decisions about assisted reproductive technologies.

Introduction

Assisted reproductive technology (ART) entails all fertility treatments in which both oocytes and embryos are handled.

Women who undergo ART procedures are more likely than women who conceive spontaneously to deliver multiple-birth pregnancies. Multiple births resulting from fertility treatments have been associated with higher morbidity and mortality rates, including preterm births and low birth weight infants, as well as substantial financial costs to families and society (Kulkarni *et al*., 2013).

The contribution of ART to preterm births, most of which are also low birth weight, is a significant public health problem. Healthy People 2020 includes specific target objectives for reducing low birth weight and preterm births. In the USA in 2013, there were 53 252 live-birth deliveries and 66 691 infants resulting from ART (Sunderam *et al*., 2015). The percentage of ART-conceived infants who were preterm ranged from 13.3% among singletons to 61.0% among twins and 97.5% among triplets and higher-order multiples (Sunderam *et al*., 2015). Infants conceived with ART contributed to 4.6% of preterm births in 2013. Rates of preterm and very preterm infants were higher among infants conceived with ART, 33.6%, compared with the rates among all infants, 11.4% (Sunderam *et al*., 2015). There was only a slight change in 2014, with 33.2% of the 68 782 infants resulting from ART born preterm (compared with 11.3% among all infants), contributing to ∼4.7% of all preterm infants and 5.5% of all very preterm infants (Sunderam *et al*., 2017). Other countries have seen declines in multiple pregnancy rates with the use of ART. The UK has seen a relative reduction of 40% in the multiple pregnancy rate from 2008 to 2014 (El-Toukhy *et al*., 2018).

While the contribution of ART-conceived infants to all triplet and higher-order multiples continues to decline, there is less of a decline in the percentage of twins who are ART-conceived. Approximately 37.5% of ART-conceived infants were twins in 2014 and they contributed to 18.0% of all twins nationally (CDC-MMWR, 2017). In this report, we sought to describe demographic, financial and social issues that impact families who have singleton, twin and triplet or higher-order multiple gestations following ART treatments.

Materials and Methods

Study population

The study was conducted at sites of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Cooperative Multicenter Reproductive Medicine Network (RMN). The study population included families who have higher-order multiples resulting from ART and families who have singletons and twins resulting from ART. The age range of 2–12 years for the children was designed to include families who have children who require a high degree of parental involvement in their daily activities in contrast to families who have young adult children residing independently outside of the home. For each cohort of families with either higher-order multiples, twins or singletons, the eligibility criteria included the following: (i) being the mother or father in a family who has ART-conceived children; (ii) having higher-order multiples, twins or singletons 2–12 years of age; and (iii) being able to respond to questions during an interview and on standardised instruments.

Recruitment

The Institutional Review Board at each of the participating RMN sites approved this study. Written informed consent was obtained from all study participants. The RMN study coordinators coordinated the recruitment, enrolment and data collection at their respective RMN sites. Families who met the eligibility criteria were provided an introduction to the study describing the goals of the study along with an invitation to participate. Families interested in participating were instructed to follow-up with a telephone call to the study coordinator to schedule an interview.

Data collection instruments

A semi-structured interview guide was developed to address the following categories of family information: (i) demographic characteristics—parental age, employment, housing, race/ethnicity, income and educational obtainment; (ii) family characteristics—numbers of children, ages, gender, extended family and friends; (iii) health status of the ART-conceived children—gestational age, medical complications at birth and chronic conditions related to prematurity or low birth weight; and (iv) obstetric history—infertility history, type of ART, health insurance status, pregnancy history and health complications.

In addition to the family characteristics, the semi-structured interviews collected information on direct costs including the following: (i) housing modifications; (ii) transportation adjustments; (iii) child care costs; and (iv) mother's ability to maintain employment. Indirect costs interview items included (i) physical and emotional demands of direct care; (ii) follow-up care for health and/or developmental sequelae; (iii) time away from other children, social activities, time with spouse; and (iv) sibling adjustment. An assessment of financial strain included 'How hard is it for you to pay for the very basics like food, housing, medical care, and heating? Would you say it is very hard, somewhat hard, or not hard at all? (Santoro *et al*., 2011).

Standardised instruments

Family systems theory served as the conceptual guide for this study (Henggeler, 1990; Cummings, 2000). The psychosocial implications were operationalised as impact on the family, parenting stress, depression, marital satisfaction and child behavioural outcomes. The standardised instruments were selected based on the alignment with family systems theory, reliability, validity, availability of normative data, use with a single informant and self-report from the parent. The instrument scores reported were from/for the primary care giver; a mean score was calculated for the twins and multiples.

The *Impact on Family Scale* (Stein and Riessman, 1980; Stein and Jessop, 2003), a 33-item, self-report scale, was used to assess the impact on four dimensions on family adaptation and functioning: financial burden, social/familial impact, personal strain and mastery. The financial burden subscale includes items regarding the economic consequences for the family. The familial/social impact subscale includes items relating to disruption of social interactions within and outside the family. The personal strain subscale includes items of parental fatigue, uncertainty and difficulty planning the future. The mastery subscale includes familial coping strategies such as offering support to other family members that can lead to a sense of mastery. The Cronbach alphas are high for the overall score. The Pearson correlations among the coping items exceed 0.90 and range from 0.76 to 0.86 on the financial items (Stein and Jessop, 2003). Statements are scored 1 to 4 to determine the amount of impact parents' experience. Since the development of the original scale, additional validation studies support the use of 15 of the 33 questions to assess the overall negative personal, social and familial impacts of childhood illness. The maximum obtainable score for the 15-item total score is 60, with a lower score indicating more negative impacts on the family.

The *Child Behaviour Checklist* (Achenbach, 1991) is a group of standardised instruments for assessing children's behaviour/emotional problems. The CBCL/$1\frac{1}{2}$-5, designed for children aged $1\frac{1}{2}$ to 5 years, was used to obtain standardised ratings of aspects of behavioural, emotional and social functioning of the children (Achenbach and Rescorla, 2000). They include 99 problem items rated 0, 1 or 2 (0, not true, 1, somewhat/sometimes true; 2, very/often true). Seven syndrome scales are constituted: emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems and aggressive behaviour. Three composite or summary scales are computed: internalising scale (sum of emotionally reactive, anxious/depressed, somatic complaints, and withdrawn), externalizing scale (sum of attention problems and aggressive behaviour) and total problems scale (all syndrome scores). The language development survey for ages 18–35 months, assessing children's word and vocabulary, was also included. Average length of phrases and vocabulary score were calculated. Scores $\leq$20th percentile were defined as delayed phrase or $\leq$15th percentile as delayed vocabulary development.

The CBCL 6–18, designed for children aged 6 to 18 years, was used to obtain standardised ratings of social and behavioural aspects of the children. This is a validated normative questionnaire with 113 items rated 0, 1 or 2 (0, not true; 1, somewhat/sometimes true; 2, very/often true), completed by parents (Achenbach, 1991; Achenbach and Dumenci, 2001). Behavioural and emotional problems were grouped into eight syndrome scales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour and aggressive behaviour. The internalising problems included following the scales: anxious/depressed, withdrawn/depressed and somatic complaints. The externalising problems comprised the rule-breaking behaviour and aggressive behaviour scales. The total problems scale was the sum of all syndrome scores.

The Parenting Stress Index (PSI) (Abidin, 1995) is a 36-item questionnaire used to assess stress in the parent–child relationship. Normalised on more than 2500 parents, the PSI includes parent characteristics such as isolation, depression and attachment as well as a total stress score. The PSI is designed for the early identification of family and parenting characteristics that do not promote normal development and functioning in children. Further, the PSI predicts the potential for parental behaviour problems as well as child adjustments difficulties within the family system (Abidin, 1995). The Cronbach's alpha, has been reported to be 0.91 in the total stress score on the PSI short form. Test–retest reliability ranges from 0.65 to 0.96 for the total stress score on the short form (Abidin, 1995). This validated scale consists of three question domains: (i) level of parental distress (PD), (ii) amount of parent-child dysfunctional interaction (PCDI) and (iii) dealing with a difficult child (DC). For each item, a parent records agreement with

a statement on a 5-point scale, from 1 (strongly agree) to 5 (strongly disagree). Subscale scores range from 12 to 60, and the total stress score ranges from 36 to 180 with lower scores indicating greater levels of parental stress.

Kansas Marital Satisfaction Scale (KMSS) is a self-report questionnaire that assesses marital satisfaction (Nichols *et al*., 1983). It consists of three questions including satisfaction with spouse, marriage and relationship. The three items are measured on a 7-point scale ranging from extremely dissatisfied to extremely satisfied. The scores range from 21 to 3 with higher scores indicating higher marital satisfaction.

Beck Depression Inventory—2nd Edition (Beck *et al*., 1996) is a 21-question, multiple-choice, self-report instrument to assess depression symptoms as detailed in the DSM-IV. Each question is scored on a scale from 0 (absence of symptoms) to 3 (most severe symptoms), and participants are instructed to consider each item related to how they have felt in the past 2 weeks. The 21 items are summed for a single score for the BDI-II. The coefficient alpha for an outpatient population is 0.92.

Statistical analysis

Data are presented as frequency and percentage for categorical variables for each group. Differences between groups are assessed by chi-square analysis, with application of Fisher's exact test if any expected frequencies were < 5. Data are expressed as mean (SD) for continuous variables, with a Kruskal–Wallis test used for testing differences among the three groups and Wilcoxon rank-sum test used for testing differences between two groups. Multivariable analyses were performed to assess the association between instrument scores and study groups and related factors including total number of children in the family, annual family income, extended family and friends assisting with care-giving, education and occupation of primary care giver. Analyses were performed using the Statistical Analysis System, version 9.4 (SAS Institute) led by the RMN Data Coordination Center (DCC). Significance was defined as a two-sided $P < 0.05$.

Ethical Approval was obtained from Institutional Review Boards at each participating institution.

Results

A total of 348 mothers (121 singletons, 125 twins, 102 higher-order multiples) and 338 fathers (118 singletons, 122 twins, 98 higher-order multiples) were enrolled in the study, led by the RMN Data Coordinating Center (DCC).

Family characteristics

The demographics of the mothers' and fathers' age, race, educational attainment and home ownership were not significantly different between the families with singletons, twins or higher-order multiples (Table I). Overall, the mean years of education among the mothers was 17.0 (SD = 2.8) and 16.4 (SD = 3.1) among the fathers. Over 50% of fathers and mothers were in professional occupations. Regarding annual income, among all families, 54.5% had annual incomes over $100 000, 36.4% had incomes $50 000–$100 000 and 9.0% had annual incomes less than $50 000. Over 60% of the families with twins and singletons reported incomes greater than $100 000 compared to only 37.1 percent of the families with higher-order multiples ($P < 0.001$). Significant differences were also identified in two areas related to family size: the mean number of children in the family ($P < 0.001$) and the mean number of individuals supported by the annual family income ($P < 0.001$).

Health-related characteristics

No significant differences between the families with singletons, twins or higher-order multiples were identified for the length of time pregnancy was attempted prior to seeking fertility treatment (Table II) or the type of infertility diagnoses. Regarding health insurance, the majority of all families were covered by a HMO or other private insurance. Among all families, 7.1% reported Medicaid as their health insurance, while 14.1% of the families with higher-order multiples indicated Medicaid as their health insurance (NS). A significant difference in the gestational ages at delivery of the singletons, twins and higher-order multiples was identified: mean weeks (standard deviation) 38.9(1.9); 34.8(3.2) preterm; and 31.9(2.9) very preterm, respectively, ($P < 0.001$).

Family implications

Among the mothers employed during their pregnancy, 81.7% of the mothers of singletons and 51.6% of mothers of twins reported being able to maintain their normal hours of employment throughout pregnancy (Table III). Among employed mothers with higher-order multiples, only 26.3% maintained their normal hours of employment throughout their pregnancy ($P < 0.001$). Over 90% of the mothers in each group were described as the primary caregiver. Among families with singletons, 72.5% indicated having family or friends to assist with caregiving. This was the case among 69.5% of families with twins and 68.4% of families with higher-order multiples.

When asked about longer-term follow-up care for health and/or developmental outcomes of their children, among all families, 50.0% reported needing follow up care. Among families with higher-order multiples, 75.7% relayed requiring follow-up care, compared with 54.3% among twins and 23.8% among singletons ($P < 0.001$). Regarding the need to make housing modifications to accommodate the needs of the children, among the families with higher-order multiples, 36.3% reported needing modifications, while among families with twins and singletons, the percentages were 30.2 and 19.8%, respectively ($P = 0.021$).

There were no significant differences among families with singletons, twins, or higher-order multiples experiencing separation or divorce since the birth of their children. When asked about financial strain, i.e. how hard is it for you to pay for the very basics, like food, medical care and heating, among families with higher-order multiples, 53.5% indicated it was somewhat hard, 5.9% reported it to be very hard; and 28.3 and 3.1% of families with twins reported it was somewhat hard and very hard. In contrast, among families with singletons, 19.5% indicated it was somewhat hard and no one reported it was very hard ($P < 0.001$).

Standardised instrument scores

Unadjusted Scores on the standardised instruments are presented in Table IV. A lower personal strain domain score (20.0 vs 21.1, $P = 0.003$) and the revised 15-item score (51.1 vs 53.0, $P = 0.010$) of

Table 1 Characteristics of the families in three arms (singletons, twins, and higher-order multiples).

	Singletons	Twins	Higher-order multiples	All	*P* value*
Father's age (years)					
N	118	122	98	338	
Mean (SD)	40.2 (8.2)	40.4 (7.3)	40.0 (6.7)	40.2 (7.4)	0.907
Mother's age (years)					
N	121	125	102	348	
Mean (SD)	37.8 (5.7)	38.1 (5.9)	37.2 (5.0)	37.7 (5.6)	0.547
Father—Hispanic	6/119 (5.0%)	2/121 (1.7%)	9/98 (9.2%)	17/338 (5.0%)	0.032
Father's race					0.239
White	104/117 (88.9%)	112/122 (91.8%)	90/96 (93.8%)	306/335 (91.3%)	
Black	8/117 (6.8%)	2/122 (1.6%)	3/96 (3.1%)	13/335 (3.9%)	
Asian	5/117 (4.3%)	8/122 (6.6%)	3/96 (3.1%)	16/335 (4.8%)	
Other	0/117 (0.0%)	0/122 (0.0%)	0/96 (0.0%)	0/335 (0.0%)	
Mother—Hispanic	4/120 (3.3%)	4/126 (3.2%)	4/102 (3.9%)	12/348 (3.4%)	1.000
Mother's race					0.318
White	105/121 (86.8%)	114/125 (91.2%)	95/102 (93.1%)	314/348 (90.2%)	
Black	7/121 (5.8%)	3/125 (2.4%)	2/102 (2.0%)	12/348 (3.4%)	
Asian	7/121 (5.8%)	8/125 (6.4%)	3/102 (2.9%)	18/348 (5.2%)	
Other	2/121 (1.7%)	0/125 (0.0%)	2/102 (2.0%)	4/348 (1.1%)	
Father's occupation					0.609
Unemployed/stay at home	5/118 (4.2%)	3/120 (2.5%)	6/97 (6.2%)	14/335 (4.2%)	
Self-employed/management/business	18/118 (15.3%)	13/120 (10.8%)	12/97 (12.4%)	43/335 (12.8%)	
Office/administrative support	12/118 (10.2%)	11/120 (9.2%)	13/97 (13.4%)	36/335 (10.7%)	
Service/retail/sales	15/118 (12.7%)	9/120 (7.5%)	8/97 (8.2%)	32/335 (9.6%)	
Construction/transportation/maintenance	14/118 (11.9%)	12/120 (10.0%)	11/97 (11.3%)	37/335 (11.0%)	
Professional	54/118 (45.8%)	72/120 (60.0%)	47/97 (48.5%)	173/335 (51.6%)	
Mother's occupation					0.303
Unemployed/stay at home	24/120 (20.0%)	26/126 (20.6%)	28/102 (27.5%)	78/348 (22.4%)	
Self-employed/management/business	12/120 (10.0%)	5/126 (4.0%)	2/102 (2.0%)	19/348 (5.5%)	
Office/administrative support	11/120 (9.2%)	13/126 (10.3%)	11/102 (10.8%)	35/348 (10.1%)	
Service/retail/sales	8/120 (6.7%)	6/126 (4.8%)	7/102 (6.9%)	21/348 (6.0%)	
Construction/transportation/maintenance	2/120 (1.7%)	5/126 (4.0%)	5/102 (4.9%)	12/348 (3.4%)	
Professional	63/120 (52.5%)	71/126 (56.3%)	49/102 (48.0%)	183/348 (52.6%)	
Number of children 1.5–5 years of age	100	99	76		
Total number of children in the family					
N	122	129	103	354	
Mean (SD)	1.8 (0.7)	2.5 (0.8)	3.8 (0.9)	2.6 (1.1)	<0.001
Annual income					<0.001
<$50 000	9/117 (7.7%)	10/129 (7.8%)	12/97 (12.4%)	31/343 (9.0%)	
$50 000–$100 000	37/117 (31.6%)	39/129 (30.2%)	49/97 (50.5%)	125/343 (36.4%)	
>$100 000	71/117 (60.7%)	80/129 (62.0%)	36/97 (37.1%)	187/343 (54.5%)	
How many individuals in the household does this income support?					
N	120	129	103	352	
Mean (SD)	3.7 (0.8)	4.4 (0.9)	5.7 (0.9)	4.5 (1.2)	<0.001

*Kruskal–Wallis test was used for continuous variables and chi-square or Fisher's exact test was used for categorical variables. Data are presented as *N*, mean (SD) or number of subjects/total number (percentage).

Table II Health-related characteristics.

	Singletons	Twins	Higher-order multiples	All	*P* value*
Study child—gestational age (weeks)					
N	122	129	103	354	
Mean (SD)	38.9 (1.9)	34.8 (3.2)	31.9 (2.9)	35.4 (3.9)	<0.001
Length of time (years) pregnancy attempted before seeking infertility treatment?					
N	122	127	101	350	
Mean (SD)	2.4 (2.6)	2.3 (1.8)	2.4 (2.4)	2.3 (2.3)	0.740
Health insurance type					0.103
HMO	73/114 (64.0%)	79/126 (62.7%)	54/99 (54.5%)	206/339 (60.8%)	
Other private insurance	34/114 (29.8%)	38/126 (30.2%)	29/99 (29.3%)	101/339 (29.8%)	
Medicaid	3/114 (2.6%)	7/126 (5.6%)	14/99 (14.1%)	24/339 (7.1%)	
Medicare	2/114 (1.8%)	1/126 (0.8%)	1/99 (1.0%)	4/339 (1.2%)	
Self-pay uninsured	2/114 (1.8%)	1/126 (0.8%)	1/99 (1.0%)	4/339 (1.2%)	
History of multiple gestations, excluding this pregnancy?	5/121 (4.1%)	15/126 (11.9%)	3/101 (3.0%)	23/348 (6.6%)	0.016

*Kruskal–Wallis test was used for continuous variables and chi-square or Fisher's exact test was used for categorical variables. Data are presented as *N*, mean (SD) or number of subjects/total number (percentage).

Table III Family implications*.

	Singletons	Twins	Higher-order multiples	All	*P* value
Able to maintain normal hours of employment throughout pregnancy	94/115 (81.7%)	63/122 (51.6%)	25/95 (26.3%)	182/332 (54.8%)	<0.001
Follow-up care required after delivery for the child/children for any health and/or developmental sequelae	29/122 (23.8%)	69/127 (54.3%)	78/103 (75.7%)	176/352 (50.0%)	<0.001
Local extended family/friends	110/122 (90.2%)	106/128 (82.8%)	79/102 (77.5%)	295/352 (83.8%)	0.034
Extended family and friends assist with care-giving	79/109 (72.5%)	73/105 (69.5%)	54/79 (68.4%)	206/293 (70.3%)	0.810
Financial strain	24/121 (19.8%)	39/129 (30.2%)	37/102 (36.3%)	100/352 (28.4%)	0.021
Had to make housing modification for the study child/children					
Had to make transportation modifications for the child/children	72/120 (60.0%)	100/129 (77.5%)	90/102 (88.2%)	262/351 (74.6%)	<0.001
How hard is it for you to pay for the very basics like food, medical care and heating?					<0.001
Very hard	0/118 (0.0%)	4/127 (3.1%)	6/101 (5.9%)	10/346 (2.9%)	
Somewhat hard	23/118 (19.5%)	36/127 (28.3%)	54/101 (53.5%)	113/346 (32.7%)	
Not hard at all	95/118 (80.5%)	87/127 (68.5%)	41/101 (40.6%)	223/346 (64.5%)	
Mother as the primary caregiver	111/119 (93.3%)	115/125 (92.0%)	96/102 (94.1%)	322/346 (93.1%)	0.817
Single parent	3/122 (2.5%)	7/128 (5.5%)	5/103 (4.9%)	15/353 (4.2%)	0.504
Became divorced or separated from spouse/significant other since the birth of child/children	6/118 (5.1%)	8/126 (6.3%)	5/103 (4.9%)	19/347 (5.5%)	0.862

*Data are presented number of subjects/total number (percentage). Chi-square or Fisher's exact test was used for *P* values.

the Impact on Family Scale were shown for twins when compared to singletons, indicating a more negative impact on family; similar results were shown for multiples when compared to twins (Table IV). In addition, a lower total and domain scores for Parenting Stress Index, a lower total score of Kansas Marital Satisfaction Scale and a higher Beck Depression Inventory total score were found for twins when compared to singletons; parts of these results (total and parental stress domain score for Parenting Stress Index, total score for Beck Depression Inventory) were similarly affected for multiples when compared to twins (Table IV). Turning to the Child Behaviour Checklist, among children

Table IV Instruments scores by study groups*.

	Singletons	Twins	Higher-order multiples	*P* value for comparison between singletons and twins	*P* value for comparison between twins and multiples
Impact on Family Scale score[&]					
n	118	125	102		
Domain score					
Financial impact	13.9 ± 2.2	13.9 ± 2.0	13.6 ± 2.2	0.476	0.347
Familial/social impact	31.9 ± 4.4	31.1 ± 4.5	29.4 ± 5.2	0.081	0.013
Personal strain	21.1 ± 3.1	20.0 ± 3.0	19.0 ± 3.4	0.003	0.013
Mastery (lack of)	9.2 ± 3.1	9.2 ± 2.6	9.1 ± 2.3	0.512	0.786
Revised 15-item score	53.0 ± 7.2	51.1 ± 7.0	48.4 ± 8.1	0.010	0.011
Parenting Stress Index score[#]					
n	118	128	103		
Total score	148.8 ± 16.4	141.5 ± 16.9	135.4 ± 17.1	<0.001	0.011
Domain score					
Parental stress	48.6 ± 7.6	45.9 ± 8.6	41.6 ± 8.9	0.013	<0.001
Parent–child interaction	55.8 ± 4.5	54.2 ± 5.4	53.4 ± 4.9	0.003	0.072
Difficult child	44.3 ± 7.0	41.4 ± 7.2	40.3 ± 6.8	0.001	0.277
Kansas Marital Satisfaction Scale score[^]					
n	119	124	102		
Total score	17.6 ± 4.2	16.4 ± 4.7	16.1 ± 4.7	0.045	0.476
Beck Depression Inventory score[$]					
n	119	128	102		
Total score	7.3 ± 6.5	8.8 ± 6.5	12.0 ± 7.7	0.023	0.002
CBCL/1 $^1/_2$–5[^^]					
n	100	99	76		
Syndrome scales					
Emotionally reactive	1.6 ± 1.7	1.9 ± 1.6	1.7 ± 1.4	0.019	0.391
Anxious/depressed	1.3 ± 1.7	1.8 ± 1.6	1.5 ± 1.4	0.001	0.269
Somatic complaints	1.2 ± 1.2	1.5 ± 1.5	1.2 ± 1.0	0.313	0.612
Withdrawn	0.5 ± 0.9	0.8 ± 1.1	0.8 ± 0.9	0.004	0.236
Sleep problems	2.0 ± 2.0	2.0 ± 2.0	1.6 ± 1.5	0.591	0.192
Attention problems	1.4 ± 1.6	1.5 ± 1.3	1.4 ± 1.2	0.080	0.863
Aggressive behaviour	6.1 ± 4.7	7.2 ± 5.0	7.0 ± 4.7	0.090	0.866
Internalising scale	4.5 ± 4.4	6.0 ± 5.0	5.2 ± 3.7	0.018	0.585
Externalising scale	7.4 ± 5.8	8.7 ± 5.8	8.4 ± 5.6	0.085	0.800
Total problems scale	18.7 ± 14.2	23.2 ± 15.4	20.8 ± 12.7	0.032	0.478

*Plus–minus values are means ± SD. CBCL/1 $^1/_2$–5, child behaviour checklist for ages 1.5–5.
[&]A lower score indicates a more negative impact on the family.
[#]A lower score indicates a greater level of parental stress.
[^] A higher score indicates a higher marital satisfaction.
[$]A higher score indicates a more severe depression symptom.
[^^] A higher score indicates a more severe problem.

1.5–5 years of age, a higher syndrome scales of emotionally reactions, anxiety/depression and withdrawal, the combined internalising scale and the total problems scale were shown for twins when compared to singletons; no difference was shown for multiples when compared to twins (Table IV). No difference in the language development profile or the scales for CBCL/6–18 was found for twins when compared to singletons, or for multiples when compared to twins (Table VI). It should be noted that the number for the language development and for children CBCL/6–18 questionnaire was low.

Results for multivariable analyses are shown in Table V. After adjusting for total number of children in the family, annual family income, extended family and friends assisting with care-giving, education and

Table V **Association between instrument scores and study groups and related factors (multivariate analysis)*.**

	Impact on Family Scale: revised 15-item score		Parenting Stress Index total score		Kansas Marital Satisfaction Scale total score		Beck Depression Inventory total score		CBCL/1 1/2–5 total problem score	
	Beta (95% CI)	***P* value**	**Beta (95% CI)**	***P* value**	**Beta (95% CI)**	***P* value**	**Beta (95% CI)**	***P* value**	**Beta (95% CI)**	***P* value**
Group										
Singletons	Reference		Reference		Reference		Reference		Reference	
Twins	−2.6 (−4.7, −0.5)	0.014	−9.0 (−13.8, −4.2)	<.001	−1.0 (−2.3, 0.3)	0.150	2.0 (0.1, 3.9)	0.039	5.2 (0.6, 9.8)	0.026
Higher-order multiples	−7.4 (−10.4, −4.5)	<.001	−19.6 (−26.2, −13.0)	<.001	−1.7 (−3.5, −0.2)	0.073	6.1 (3.4, 8.7)	<.001	4.1 (−2.5, 10.6)	0.225
Total number of children in the family	1.6 (0.6, 2.7)	0.002	2.8 (0.5, 5.1)	0.020	0 (−0.6, 0.7)	0.878	−0.7 (−1.7, 0.2)	0.134	−1.2 (−3.5, 1.1)	0.300
Annual family income										
<$50 000	Reference		Reference		Reference		Reference		Reference	
$50 000–$100 000	−1.6 (−4.7, 1.5)	0.298	−0.5 (−7.5, 6.6)	0.895	0.2 (−1.8, 2.2)	0.865	1.3 (−1.5, 4.1)	0.348	0 (−7.0, 7.0)	0.998
>$100 000	−0.8 (−3.9, 2.3)	0.617	−1.2 (−8.2, 5.8)	0.741	0.4 (−1.6, 2.4)	0.722	0.8 (−2.0, 3.6)	0.565	−2.5 (−9.7, 4.6)	0.482
Highest level of education in years for primary care giver	0 (−0.3, 0.3)	0.841	0 (−0.7, 0.7)	0.978	0 (−0.2, 0.2)	0.867	0 (−0.3, 0.2)	0.593	−0.7 (−1.4, 0)	0.049
Primary care giver working or not										
No	Reference		Reference		Reference		Reference		Reference	
Yes	1.4 (−0.6, 3.5)	0.161	2.2 (−2.3, 6.8)	0.338	−0.7 (−1.9, 0.6)	0.287	−0.2 (−2.0, 1.6)	0.849	−0.7 (−5.1, 3.7)	0.754
Extended family and friends assist with care-giving										
No	Reference		Reference		Reference		Reference		Reference	
Yes	0.7 (−0.9, 2.4)	0.389	1.2 (−2.6, 5.0)	0.546	0 (−1.0, 1.1)	0.933	0.3 (−1.2, 1.8)	0.688	0.4 (−3.2, 4.1)	0.811

*CBCL/1 1/2–5, Child Behavior Checklist for ages 1.5–5. CI, confidence interval.

Table VI CBCL/18–35 months language development profile and CBCL/6–18 scales for singletons, twins and multiples*.

	Singletons	Twins	Higher-order multiples	P value for comparison between singletons and twins	*P* value for comparison between twins and multiples
For CBCL/18–35 months, % (no./total no.)					
Language development					
Delayed phrase development	7.9 (3/38)	23.8 (10/42)	40.0 (10/25)	0.071	0.161
Delayed vocabulary development	9.5 (4/42)	11.1 (5/45)	39.3 (11/28)	1.000	0.005
For CBCL/6–18^, mean ± SD					
n	14	28	25		
Syndrome scales					
Anxious/depressed	2.9 ± 2.1	2.7 ± 2.7	2.2 ± 2.0	0.502	0.537
Somatic complaints	1.1 ± 1.1	1.2 ± 1.3	0.9 ± 0.7	0.880	1.000
Withdrawn/depressed	0.6 ± 0.9	1.0 ± 1.3	0.6 ± 0.9	0.182	0.097
Social problems	1.6 ± 1.6	1.8 ± 2.0	1.3 ± 1.3	1.000	0.747
Thought problems	1.8 ± 2.1	2.0 ± 2.5	1.0 ± 0.9	0.746	0.303
Attention problems	2.9 ± 2.9	2.9 ± 3.0	2.0 ± 1.5	0.788	0.464
Rule-breaking behaviour	0.7 ± 0.9	1.1 ± 1.2	0.8 ± 0.9	0.227	0.448
Aggressive behaviour	2.3 ± 2.1	3.5 ± 3.2	3.7 ± 3.2	0.238	0.943
Internalising problems	4.6 ± 3.7	4.8 ± 4.8	3.7 ± 3.3	0.894	0.538
Externalising problems	3.0 ± 2.7	4.6 ± 4.2	4.5 ± 3.8	0.218	0.979
Total problems scale	16.6 ± 8.5	19.1 ± 15.8	14.7 ± 11.1	0.904	0.250

*CBCL/Language Development Survey for Ages 18–35 months. CBCL/6–18, Child Behavior Checklist Ages 6–18.
^A higher score indicates a more severe problem.

occupation of primary care giver, the revised Impact on Family Scale 15-item score for twins (beta = −2.6, 95% confidence interval (CI), −4.7, −0.5, $P = 0.014$) and multiples (beta = −7.4, 95% CI, −10.4, −4.5, $P < 0.001$) were significantly lower than that for singletons. Similar results were found for the Parenting Stress Index total score. In addition, the Beck Depression Inventory total score was significantly higher for twins (beta = 2.0, 95% CI, 0.1, 3.9, $P = 0.039$) and multiples (beta = 6.1, 95% CI, 3.4, 8.7, $P < 0.001$), and the CBCL/11/2–5 total problem score was significantly higher for twins (beta = 5.2, 95% CI, 0.2, 9.8, $P = 0.026$) when compared to singletons (Table V).

Discussion

In this group of well-educated, high-income families, there were no significant differences between the groups in the domains of primary caregiving, having family or friends to assist with caregiving or parental separation or divorce since the children's birth. These are reassuring longer-term family outcomes. It is important to note the statistically significant differences between the families' annual incomes and difficulty paying for the basics. Families with higher-order multiples experienced more difficulty paying for basics and had lower incomes than families with twins or singletons.

An important factor related to family well-being is parity. Vilska *et al.* (2009) conducted a 1-year prospective study on the psychological well-being of parents with ART conceived and spontaneously conceived twins and singletons. The authors concluded that parenthood with twins, but not the use of ART, has a negative impact on the mental health of mothers and fathers during the transition to parenthood. Similarly, Roca-de Bes *et al.* (2011) conducted a study to determine if psychosocial risks associated with multiple births are increased as a consequence of ART in comparison to multiple births not resulting from ART. Parents of children, singletons and multiples, ages 6 months and 4 years, were divided into ART and non-ART groups. The results indicated that no effect was observed based on the use of ART on the psychosocial variables examined. However, there were differences between the groups of singletons and multiple births regarding material necessities, social stigma, marital satisfaction, depression and quality of life. The authors concluded that having more than one child per birth, whether conceived with ART or not, increases psychosocial risks for the parents. Our findings mirror this observation as reflected in the significant differences among families with twins and those with singletons on the Impact on Family Scale and the Parenting Stress Index.

Turning to other psychosocial issues, Jena *et al.* (2011), noting that the effects of multiple births in the published literature is limited, examined the association of twins and parental divorce using 1980 census data. The authors reported that the potential impact of twins on divorce may be greater in the longer term, when the children are older. However, given the age of the census data and since women conceiving via ART may be different from women conceiving twins

spontaneously, the results may not be directly extrapolated to twins conceived via ART. In our sample, there were no significant differences among the groups of families regarding divorce or separation since the birth of the child/children. Regarding the children requiring follow-up care for health or developmental outcomes, there were statistically significant differences. Among families with higher-order multiples, 75.7% required follow up care health and/or developmental outcomes in contrast to 54.3% among twins, and 23.8% among singletons. A 2004 report by Risdal *et al*. examined the literature on comparative levels of divorce and marital dissatisfaction in parents of children with and without developmental disabilities. The authors noted the historically negative views on the influence of children with disabilities on marital satisfaction; however, the meta-analysis reported a smaller than expected effect size.

Among the limited number of studies that have addressed the outcomes of children resulting from ART and their families, one difficulty is controlling for parental attitudes and expectations. Children born following ART, noted in multiple studies, are born to older parents, at earlier gestational ages and lower birth weights in families of smaller size and higher economic status compared to naturally conceived children (Hvidtjorn *et al*., 2011; Hart and Norman, 2013). A study by Anderson *et al*. (2014) reported that the negative effect of twin status improved by middle childhood and that twins may even have more optimum psychosocial adjustment than singletons. In a review of outcomes among children resulting from ART conducted by Wagenaar *et al*. (2008), the authors observed that the psychological well-being of children born following IVF is reassuring. Related to behaviour and socioemotional functioning in 9–18-year-old children born after *in vitro* fertilisation, Wagenaar *et al*. (2009) reported, based on the CBCL and the Teacher Report Form (TRF), that behaviour and socioemotional functioning is normal. However, the authors called for continued follow-up studies to learn about longer term outcomes into adolescence. Multiple authors have recommended continued research on the longer-term follow-up of children born following ART as they progress through adolescence and into adulthood. In 2012, Eisenberg submitted that studying long-term outcomes was needed to improve the health of children born following ART. Hediger *et al*. (2013) noted that further longitudinal research is needed to inform clinical guidelines and population health.

Our study has several notable strengths. As a part of the RMN, enrolling families, including mothers and fathers, from the cooperative clinical sites provided a sample size larger than studies conducted at a single site and incorporated the perspectives from both parents. Further, enrolment from the cooperative clinical sites included families from multiple geographic regions and provided for uniform recruitment and data collection procedures. For more than two decades, researchers have called for studies addressing the longer-term outcomes for the ART-conceived children and their families. By focusing on children of two to 12 years of age, our study explored longer-term psychosocial and financial issues during an 11-year timeframe when parents are often heavily involved with their children's educational and social activities.

In addition to the strengths of the study, there were several limitations. While the study population included families from the RMN sites across the country, it was limited to families who received fertility treatment services. Our sample population included over 90% white, well-educated, higher income families. This sampling bias limits the generalisability of the findings to families with less education and lower incomes. For a variety of reasons, including financial status, health insurance coverage, access to and/or availability of services, some families who desire fertility treatment services may not receive them. Further, the interview data were self-reported and subject to recall and response biases. Turning to the scores for the CBCL, the number of children available in the 6–18-year age range (28 twins, 14 singletons) was lower than in the 1.5–5 years age range (99 twins, 100 singletons).

Future prospective studies addressing longer-term family psychosocial and financial outcomes will expand and enhance educational and counselling information available to clinicians while working with families to inform their decision-making surrounding ART.

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Authors' roles

Virginia Miller, DrPH, MS, MPH—conceived of study, protocol design, critical review of data, manuscript preparation. Michael P. Diamond MD—conceived of study, protocol design, critical review of data, manuscript preparation. Karl R. Hansen, MD, PhD—review of study protocol design, study conduct, manuscript review. Anne Z. Steiner, MD, MPH—review of study protocol design, study conduct, manuscript review. Marcelle Cedars, MD—review of study protocol design, study conduct, manuscript review. Richard S. Legro, MD—review of study protocol design, study conduct, manuscript review. Stephen A. Krawetz, PhD—review of study protocol design, study conduct, manuscript review. Christos Coutifaris, MD, PhD—review of study protocol design, study conduct, manuscript review. Hao Huang, MD, MPH—review of study protocol design, statistical analysis, manuscript critical review. Nanette Santoro, MD—review of study protocol design, study conduct, manuscript review. Heping Zhang, PhD—review of study protocol design, statistical analysis, manuscript critical review.

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Conflict of interest

Dr Virginia Miller—no conflicts; Dr Michael P. Diamond—NIH funding, AbbVie, Bayer and ObsEva Funding; Board of Directors and Stockholder for Advanced Reproductive Care; Dr Karl R. Hansen—Yale University/Reproductive Medicine Network/NICHD, Roche Diagnostics and Ferring International Pharmascience Center US funding; Dr Anne

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