Advanced Access publication on January 23, 2018 doi:10.1093/humrep/dey002

human reproduction

ORIGINAL ARTICLE Psychology and counselling

The impact of ART on union dissolution: a register-based study in Denmark 1994–2010

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Submitted on October 15, 2017; resubmitted on December 19, 2017; accepted on January 2, 2018

STUDY QUESTION: Are couples initiating ART treatment at higher risk for future union dissolution compared to other couples?

SUMMARY ANSWER: There is no effect of ART treatments in future marital dissolution over a period of 16 years when adjusting for all confounders.

WHAT IS KNOWN ALREADY: Findings regarding marital stability and infertility treatments have been sparse and controversial. While there is data showing higher divorce rates among women who go through infertility treatments, there is also some evidence of this experience bringing couples closer by forcing them to communicate more and to deal with the surrounding stigma. Using a population-based study and couple-level data, we investigated the extent to which ART treatment increases the risk for divorce/marital dissolution during up to 16 years of follow-up.

STUDY DESIGN SIZE, DURATION: Register-based national cohort study including all women registered with ART treatment in Denmark between I January 1994 and 30 September 2009 ($n = 42\,845$). Marital/cohabiting status was confirmed by matching these women to partners who they were married to or shared an address with. To account for having a significant relationship at baseline (2 years), marital/cohabiting status was confirmed by accessing this variable before the establishment of the cohort back to I January 1992.

PARTICIPANTS/MATERIALS, SETTING, METHODS: A comparison group from the background population including five controls per case and matched to female age at baseline was prospectively sampled. Participants could change status during follow-up if they entered ART. The final sample had 148 972 couples, followed until marital dissolution, death of self/spouse, migration or until 31 December 2010. We used Cox regression models adjusting for female and male age, education, marriage, common child at baseline and live-born child during follow-up.

MAIN RESULTS AND THE ROLE OF CHANCE: At baseline, the majority of couples were married (69%). More non-ART couples opted for marriage (70% versus 64%; P < 0.0001) and already had common children at study entry (43% versus 9%; P < 0.0001). During the 16 years of follow-up the majority of couples had children with their baseline partners (56% non-ART versus 65% ART), and 22% ended up separated or divorced (20% ART versus 22% non-ART). Findings revealed a lower risk of break-up among ART couples (crude HR 0.84, 95% CI 0.82–0.86), even after adjusting for both partners' age, education, partnership status and having a common child at baseline (adj HR 0.83, 95% CI 0.80–0.86). However, when subsequent common children (time-dependent) was added to the model, no difference in the risk of dissolution was found (adj HR 1.00, 95% CI 0.99–1.01). A significant interaction between ART status and common children showed that the risk of break-up was attributed to childlessness regardless of having gone through ART treatment.

LIMITATIONS REASON FOR CAUTION: This study did not control for involuntary childlessness, non-ART fertility care (ovulation induction, IUI) and biological parenthood. Additionally, there are important predictors of divorce that were not considered. We were unable to adjust for religion, existence of previous marital relationships, income, employment, health status of parents and child(ren), and quality of relationship.

WIDER IMPLICATION OF FINDINGS: The finding that going through ART does not increase the risk of break up per se is reassuring for couples who underwent ART and have children or are contemplating to start ART.

STUDY FUNDING/COMPETING INTEREST(S): This work was supported by FCT (Portuguese Foundation for Science and Technology), grant ref. SFRH/BPD/85789/2012. The authors have no conflicts of interest.

TRIAL REGISTRATION NUMBER: N/A

Key words: ART / parenting / marital relationship / union dissolution / divorce / registries / cohort studies

Introduction

The impact of ART on couples' well-being and stability has been documented in both research and social media for the last decades. Despite this strong interest and an associated increase in the number of studies analyzing the relationship between (in)fertility and the marital relationship, mixed findings have been reported.

For example, studies comparing couples going through fertility treatments with fertile couples regarding their marital adjustment or stability have yielded conflicting results. Using for comparison a group of women seeking elective sterilization, Monga et al. (2004) found that women going through ART had significantly poorer levels of marital adjustment. Similar results were found by Wang et al. (2007), with women going through IVF or ICSI treatments presenting worse and less stable relationships than women with no known history of infertility. However, opposite conclusions were also suggested by findings of significantly higher marital adjustment levels presented by groups of both men and women (Onat and Kizilkaya Beji, 2012), or couple-level data (Sydsjö et al., 2002) compared to fertile groups. There is also research postulating that while infertile women present higher marital adjustment than their fertile counterparts, there are no significant differences regarding male adjustment to their marriages (Drosdzol and Skrzypulec, 2009).

Prospective studies following couples after treatment also present mixed findings. Sydsjö et al. (2005) found no differences in marital adjustment comparing male and female scores during treatment, 6 months after and 1.5 years after, but Schanz et al. (2013) found that men and women in fertility treatments reported a decrease in partner satisfaction 5 years after beginning treatment. Evidence seems more stable when the focus is only on the transition to parenthood: Studies assessing marital adjustment during and after pregnancy found no differences between couples who achieved pregnancy through ART treatment and couples who had spontaneously conceived (Slade et al., 1992; Hjelmstedt et al., 2004; Repokari et al., 2007). These studies also describe a parallel tendency for deterioration of marital adjustment after parenting, even though there is evidence of a more stable dyadic consensus only for couples who went through ART (Repokari et al., 2007).

Finally, studies focusing on marital stability or dissolution also contributed to intensify the ongoing debate on the impact of fertility treatments. Some authors claim that separation rates in couples who went through ART are probably lower than the general population, with reports of as low as 5% (Schanz et al., 2013), or of 14% (Martins et al., 2014) in studies following couples over 5 years, and of 17% at 10 years of follow-up (Sundby et al., 2007; Wischmann et al., 2012). This is justified with available evidence on how going through the experience of infertility brings couples closer by forcing them to communicate more and deal with the surrounding stigma (Schmidt et al., 2005a,b). The

transition to parenthood also seems to play an important role, since Wirtberg et al. (2006) found that half of the participants interviewed 20 years after unsuccessful tubal surgery had separated; and Kjaer et al. (2014) found that women who did not have a child 12 years after their fertility evaluation had an estimated higher probability of separation than those who had a child, regardless of previous children.

Taking these findings together, there are reasons to believe that the controversial evidence pointing to either an improvement or deterioration of the marital relationship due to fertility treatment can be due to several important confounders, such as the lack of long-term prospective data, high participation and retention rates, and appropriate comparison groups. Additionally, besides treatment success, preferably measured by live-born child, other established predictors of divorce such as education, partnership status, common children and age (Lyngstad and Jalovaara, 2010; Matysiak et al., 2014; Lundberg et al., 2016; Rotz, 2016) should be taken into consideration when examining the impact of infertility on the relationship.

The goal of this study was to determine the risk of marital dissolution among heterosexual couples who have gone through assisted reproductive technology (ART) treatment. Using couple-level data in a population-based study, we explored whether having ART treatment increases the risk of relationship dissolution during up to 16 years after initiation of ART treatment, controlling for the aforementioned established predictors of dissolution.

Materials and Methods

Setting

In Denmark 8–9% of the annual national birth cohort are children conceived with medically assisted treatment, and 50% of these are a result of ART treatments. In total 50% of all treatments are offered in a tax-financed public health care system, with the remaining treatments offered in a private health care system. In the public health care system treatment is accessible for all single women or women in a partnership with no common children up to 40 years old. In the private sector women/couples are offered treatment up to a female age of 45. The public health care system offers up to three fresh ART treatment cycles and an unlimited number of cycles with intrauterine insemination (IUI) treatment (in practice 3–6 cycles).

Study population

The Danish National ART-Couple (DANAC) cohort (Schmidt et al., 2013) includes all women registered with at least one ART treatment between I January 1994 and 30 September 2009 ($n=42\,845$), after excluding 35 women who were under 18 or over 49 years old or had missing information on the first or last treatment (see Blenstrup and Knudsen, 2011 and Thygesen

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et al., 2011 for validity of Danish registers). In the current study, 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). A random age-matched comparison group of women including approximately five controls per case (n = 214519) was sampled prospectively. When a woman initiated the first ART treatment (baseline), five age-matched women not previously treated with ART were randomly selected from the Central Population Register, which includes all people in Denmark. This matching allowed women in the comparison group to change status during follow-up if participants entered ART treatment. Thus, the total initial sample had 257 364 observations.

Each of these women has a unique personal identification number (PIN), as well as the partners with whom they are married or share an address. This allowed us to match partners and extract sociodemographic data. Since couples in Denmark are equally likely to be married or to cohabit without formal marriage, we included both categories in our data analyses. First, we excluded women without a partner (n = 70918), and women with female partners (n = 361) at baseline. Participants were also excluded at baseline if they did not share a common address for at least 2 years (n = 33297). Relationship length was estimated from the time a couple initiated ART treatment or were selected for the comparison group to the last year before change in civil status/cohabiting status (to living alone or living with another partner). If in the following year after change in status the same partner from baseline was reported, marital dissolution was not registered. In the comparison group 385 women had migrated before inclusion, and these women were thus excluded. After exclusions, the final sample for analyses was n = 152403 observations distributed among 148 972 couples. They were followed from the date of the first ART treatment or study entry (comparison group) until marital dissolution, death or death of a spouse, migration or end of follow-up on 31 December 2010.

This research projects was approved by the Danish Data Protection Agency (J.nr. 2008-41-2076), the National Board of Health (J.nr. 7-505-29-1658/1), the Danish Medical Agency, and Statistics Denmark (J.nr. 703481). According to the Danish law, register-based studies do not require approval from the ethics committee system.

Statistical analyses

All statistics were performed with SAS version 9.4. Differences between ART-treated couples and non-ART couples were investigated with chisquare test for categorical variables and t-test for continuous variables. Differences in the probability of break-up among the ART and non-ART couples were investigated using Cox proportional hazards regression with time to break-up as the dependent variable. Covariates tested in the analyses were the couple's highest educational level attained according to the International Standard Classification of Education System (ISCED; low I, up to 10 years of education; medium II, upper secondary education, vocational education and academy profession; high III, professional bachelor programs; highest IV, bachelor and master's program and PhD), partnership status (married or cohabiting), and female and male age at the start of observation. Although ART and non-ART couples in average start trying to conceive at a similar age (Schmidt et al., 2003), the transition to parenthood is made at a later age for ART couples due to their infertility. Hence, whether and when the couple had a first common child (spontaneously or ART conceived, biological or adopted) was included as a time-dependent covariate using the %stratify macro (Rostgaard, 2008). Relevant two-way interactions were further tested.

Results

Descriptive results and significant differences between couples who underwent ART treatment and non-ART couples are shown in Table I.

At baseline, the majority of couples were married (69%), with more non-ART couples opting for marriage than ART couples (ART 64%; non-ART 70%). During up to 16 years of follow-up, 22% of the study population ended up separated or divorced (ART 20%; non-ART 22%). Of these relationship dissolutions, almost three quarters (73%) happened within 5 years after baseline. The majority of women were between 30 and 35 years old, with more ART women in the 25-29 category than non-ART women (ART 28%; non-ART 18%), and fewer in the 35-39 category (ART 23%; non-ART 30%). The tendency for couples in the ART group to be younger was also shown by male age, with more ART men younger than 30 than non-ART men (ART 17%; non-ART 11%), and fewer between 40 and 49 (ART I4%; non-ART 23%). Distribution regarding education was the same in both genders, revealing a slight tendency for ART men and women to have higher education degrees than non-ART couples. More non-ART couples than ART couples already had common children at study entry (43% versus 8%), which reflects the fact that these couples succeed in having children earlier than ART couples. At the end of follow-up, 56% of non-ART couples and 65% of ART couples had children with the partner they had at study entry.

Table II depicts hazard ratios for relationship dissolution in all couples. Crude analyses showed a lower risk of break-up among ART couples (crude HR 0.84, 95% CI 0.82–0.86). These findings were sustained after adjusting for both partners' age, education, partnership status and children at baseline (adj HR 0.83, 95% CI 0.80–0.86). However, after adding subsequent common children (time-dependent) to the model, no difference in the risk of relationship dissolution was found between ART and non-ART couples (adj HR 1.00, 95% CI 0.99–1.01).

To further illustrate this relationship, a two-way interaction including time-dependent effect of common children and effect of ART treatment on relationship dissolution is shown in Table III. Regardless of having gone through ART treatments, childless couples had a higher risk of break-up compared to couples that had children during the 16-year follow-up.

Discussion

This follow-up study included all couples who had ART treatment during the period 1994–2009 in Denmark and a female age-matched comparison group of couples to examine the impact of ART in the stability of the marital relationship. This is the first nationwide study comparing relationship dissolution rates between couples that went through ART treatment and those who did not, and controlling for pre-existing and time-dependent live-born common children, education, partnership status and age.

When compared with an age-matched comparison group from the general population, couples in the ART group revealed a slighter tendency towards cohabitation and seemed less inclined for marriage. This result is in accordance with the recent increase of postconception marriage (Gibson-Davis and Rackin, 2014; Holland, 2017), considering that more couples from the comparison group were parents at study entry. Regardless of the type of union, one in five couples (22%) separated or divorced over a 16-year follow-up. The majority of these dissolutions occurred within the first 5 years after baseline (73%), both to couples who went through ART treatment (66%) and to those who did not (74%).

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Table I Population characteristics of ART couples in the Danish National ART-Couple cohort and a non-ART comparison group, N = 148972.

	All couples		ART couples		Comparison group, non-ART couples		P-value
	n	%	n	%	n	%	
Couples	148 972	100	25 515	17	123 457	83	NA
Partnership status							
Married	95 126	69	14739	64	80 387	70	<0.000
Cohabiting	42 163	31	8456	36	33 707	30	
missing	11 683						
Marital dissolution							
Stability	116832	78	20 35 1	80	96 48 1	78	
Dissolution	32 140	22	5164	20	26 976	22	<0.000
Dissolution: relationship length ^a							
2–5	23 45 1	73	3431	66	20 020	74	<0.001
6–10	6269	20	1260	24	5009	19	<0.001
11–16	2420	8	473	9	1947	7	<0.001
Female age							
<25	1899	1	725	3	1174	ı	<0.000
25–29	29 780	20	7041	28	22 739	18	
30–34	63 013	42	10831	42	52 182	42	
35–39	43 448	29	5855	23	37 593	30	
≥40	10 832	7	1063	4	9769	8	
Male age							
<30	18 375	12	4442	17	13 933	11	<0.000
30–39	94 997	64	17 046	67	77 95 I	63	
40–49	32 623	22	3692	14	28 93 1	23	
≥50	2977	2	335	1	2642	2	
Female education							
I. Low	28 191	19	3984	16	24 207	20	<0.000
II. Middle	76 922	52	12 840	51	64 082	52	
III. High	28 361	19	5370	21	22 99 1	19	
IV. Highest	13 903	9	3060	12	10 843	9	
missing	1595						
Male education							
I. Low	27 924	19	3923	16	24 00 1	20	<0.000
II. Middle	77 038	52	12 865	51	64 173	52	
III. High	28 37 1	19	5368	21	23 003	19	
IV. Highest	14 289	10	3150	12	11139	9	
missing	1350						
Child(ren) with baseline partner before treatment/study entry	55 338	36	2599	9	52 739	43	<0.000
Child(ren) with baseline partner at end of follow-up	85 084	57	16 535	65	68 549	56	<0.000

However, more non-ART couples separated within the first 5 years than ART couples, which in turn had higher separation rates between 6

and 16 years. This tendency accords with the lower divorce rates found in ART couples in studies who did follow-ups of 5 years (e.g. Schanz et al., 2013; Martins et al., 2014). Moreover, the finding that ART couples seem to separate later than non-ART couples might be explained by the

high levels of communication and closeness previously found on couples seeking fertility treatment (Schmidt et al., 2005a,b; Peterson et al., 2011; Ying and Loke, 2016); if the aim of pursuing parenthood through treatments and the associated uncertainty of the outcome brings more cohesion, it is likely that dissolution might occur sooner in non-ART couples who have not experienced this process.

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Table II Hazard ratios (HR) for marital dissolution (divorce or end of cohabitation) of couples who went through ART treatment compared with couples who did not (reference), followed over 16 years (N = 148 972).

	ART couples versus non-ART couples			
	HR	95% CI	P-value	
Model I. Crude HR	0.84	0.82–0.86	<0.0001	
Model 2. Adjusted HR for baseline factors ^a	0.83	0.80-0.86	<0.0001	
Model 3. Adjusted HR + common child ^b	1.00	0.99-1.01	0.99	

^aModel 2 included female age, male age, couple's highest educational level, children at baseline and partnership status at baseline.

Table III Two-way interactions between ART treatment and having at least one child in common for marital dissolution (divorce or end of cohabitation).

	HR	95% CI	P-value
Common child and non-ART	1.00	ref	NA
Common child and ART	1.02	1.00-1.04	<0.05
No child and non-ART	1.24	1.22-1.25	<0.0001
No child and ART	1.22	1.20-1.24	<0.0001
HR hazard ratio			

These results are also in line with the finding of a lower risk of relationship dissolution for ART couples. While these findings were sustained after adjusting for male and female age, education and partnership status, the differences in the risk for separation between couples who went through ART treatments and those who did not ceased to be significant after couples' common children over the course of 16 years entered the model.

A further two-way interaction (ART × common child) showed that the risk for dissolution is higher for childless couples regardless of having sought for ART treatment. Kjaer et al. (2014) had previously found that women who underwent unsuccessful ART treatment and did not become mothers over the following 17 years had a higher probability of marital dissolution than those who were mothers, regardless of previous children. The authors suggested that unsuccessful fertility treatment could be contributing to relationship dissolution in couples who sought fertility treatment. Our findings suggest that having common child(ren) is a protective factor of relationship dissolution independently of recurring to ART.

This paper corroborates the available evidence regarding the beneficial effect of parenthood on divorce (e.g. Coleman et al., 2000; Vuri, 2003; Hart et al., 2017; Wehner et al., 2004). However, there has been a recent debate on whether these results are biased by the fact that those who plan to have a child are more prone to union stability (Lawrence et al., 2008; Hart et al., 2017). This study suggests that those plans have to effectively become real in order to prevent union

dissolution. A recent meta-analysis concluded that people who went through unsuccessful ART treatments tend to show low scores in mental health and well-being measures compared to those who achieved the desired child(ren) (Gameiro and Finnigan, 2017).

Our results emphasize the importance of referring couples to psychosocial support after unsuccessful treatment. Counseling should focus on the marital relationship and the couple's reproductive life plan, allowing a joint and conscious decision-making process towards pursuing parenthood or transitioning to a childfree lifestyle. Given that psychological burden is the main reason for treatment discontinuation (Gameiro et al., 2012), psychosocial support for couples after failed treatment can also prevent dropout and consequently increase the chance of having a liveborn child. Our findings can also help couples and reproductive health professionals to be reassured that going through (additional) treatments will not lead to marital dissolution per se.

However, because we were not able to control for child wish in the register-based study, and assuming that a significant proportion of non-ART couples were also experiencing at least at some point in their relationship involuntary childless, we cannot draw conclusions on its relationship with marital dissolution. An important limitation to consider in interpreting our findings is the fact that couples trying to conceive for more than 12 months and not seeking treatment, and couples going through non-ART fertility care (e.g. ovulation induction or IUI) were included in the comparison group. Future studies should try to address these limitations and also other factors such as the interference of the waiting period to initiate treatment and of nonbiological parenthood, both through gamete donation and adoption. Additionally, there were other potential predictors of marital dissolution that were not considered, such as employment and income (Lyngstad and Jalovaara, 2010), gender perspectives (Hart et al., 2017), health status (Monden and Uunk, 2013), mental health, acute life events (Røsand et al., 2014), relationship satisfaction (Lawrence et al., 2008), and number (Vinberg et al., 2015) and age of children (Vuri, 2003).

Despite the many factors that are believed to influence the outcome of marital unions, this study has controlled for most well-known confounding variables. Its main strengths include a complete registered national cohort of all Danish women treated with ART over a long follow-up period and the cross-linkage with their male partners, allowing the examination of couple-level based data, an age-matched comparison group, and the inclusion of live-born children over the studied period of 16 years.

This paper showed that going through ART does not increase the risk of union dissolution over the course of 16 years after the first treatment. These findings are reassuring both for health professionals and mainly for patients considering enduring the challenges of ART. A patient-centered care approach and referral to psychosocial support when possible should be given to patients after failed treatment, who have a higher risk of ending their relationships. Further studies should analyze differences according to previous aspirations for parenthood, variations in childlessness status (i.e. voluntary versus involuntary), and trying to conceive status.

Authors' roles

M.V.M. roles included study conception and manuscript writing. All authors were involved in study design and obtaining data. D.V. and C.

^bModel 3 included female age, male age, couple's highest educational level, partnership status and common children as a time-dependent variable.

O.H. performed data analyses. All authors were involved in data interpretation and manuscript revision.

Funding

M.V.M.'s work was supported by Fundação para a Ciência e a Tecnologia (Portuguese Foundation for Science and Technology), grant ref. SFRH/BPD/85789/2012

Conflict of interest

None declared.

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