

Medically assisted reproduction and mental health in adolescence: evidence from the UK Millennium Cohort Study

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Background: The number and proportion of children conceived through medically assisted reproduction (MAR) is steadily increasing yet the evidence on their mental health in adolescence is inconclusive. Two main mechanisms with opposite effects can explain differences in mental health outcomes by conception mode: while more advantaged parental characteristics could positively influence it, higher parental stress could have a negative influence. **Methods:** Linear and logistic estimations on a longitudinal population-based birth cohort study of 9,897 individuals to investigate whether adolescents conceived through MAR are more likely than naturally conceived (NC) children to experience mental health problems at age 17, as reported by adolescents themselves and their parents. We test whether this association is confounded and/or mediated by parental background characteristics collected when the cohort member was around 9 months old (maternal age, maternal education level, ethnicity, income quintile), family structure variables measured in adolescence (number of siblings in the household at age 15, parental household structure at age 14) or maternal distress at age 14. **Results:** Children conceived naturally and through MAR self-reported similar mental health outcomes. The only differences between MAR and NC adolescents are in the parental reports, with parents who conceived through MAR reporting their children had 3.82 (95% CI: 1.140 to 11.54) and 2.35 (95% CI: 1.145 to 4.838) higher odds of falling within the high category of SDQ total difficulties and emotional symptoms scales, respectively. The results did not change on adjustment for mediators, such as maternal distress, number of siblings in the household and parental household structure. **Conclusions:** The results reveal a lack of or small differences in MAR adolescents' mental health outcomes compared to children who were conceived naturally. While the results based on the parental reports could suggest that MAR adolescents are at higher risk of suffering from mental health problems, the differences are small and not supported by adolescents' own reports. The difference between MAR and NC adolescent's parental report might reflect differences in parental concern, their relationship or closeness and can help to reconcile the mixed findings of previous studies. **Keywords:** Medically assisted reproduction; fertility treatments; mental health; risk behaviours; depression; adolescence.

Introduction

Given the increasingly important role of medically assisted reproduction (MAR), an abundance of research has documented similarities and differences between MAR and naturally conceived (NC) children in various dimensions of early life health (for a recent review, see Berntsen et al., 2019). While the literature has consistently reported MAR-conceived children have poorer perinatal outcomes such as low birthweight, preterm delivery, birth defects (Pinborg et al., 2013; Qin et al., 2017) and higher infant mortality (Rodriguez-Wallberg et al., 2020); the link between MAR conception and other aspects of child well-being is less well established. In particular, the evidence on mental health and behavioural outcomes among MAR-conceived children is mixed. While many studies have found no or negligible associations between MAR and mental health or behavioural problems in childhood and adolescence (Hart & Norman, 2013; Wagenaar et al., 2009; Wilson, Fisher, Hammarberg, Amor, &

Halliday, 2011; Zhu et al., 2011), the literature has also indicated increased risks of mental health disorders, depression and binge drinking (Bay, Mortensen, Hvidtjørn, & Kesmodel, 2013; Hart & Norman, 2013; Rissanen, Gissler, Lehti, & Tiitinen, 2019; Svahn et al., 2015; Wagenaar et al., 2009). Previous studies have also reported moderately increased risks of other specific psychiatric diagnoses such as autism spectrum disorder (Liu et al., 2017) and attention-deficit/hyperactivity disorder (Berntsen et al., 2019; Kallen et al., 2011; Rissanen et al., 2019).

Previous findings' inconsistency can be attributed to the use of small or non-representative samples and the variation across studies in the exclusion or not of multiple births, which increases comparability with NC children but excludes a notable proportion of MAR children (Berntsen et al., 2019; Rumbold et al., 2017). In addition, differences across studies in the use of parental or child self-report, the types of MAR techniques and outcomes analysed, time periods and methods used make it difficult to compare studies and reconcile their findings. Remes, Palma, Peltonen, Martikainen, and Goisis (2022)

Conflict of interest statement: No conflicts declared.

overcame sample size and representativeness limitations using Finnish administrative registers and found slightly higher risks of hospitalization for internalizing and developmental disorders among MAR compared to NC adolescents when adjusting for family sociodemographic characteristics. However, administrative registers provide limited information on family characteristics which might confound the association between MAR and mental health and prevent us from analysing mental health outside of severe and formal hospital diagnoses, which are subject to biases based on access and ascertainment.

Regarding theoretical explanations, the literature has posited that mental health outcomes could be linked to MAR conception through two main mechanisms with potentially opposite effects. On one side, parents conceiving through MAR tend to be older and socioeconomically more advantaged than parents who conceive naturally (Chambers et al., 2014; Chandra, Copen, & Stephen, 2014; Goisis, Håberg, Hanevik, Magnus, & Kravdal, 2020). Such selection is likely to play a significant role as higher parental education and earnings are related to lower risk of mental disorders and psychosocial problems (Lewis, Hope, & Pearce, 2014; Patalay & Fitzsimons, 2017; Reiss, 2013). On the other side, compared to natural conception, the often-long process of conceiving through MAR is associated with higher parental stress levels and higher expectations for both child and parents, which could negatively influence the parent–child relationship and children’s psychosocial development (Bernstein, 1990; Colpin & Soenen, 2002; Golombok, Cook, Bish, & Murray, 1995; Wagenaar et al., 2009; Wagenaar, Huisman, Cohen-Kettenis, & Waal, 2008). Although there is evidence that the stress experienced around the time of conception and birth might not last into the adolescent period (Goisis et al., 2022; Sarantaki, Anagnostopoulos, Loutradis, & Vaslamatzis, 2015), the evidence is still limited.

This study aims to widen our understanding of the mental health of MAR-conceived children as they approach adulthood, which is relevant because of their increasing numbers and the lack of information on their mental health. We investigate whether adolescents conceived through MAR experience more mental health problems than their NC peers, and how their family characteristics influence the association. Moreover, we investigate whether the association between MAR conception and mental health differs by whether it is reported by the adolescents themselves or by their parents.

This paper contributes to the existing literature on several grounds: First, it uses national population-based U.K. cohort data that allows us to overcome the issues of findings’ generalizability encountered in previous studies. Second, the richness of the data allows us to control for a wide range of characteristics such as parental background, family structure

and maternal distress that might explain the association between MAR conception and mental health. Third, we evaluate mental health using a broad range of outcomes which allows us to obtain a more comprehensive understanding of the association compared to previous studies relying on fewer or single outcomes (Rissanen et al., 2019; Svahn et al., 2015; Wagenaar et al., 2009; Zhu et al., 2011) or hospitalization records (Remes et al., 2022). Finally, we look at and compare children’s and parental reports which allows us to test whether the mixed findings of prior studies—which have tended to rely on either children’s or parental reports—can be explained by their different reporting patterns.

Methods

Study population

The UK Millennium Cohort Study (MCS) is a nationally representative longitudinal survey that follows 19,244 children born in the UK in 2000–2002. The sample is geographically clustered and stratified to over-represent areas of England with relatively high proportions of ethnic minorities and high levels of child poverty, as well as areas in the three smaller countries of Wales, Scotland and Northern Ireland. Baseline interviews were conducted when the children were approximately 9 months old (Sweep 1) and follow-up interviews were conducted at ages three (Sweep 2), five (Sweep 3), seven (Sweep 4), 11 (Sweep 5), 14 (Sweep 6) and 17 (Sweep 7). In each wave, interviewers visited the cohort members’ homes and conducted face-to-face interviews with both resident parents. Parents also answered some questions via self-completion. Sweep 4 is the first one in which cohort members completed their own questionnaire.

Identification of MAR treatments

MAR children refer to children conceived through assisted reproductive technology (ART), such as IVF and ICSI, or other kinds of fertility treatments such as ovulation induction (OI) and intrauterine insemination (IUI). At the baseline interview, respondents (the cohort member’s mother in 99% of cases) were asked whether they had used any fertility treatment to conceive. The analytical sample contains cohort members whose parents answered this question in Sweep 1 and for whom we have data on at least one mental health outcome measured at age 17, in Sweep 7. In the analytical sample ($N = 9,897$), in total, 298 children were conceived with the help of MAR. Of these, 120 (40.3%) were conceived through ART (either IVF, ICSI or Frozen embryo transfer), 15 through IUI (5%), 125 (41.9%) with the aid of ovarian stimulation drugs not followed by any further treatment and 38 (12.8%) with surgery involving the wombs, tubes or ovaries. In the analyses, the different kinds of MAR treatments are included in the same category because of the small numbers.

Outcomes

We rely on a range of measures collected at Sweep 7 (when the cohort members were around age 17) which provides us with a comprehensive view on the cohort members’ level of mental health and socioemotional well-being. All questions used to construct the outcomes were answered as part of self-completion questionnaires.

Outcomes reported by the cohort member (self-reported) and their parent (the mother for 99.8% of participants). Strengths and difficulties questionnaire (SDQ) scales (continuous and binary): The SDQ was developed by the English child psychiatrist Robert N. Goodman to assess mental health problems by asking respondents to select one of three response options (not true/somewhat true/certainly true) for statements such as 'I try to be nice to other people. I care about their feelings'. We use the total scale and its 5 subscales: emotional symptoms (self-reported $\alpha = .85$, parent-reported $\alpha = .98$), conduct problems (self-reported $\alpha = .83$, parent-reported $\alpha = .96$), hyperactivity/inattention (self-reported $\alpha = .81$, parent-reported $\alpha = .96$), peer problems (self-reported $\alpha = .82$, parent-reported $\alpha = .97$) and prosocial (self-reported $\alpha = .92$, parent-reported $\alpha = .99$) scales. We use SDQ as a continuous and as a categorical variable. For the continuous form, higher scores indicate higher levels of mental health problems. Binary variables take value 1 for high ranges of SDQ score and 0 for normal and borderline levels. The variable is created by the MCS data team and made available in the derived variables dataset.

Self-reported and parent-reported binary variables use different thresholds for defining the clinical categories, as reported in Table S1. More information about SDQ can be found at <https://www.sdqinfo.org>. The validity and reliability of SDQ scales in the Millennium Cohort Studies have been reported in great detail by Bridger Staats, Kelly, Lacey, and Hardy (2023) and Croft, Stride, Maughan, and Rowe (2015), among others.

Outcomes answered only by cohort members. Kessler Psychological Distress scale (continuous and binary): Six-item psychological distress self-report measure assesses the risk of serious mental illness by asking participants how often in the past 30 days they felt, for example, hopeless, with five response options ranging from none of the time to all the time (Patalay & Fitzsimons, 2021). Total scores range from 0 to 24, with higher scores indicating greater distress (Kessler et al., 2003). The scale has moderate and severe thresholds. The binary variable takes value 1 if the score is above the severe threshold (≥ 13), which is considered indicative of serious mental illness (Kessler et al., 2010; Prochaska, Sung, Max, Shi, & Ong, 2012), hereafter referred to as 'high psychological distress'. The variable is created by the MCS data team and made available in the derived variables dataset ($\alpha = .93$).

Attempted suicide (binary): We construct this binary variable based on the response to the question: 'Have you ever hurt yourself on purpose in an attempt to end your life?' and coded it with value 1 if the cohort member answered yes, and 0 otherwise.

Anti-social behaviour (continuous): We construct this index variable by counting the anti-social behaviour actions respondents reported they had done in the 12 months prior to the interview. The index ranges from 0 to 15, with stealing, doing graffiti or damaging public space as some of its items ($\alpha = .99$). All items of this scale are described in Appendix S1. This variable has been previously used in the literature by Gage and Patalay (2021) and Patalay and Gage (2019), among others.

Self-harm (binary): We construct this index variable by combining the answers (yes or no) to the question 'During the last year, have you hurt yourself on purpose in any of the

following ways? cut or stabbed, burned, bruised, or pinched, overdose, pulled out hair, and others'. The binary variable takes value 1 if the cohort member responded yes to any of the items (described in Appendix S1), and 0 otherwise. This variable has been previously used in the literature by Patalay and Fitzsimons (2021) and Patalay and Gage (2019), among others.

Substance abuse (binary): We construct this index variable by assigning it value 1 if the cohort member reported he/she ever had five or more alcoholic drinks at a time, smoked more than 6 cigarettes a week, or had ever used drugs and 0 otherwise. This variable has been previously used in the literature by Gage and Patalay (2021) and Patalay and Gage (2019), among others.

Covariates

We adjust for basic characteristics of the cohort member: the child's sex, whether s/he was the first-born and whether the child was delivered in a multiple birth. We also include parental background characteristics collected in sweep 1: mother's age at birth (continuous), parents' marital status at birth (categorical: married, cohabiting, single), mother's educational level (categorical: NVQ 1/2 = up to GCSE: primary/secondary education or relevant vocational qualifications, NVQ 3 = A/AS/S Levels/SCE Higher, Leaving Certificate or equivalent, or relevant vocational qualifications, NVQ 4/5 = higher degree or relevant vocational qualifications), ethnicity (6 categories: White, Mixed, Indian, Pakistani and Bangladeshi, Black or Black British, Other) and household's income quintile using the modified OECD scale (categorical).

We also control for family structure characteristics: number of siblings in sweep 5 (continuous) to capture siblings who may have left the parental home before age 17, and parental household structure in Sweep 6 (Categorical: one biological parent, two biological parents, one biological and other parent). Finally, we adjust for maternal distress using maternal Kessler measured in Sweep 6 (Continuous: Kessler scales for parents ranging from 0 to 24).

Inclusion/Exclusion criteria

Analytical samples include cohort members who live with at least one biological parent in sweeps 1 ($N = 18,774$) and 7 ($N = 10,345$), for whom information on their mental health at Sweep 7 (age 17) and mode of conception measured at sweep 1 (collected when the cohort members are around 9 months old) is available ($N = 9,896$) (See Table S2). Children conceived via donor insemination ($n = 2$) were excluded as prior studies have shown that the (lack of) disclosure about parental identity might be associated with worse mental health, but their small numbers precluded a separate investigation (Golombok et al., 2002; Owen & Golombok, 2009). Because of missing values on covariates (14–29% depending on the outcome), we performed multiple imputations on the covariates for each mental health outcome (Table S3). Analytical samples (Table S4) ranged from 9,031 to 9,736 observations depending on the outcome, which represents 87.3–94.1% of Sweep 7 sample ($n = 10,345$).

In the analytical sample ($N = 9,897$) 48.8% of cohort members are male, 82% are white, 42.3% were firstborns and 2.2% were born in a multiple birth. The average age at which cohort members' mothers gave birth to them is 29.5 years, and most of the cohort member's parents were married when having their children (65.1%). The average number of siblings in the household in Sweep 5 was 1.5. Finally, 39% of cohort member's mothers had completed NVQ educational level 4/5.

Statistical analysis

We estimate linear regression models for continuous outcomes and logistic regression models for binary outcome variables using attrition weights. Model 0 reports the association between MAR and the outcomes adjusting for cohort member's characteristics (sex, birth order, multiple birth and their age at sweep 7). Model 1 controls for family background characteristics that could be associated both with undergoing MAR and mental health, that is, confounders of the association (maternal education, parental marital status, income quintile, ethnicity and maternal age all measured at Sweep 1). Model 2 adjusts for variables that could act as mechanisms for the effect of MAR on the outcomes, that is, mediators. We include maternal distress at Sweep 6 (age 14 interview), parental household structure at Sweep 6 and the number of siblings in the household in Sweep 5 (age 11 interview) as mediators. However, the categorization of number of siblings in the household as confounders or mediators is not as clear-cut as for parental household structure and maternal distress at Sweep 6. For this reason, in Model 1, we adjust for variables which represent clear confounders, and in Model 2, we further adjust for variables that could mediate or confound the association.

Results

Tables 1 and 2 present descriptive statistics for the continuous and binary outcome variables, respectively. The descriptive differences observed in some continuous outcomes suggest that while MAR adolescents report higher levels of emotional problems at age 17 than their NC counterparts, the opposite is true for peer problems. Among the binary outcomes, the incidence of mental health problems is similar between NC and MAR adolescents for all the self-reported outcomes. In contrast, we observe the parents of adolescents conceived through MAR to report for their children a higher prevalence of high levels of emotional symptoms and total difficulties in SDQ scales than parents who conceived naturally.

Table S5 shows that MAR parents tend to be more educated, with higher levels of income and more likely to be married at the time of birth. In addition, MAR children are born to older mothers and are more likely to be first-born and to be born in a multiple birth than NC children. Also, MAR children have fewer siblings in the household when aged 12 and are more likely to live with two parents/carers at age 17 than NC children. Finally, parents of MAR-conceived adolescents have lower Kessler scores than parents who conceived naturally, which indicates they suffer from lower levels of psychological distress.

Table 3 Summarizes MAR coefficients and/or odd ratios for the estimations on the 17 outcome variables measured at age 17 across three model specifications, for the binary and/or continuous version of the outcomes. Full results for each outcome are presented in Tables S6–S35.

Model 0 (which adjusts for cohort members' characteristics) shows no association between MAR conception and all continuous outcomes (left panel in Table 3). The adjustment for family sociodemographic characteristics (Model 1) shows no statistically significant difference between MAR and NC adolescents in the self-reported outcomes. Nonetheless, the adjustment reveals significant differences between MAR and NC adolescents in parent-reported outcomes, with MAR adolescents having between 0.36 (95% CI: –0.0345 to 0.690) and 1.73 (95% CI: 0.0489 to 3.406) higher scores than their NC peers in parent-reported SDQ scores for total difficulties and the subscales of emotional symptoms and peer problems. Model 2 results (fully adjusted) are consistent with the results of Model 1, except for SDQ total difficulties where the association is attenuated and no longer statistically significant.

Table 1 Continuous outcomes descriptive statistics, by mode of conception

	Natural conception			MAR			Diff NC-MAR		
	Mean	95% CI	N	Mean	95% CI	N	Diff	95% CI	p-Value
Self-reported									
Anti-social behaviour	0.5	(–0.01 to 0.01)	9,438	0.47	(–0.06 to 0.06)	295	0.03	(–0.03 to 0.09)	.615
Psychological distress, Kessler K6 scale	7.2	(–0.02 to 0.08)	9,441	7.33	(–0.25 to 0.31)	295	–0.13	(–0.43 to 0.17)	.661
SDQ Emotional Symptoms	3.48	(0.11 to 0.17)	9,209	3.84	(0 to 0.28)	288	–0.36	(–0.51 to –0.21)	.014
SDQ Conduct Problems	1.75	(–0.38 to –0.34)	9,209	1.68	(–0.45 to –0.27)	288	0.07	(–0.02 to 0.16)	.451
SDQ Hyperactivity/Inattention	3.95	(0.05 to 0.09)	9,208	3.84	(–0.06 to 0.2)	288	0.11	(–0.03 to 0.25)	.417
SDQ Peer Problems	2.22	(0.09 to 0.13)	9,208	1.89	(0.01 to 0.21)	288	0.33	(0.23 to 0.43)	.001
SDQ Prosocial	7.84	(0.31 to 0.35)	9,213	7.97	(0.24 to 0.42)	288	–0.13	(–0.23 to –0.03)	.211
SDQ Total Difficulties	11.39	(–0.19 to –0.07)	9,207	11.25	(–0.46 to 0.2)	288	0.14	(–0.19 to 0.47)	.673
Parent-reported									
SDQ Emotional Symptoms	2.1	(–0.42 to –0.38)	8,769	2.63	(–0.56 to –0.24)	279	–0.53	(–0.67 to –0.39)	.000
SDQ Conduct Problems	1.18	(–0.55 to –0.51)	8,772	1.08	(–0.61 to –0.45)	279	0.1	(0.01 to 0.19)	.278
SDQ Hyperactivity/Inattention	2.64	(0.07 to 0.13)	8,766	2.49	(–0.03 to 0.23)	279	0.15	(0.01 to 0.29)	.293
SDQ Peer Problems	1.84	(0.13 to 0.17)	8,766	1.96	(0.04 to 0.26)	279	–0.12	(–0.23 to –0.01)	.286
SDQ Prosocial	8.33	(–0.14 to –0.1)	8,775	8.49	(–0.22 to –0.02)	279	–0.16	(–0.27 to –0.05)	.161
SDQ Total Difficulties	7.76	(–0.2 to –0.06)	8,752	8.16	(–0.5 to 0.24)	279	–0.4	(–0.77 to –0.03)	.284

Mean and SD weighted; N unweighted.

Table 2 Binary outcomes descriptive statistics, by mode of conception

	Natural conception			MAR			Diff NC-MAR		<i>p</i> -Value
	Mean	95% CI	<i>N</i>	Mean	95% CI	<i>N</i>	Diff	95% CI	
Self-reported									
High psychological distress, Kessler K6 scale	0.16	(0.02 to 0.02)	9,441	0.17	(0 to 0.04)	295	-0.01	(-0.03 to 0.01)	.642
Self-harm	0.24	(-0.16 to -0.16)	9,196	0.23	(-0.18 to -0.14)	288	0.01	(-0.02 to 0.04)	.697
Attempted suicide	0.07	(0.01 to 0.01)	9,191	0.07	(-0.01 to 0.03)	288	0	(-0.02 to 0.02)	1.000
Substance abuse	0.59	(-0.01 to 0.01)	9,442	0.57	(-0.03 to 0.03)	294	0.02	(-0.01 to 0.05)	.495
High SDQ Emotional Symptoms	0.14	(-0.01 to -0.01)	9,209	0.14	(-0.03 to 0.01)	288	0	(-0.02 to 0.02)	1.000
High SDQ Conduct Problems	0.06	(0.00 to 0.00)	9,209	0.04	(-0.01 to 0.01)	288	0.02	(0.01 to 0.03)	.145
High SDQ Hyperactivity/Inattention	0.14	(0.02 to 0.02)	9,208	0.11	(0 to 0.04)	288	0.03	(0.01 to 0.05)	.151
High SDQ Peer Problems	0.05	(0.03 to 0.03)	9,208	0.03	(0.02 to 0.04)	288	0.02	(0.01 to 0.03)	.110
High SDQ Prosocial	0.04	(0.02 to 0.02)	9,213	0.04	(0.01 to 0.03)	288	0	(-0.01 to 0.01)	1.000
High SDQ Total Difficulties	0.08	(0 to 0)	9,207	0.08	(-0.02 to 0.02)	288	0	(-0.02 to 0.02)	1.000
Parent-reported									
High SDQ Emotional Symptoms	0.16	(0.00 to 0.00)	8,769	0.24	(-0.03 to 0.03)	279	-0.08	(-0.1 to -0.06)	.000
High SDQ Conduct Problems	0.08	(-0.08 to -0.08)	8,772	0.05	(-0.09 to -0.07)	279	0.03	(0.01 to 0.05)	.067
High SDQ Hyperactivity/Inattention	0.07	(0.03 to 0.03)	8,766	0.05	(0.02 to 0.04)	279	0.02	(0 to 0.04)	.187
High SDQ Peer Problems	0.18	(0.02 to 0.02)	8,766	0.15	(0 to 0.04)	279	0.03	(0.01 to 0.05)	.194
High SDQ Prosocial	0.04	(0.03 to 0.03)	8,775	0.04	(0.02 to 0.04)	279	0	(-0.01 to 0.01)	1.000
High SDQ Total Difficulties	0.09	(0.00 to 0.00)	8,752	0.15	(-0.02 to 0.02)	279	-0.06	(-0.08 to -0.04)	.001

Mean and SD weighted; *N* unweighted.

Logistic estimations (right panel in Table 3) show a similar pattern: differences between MAR and NC adolescents are only significant when looking at parent-reported outcomes, and the association between MAR conception and mental health outcomes becomes larger in magnitude and statistically significant when adjusting for family sociodemographic characteristics and remains stable to further adjustment for parental mental health, number of siblings in the household and parental household structure. The fully adjusted model indicates that, conditional on family characteristics, MAR conception is associated with an average increase of 3.82 (95% CI: 1.140 to 11.54) and 2.35 (95% CI: 1.145 to 4.838) in the odds of parents reporting abnormal levels of SDQ total difficulties and emotional symptoms scales, respectively.

Sensitivity analysis

To correct for the potential occurrence of false positives in our estimations, we performed Simes and FDR multiple testing corrections using (Table S36). *p*-Value corrections did not affect the statistical significance of the associations for those outcomes in which the association between MAR conception and the outcome was robust to the adjustment for covariates.

Since the main models were run on different subsamples, we re-estimated the association between MAR conception and SDQ outcomes for families in

which both the cohort member and their parent answered the SDQ scales (see Table S37) to test whether the SDQ reported by parents and cohort members differed. The results were highly similar to the main study results.

Furthermore, to account for compositional differences in the MAR and NC subsamples as the former are considerably more likely to be part of a multiple birth and less likely to have other siblings, we estimated the models for cohort members who were only children (Table S38). The results are in line with the main results presented in the paper. On adjustment for family characteristics, parents of MAR children report their only child suffers from higher mental health problems than parents of NC only children in SDQ scores for total difficulties and the subscales of emotional symptoms, peer problems and the magnitude of effect is bigger than when estimating for the whole sample. The estimation on this subsample also reveals that MAR adolescents are less likely to report they have harmed themselves during the 12 months prior to the interview than their NC counterparts.

Finally, to test whether the adjustment for parental psychological distress measured at different sweeps affects the estimates, we repeated the analysis adjusting for maternal distress measured in sweeps 2, 3 and 4; as well as the average of maternal distress scores from Sweeps 2, 3, 4 and 6 (Table S39). Results are robust to the adjustment for distress measured at different points in time.

Table 3 Summary table, MAR coefficient resulting from OLS/Logit estimations (mental health outcomes measured at age 17)

	Continuous outcomes, Beta with 95% CI			Binary outcomes, odds ratios with 95% CI			N
	M0: CM's characteristics	M1: M0 + parental background characteristics	M2: M1 + family structure characteristics + Maternal distress	M0: CM's characteristics	M1: M0 + parental background characteristics	M2: M1 + family structure characteristics + Maternal distress	
Self-reported outcomes							
Anti-social behaviour	0.0119 (–0.162 to 0.186)	0.0225 (–0.162 to 0.207)	0.0213 (–0.163 to 0.205)	1.024 (0.613 to 1.712)	0.977 (0.565 to 1.691)	0.954 (0.538 to 1.692)	9,534
Psychological distress (K6)	0.0435 (–0.751 to 0.838)	–0.137 (–0.995 to 0.722)	–0.199 (–1.061 to 0.663)	0.982 (0.702 to 1.375)	0.986 (0.714 to 1.362)	0.969 (0.698 to 1.347)	9,533
Self-harm				1.102 (0.562 to 2.163)	1.489 (0.737 to 3.008)	1.473 (0.701 to 3.093)	9,484
Suicide attempts				0.947 (0.696 to 1.287)	0.858 (0.623 to 1.181)	0.854 (0.619 to 1.179)	9,479
Substance Abuse				0.872 (0.509 to 1.493)	0.789 (0.441 to 1.413)	0.755 (0.417 to 1.368)	9,537
SDQ Emotional symptoms	0.284 (–0.125 to 0.694)	0.220 (–0.165 to 0.606)	0.186 (–0.189 to 0.560)	0.821 (0.428 to 1.576)	1.198 (0.610 to 2.353)	1.216 (0.615 to 2.404)	9,497
SDQ Conduct problems	0.0346 (–0.332 to 0.401)	0.205 (–0.119 to 0.528)	0.201 (–0.115 to 0.516)	0.791 (0.484 to 1.291)	0.818 (0.495 to 1.352)	0.804 (0.482 to 1.342)	9,496
SDQ Hyperactivity/Inattention	0.00446 (–0.375 to 0.384)	0.0891 (–0.262 to 0.440)	0.0705 (–0.273 to 0.414)	0.661 (0.291 to 1.501)	0.817 (0.373 to 1.788)	0.785 (0.352 to 1.753)	9,496
SDQ Peer Problems	–0.295 (–0.603 to 0.0134)	–0.132 (–0.499 to 0.235)	–0.142 (–0.513 to 0.228)	0.887 (0.445 to 1.771)	1.031 (0.512 to 2.079)	1.030 (0.504 to 2.105)	9,501
SDQ Prosocial	0.0768 (–0.130 to 0.284)	0.0766 (–0.137 to 0.290)	0.0756 (–0.140 to 0.291)	1.027 (0.602 to 1.753)	1.252 (0.672 to 2.334)	1.222 (0.629 to 2.374)	9,495
SDQ Total	0.0277 (–0.960 to 1.015)	0.382 (–0.496 to 1.259)	0.310 (–0.548 to 1.167)	1.775 (0.782 to 4.031)	2.349* (1.174 to 4.699)	2.353* (1.145 to 4.838)	9,048
Parent-reported outcomes				0.755 (0.430 to 1.328)	1.260 (0.686 to 2.313)	1.292 (0.683 to 2.443)	9,051
SDQ Emotional symptoms	0.557 (–0.291 to 1.406)	0.824* (0.0693 to 1.578)	0.777* (0.0426 to 1.512)	0.889 (0.447 to 1.768)	1.310 (0.617 to 2.778)	1.325 (0.614 to 2.862)	9,045
SDQ Conduct problems	–0.0112 (–0.279 to 0.257)	0.218 (–0.0201 to 0.457)	0.212 (–0.0376 to 0.461)	0.815 (0.516 to 1.288)	1.034 (0.625 to 1.710)	1.033 (0.627 to 1.702)	9,045
SDQ	–0.0209 (–0.706 to 0.664)	0.323 (–0.227 to 0.873)	0.302 (–0.256 to 0.860)	1.226 (0.618 to 2.429)	1.391 (0.673 to 2.875)	1.428 (0.687 to 2.967)	9,054
Hyperactivity/Inattention	0.148 (–0.212 to 0.509)	0.362* (0.0347 to 0.690)	0.344* (0.0108 to 0.678)	2.198 (0.601 to 8.038)	3.603* (1.124 to 11.54)	3.821* (1.140 to 12.80)	9,031
SDQ Peer Problems	0.133 (–0.0721 to 0.338)	–0.0183 (–0.245 to 0.209)	–0.0156 (–0.248 to 0.216)				
SDQ Prosocial							
SDQ Total	0.675 (–1.339 to 2.688)	1.727* (0.0489 to 3.406)	1.624 (–0.0352 to 3.282)				

This table reports OLS coefficients and LOGIT odds ratios, with 95% confidence intervals. Multiple imputations performed using each outcome and exposure (MAR coefficient). Model 0 adjusts for cohort member's characteristics (sex, birth order, multiple birth and their age at sweep 7). Model 1 controls for parental characteristics (mother's education, parental marital status, income quintile at Sweep 1, ethnicity, maternal age). Finally, Model 2 adjusts for the number of siblings living in the cohort member's household in Sweep 5, parental household structure at Sweep 6 and maternal distress measured in Sweep 6. CM, cohort member.

***p* < .01; **p* < .05.

Discussion

We investigated the association between MAR and a range of mental health indicators measured at age 17 using a U.K. nationally representative dataset. By taking advantage of the population-based nature and richness of the data, we were able to overcome the issues of findings' generalizability and measurement of mental health outcomes encountered in previous studies and to control for a wide range of parental and family characteristics which might confound or mediate the association between MAR conception and mental health. We focused on late adolescence, a critical life period during which experiences of health and social disadvantage may disrupt successful transitions to adulthood and carry long-term consequences for later health (Dorsett & Lucchino, 2014; Viner et al., 2015).

The unadjusted results show lack of differences in the association between MAR conception and mental health outcomes for all outcomes. On adjustment for family sociodemographic characteristics, the results show MAR adolescents score slightly higher, that is, more problems, on the parent-reported SDQ total score and the subscales of emotional symptoms and peer problems. In line with previous studies (Barbuscia, Goisis, & Mirskyla, 2019; Remes et al., 2022), the results suggest that the selected and advantaged profiles of MAR families may protect against the risk of poorer mental health problems. The results did not change on adjustment for potential mediators, such as parental mental health, number of siblings in the household and parental household structure.

The magnitude of the statistically significant adjusted associations between MAR and the parent-reported SDQ outcomes is small and smaller compared to that of other covariates included in the models such as sex, multiple birth, birth parity and age, which is consistent with the findings of previous studies (Bay et al., 2013; Hart & Norman, 2013; Svahn et al., 2015). Whereas we cannot rule out the possibility that MAR adolescents are slightly more likely than their NC peers to experience mental health problems, the discrepancy between the parent- and self-reports could be related to MAR parents being overprotective, or having exaggerated expectations (Hahn & DiPietro, 2001; Ilioi & Golombok, 2015; McMahon, Gibson, Garth, Cohen, & Tennant, 2003; Wagenaar et al., 2009). Taken together, considering the magnitude of the differences in the parental reports and the lack of differences in the cohort members' reports, the evidence is not indicative of meaningful or clinically relevant differences in MAR adolescents' mental health outcomes compared to NC children.

The contrasting results we observe between the parental and adolescent self-report can help to reconcile previous studies' mixed findings. Our

results are consistent both with prior studies finding no or negligible associations between MAR and mental health problems in adolescence when analysing the children's self-report (Hahn & DiPietro, 2001; Wilson et al., 2011) and those indicating increased risks when analysing parents' report (Rodriguez-Wallberg et al., 2020). The discrepancy between the parental and child report has already been reported in previous studies (Achenbach, McConaughy, & Howell, 1987; De Los Reyes et al., 2015; Wagenaar et al., 2009, 2011; Zhu et al., 2011). Wagenaar et al. (2009) showed that parental reports suggest IVF children were more likely than NC children to score in the borderline/clinical range on the syndrome scale withdrawn/depressed behaviour. In a follow-up study, Wagenaar et al. (2011) reported no differences in self-reported mental health between MAR and NC children. The study by Zhu et al. (2011) compared self- and mother-reported SDQ scores of MAR adolescents aged between 15 and 21 years. While the maternal report suggested MAR adolescents had higher odds than NC children of having high scores in all but one SDQ scale (prosocial behaviour), the adolescent's self-reports suggested MAR adolescents had lower mental health problems in all SDQ scales except the emotional symptoms one. Our results reinforce previous studies' findings and highlight the importance of using reports not only from parents but also from the adolescents themselves when investigating the association between MAR and adolescent's mental health outcomes.

The findings of this study should be interpreted in light of its limitations. First, although we controlled for a wide range of potential confounding variables, our estimates do not reflect causal effects. Second, we are not able to identify the mechanisms underlying the observed associations in the parental reports, although we are able to exclude the possibility that they are explained by MAR parents having worse mental health. Third, due to the low number of observations, we could not investigate if the association differed by type of fertility treatment. Fourth, while our study overcomes the issue of generalizability encountered in previous studies, it is unclear if our findings are generalizable to countries where beliefs or stigma around MAR are different to those in the UK.

Despite these limitations, this paper makes a significant contribution to the literature on the mental health of adolescents and type of conception. Its main strength lies in the use of a nationally representative dataset, which allowed us to overcome the issues of the generalizability of the findings encountered in previous studies. Moreover, careful adjustments allowed us to isolate the association between MAR conception and mental health outcomes from family characteristics that could confound or mediate it. Finally, by considering the views of parents and

children, we were able to present a comprehensive assessment of MAR adolescents' mental health.

This paper also has relevant implications for future research and clinical practice. For the former, our results suggest future research should evaluate a broader set of outcomes and consider the views of different family members. For the latter, the finding of small long-term differences between MAR and NC adolescents should be part of the conversation between the doctor and the couple when discussing the risks of fertility treatments. Also, they should be considered by therapists when dealing with parents who conceived and adolescent patients conceived via MAR. Still, the results suggest that the mode of conception should, on average, not play a major role in explaining mental health problems among adolescents.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Description of items included in Self-harm and anti-social behaviour variables.

Table S1. Thresholds for SDQ and Kessler scores.

Table S2. Descriptive statistics and sample selection.

Table S3. Multiple imputation descriptive statistics.

Table S4. Sample size, by outcome and conception type.

Table S5. Covariates descriptive statistics by type of conception.

Table S6. Full OLS estimation, antisocial behaviour (continuous).

Table S7. Full OLS estimation, Kessler (continuous).

Table S8. Full Logit estimation, Kessler (binary).

Table S9. Full Logit estimation, self-harm (binary).

Table S10. Full Logit estimation, suicide attempts (binary).

Table S11. Full Logit estimation, substance abuse (binary).

Table S12. Full OLS estimation, self-reported SDQ Emotion (continuous).

Table S13. Full OLS estimation, self-reported SDQ Conduct (continuous).

Table S14. Full OLS estimation, self-reported SDQ Hyperactivity disorders (continuous).

Table S15. Full OLS estimation, self-reported SDQ Peer Problems (continuous).

Table S16. Full OLS estimation, self-reported SDQ Prosocial (continuous).

Table S17. Full OLS estimation, self-reported Total SDQ (continuous).

Table S18. Full Logit estimation, self-reported SDQ Emotion (binary).

Table S19. Full Logit estimation, self-reported SDQ Conduct problems (binary).

Table S20. Full Logit estimation, self-reported SDQ Hyperactivity (binary).

Table S21. Full Logit estimation, self-reported SDQ Peer (binary).

Table S22. Full Logit estimation, self-reported SDQ Prosocial (binary).

Table S23. Full Logit estimation, self-reported Total SDQ (binary).

Table S24. Full OLS estimation, parent-reported SDQ Emotion (continuous).

Table S25. Full OLS estimation, parent-reported SDQ Conduct (continuous).

Table S26. Full OLS estimation, parent-reported SDQ Hyperactivity (continuous).

Table S27. Full OLS estimation, parent-reported SDQ Peer Problems (continuous).

Table S28. Full OLS estimation, parent-reported SDQ Prosocial (continuous).

Table S29. Full OLS estimation, parent-reported Total SDQ (continuous).

Table S30. Full Logit estimation, parent-reported SDQ Emotion (binary).

Table S31. Full Logit estimation, parent-reported SDQ Conduct (binary).

Table S32. Full Logit estimation, parent-reported SDQ Hyperactivity (binary).

Table S33. Full Logit estimation, parent-reported SDQ Peer (binary).

Table S34. Full Logit estimation, parent-reported SDQ Prosocial (binary).

Table S35. Full Logit estimation, parent-reported Total SDQ (binary).

Table S36. Multiple tests correction.

Table S37. Summary table SDQ outcomes, MAR coefficient resulting from OLS/Logit estimations on the sample with answers of the CM and their parent.

Table S38. Estimations for only children, covariates imputed.

Table S39. Estimations of Model 2 with Kessler from different sweeps.

Acknowledgements

The authors thank the MCS families for their time and cooperation. The authors are grateful to the Centre for Longitudinal Studies (CLS), UCL Institute of Education, for the use of these data and to the UK Data Service for making them available. However, neither CLS nor the UK Data Service bear any responsibility for the analysis or interpretation of these data. M.P. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. M.P. and A.G. conceived the idea. All authors were involved in the design of the study and in interpreting the results. M.P. conducted the analyses. M.P. wrote the first draft with a substantial contribution from A.G. All authors contributed to revising the manuscript and approved the final version of the study. The authors have declared that they have no competing or potential conflicts of interest. A.G. and M.P. were supported by European Research Council (#803958). All authors were supported by the Economic and Social Research Council grant (ES/M001660/1). The funders had no role in the study design, data collection, analysis, interpretation, or writing of the report. The University of London Centre for Longitudinal Studies owns the copyright for

the Millennium Cohort Study (MCS) data used in this study. The MCS data are held/curated by the UK Data Service. Anyone wishing to use the MCS data (found at: <https://discover.ukdataservice.ac.uk/series/?sn=2000031>) must register and submit a data request to the UK Data Service at <http://ukdataservice.ac.uk/>. Additional terms and conditions of access are outlined

here: <https://www.ukdataservice.ac.uk/get-data/how-to-access/conditions>.

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Key points

- The number and proportion of children conceived through medically assisted reproduction (MAR) is steadily increasing yet the evidence on their mental health in adolescence is inconclusive.
- Using the UK Millennium Cohort Study (MCS), a nationally representative longitudinal survey, a broad range of outcomes reported by both the adolescents and their parents, we overcome some of the previous studies' limitations.
- While the results based on the parental reports could suggest that MAR adolescents are at higher risk of suffering from mental health problems, the differences are small and not supported by adolescents' own reports.
- The discrepancy in parental and child's report can help to reconcile previous studies' mixed findings.

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Accepted for publication: 18 July 2023