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Fertility treatment, twin births, and unplanned pregnancies in women with eating disorders: findings from a population-based birth cohort

N Micali,[a] I dos-Santos-Silva,[b] B De Stavola,[c] J Steenweg-de Graaf,[d,e] V Jaddoe,[d,e,f] A Hofman,[e] FC Verhulst,[g] EAP Steegers,[h] H Tiemeier[e,g,i]

[a] Behavioural and Brain Sciences Unit, UCL Institute of Child Health, London, UK [b] Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK [c] Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK [d] The Generation R Study Group, Erasmus Medical Centre, Rotterdam, the Netherlands [e] Department of Epidemiology, Erasmus Medical Centre, Rotterdam, the Netherlands [f] Department of Paediatrics, Erasmus Medical Centre – Sophia Children's Hospital, Rotterdam, the Netherlands [g] Department of Child and Adolescent Psychiatry and Psychology, Erasmus Medical Centre – Sophia Children's Hospital, Rotterdam, the Netherlands [h] Department of Obstetrics and Gynaecology, Erasmus Medical Centre, Rotterdam, the Netherlands [i] Department of Psychiatry, Erasmus Medical Centre, Rotterdam, the Netherlands
Correspondence: Dr N Micali, Brain and Behavioural Sciences Unit, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK. Email N.micali@ucl.ac.uk

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Objective To investigate fertility treatment, twin births, and unplanned pregnancies in pregnant women with eating disorders in a population-based sample.

Design A longitudinal population-based birth cohort (Generation R).

Setting Rotterdam, the Netherlands.

Sample Women from the Generation R study who reported a history of (recent or past) anorexia nervosa (n = 160), bulimia nervosa (n = 265), or both (n = 130), and a history of psychiatric disorders other than eating disorders (n = 1396) were compared with women without psychiatric disorders (n = 4367).

Methods Women were compared on the studied outcomes using logistic regression. We performed crude and adjusted analyses (adjusting for relevant confounding factors).

Main outcome measures Fertility treatment, twin births, unplanned pregnancies, and women's feelings towards unplanned pregnancies.

Results Relative to women without psychiatric disorders, women with bulimia nervosa had increased odds (odds ratio, OR, 2.3; 95% confidence interval, 95% CI, 1.1–5.2) of having undergone fertility treatment. Women with all eating disorders had increased odds of twin births (anorexia nervosa, OR 2.7, 95% CI 1.0–7.7; bulimia nervosa, OR 2.7, 95% CI 1.1–6.6; anorexia and bulimia nervosa, OR 3.795% CI 1.3–10.7). Anorexia nervosa was associated with increased odds of unplanned pregnancies (OR 1.8, 95% CI 1.2–2.6) and mixed feelings about these pregnancies (adjusted OR 5.0, 95% CI 1.7–14.4). Pre-pregnancy body mass index did not explain the observed associations.

Conclusions Eating disorders are associated with increased odds of receiving fertility treatment and twin births. Women with anorexia nervosa were more likely to have an unplanned pregnancy and have mixed feelings about the unplanned pregnancy. Fertility treatment specialists should be aware that both active and past eating disorders (both anorexia nervosa and bulimia nervosa) might underlie fertility problems.

Keywords Eating disorders, fertility, pregnancy.

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Introduction

Eating disorders mainly affect young women of reproductive age, and have important effects on reproductive and menstrual function.[1] We recently found an 8% prevalence of eating disorders in pregnant women.[2] Anorexia nervosa (AN) is characterised by low body weight, a disturbance in body image, an intense fear of gaining weight, and amenorrhoea for three or more consecutive months. Bulimia nervosa (BN) is characterised by a combination of discrete periods of binge eating and compensatory behaviours, such as vomiting, and a high

importance placed on weight and shape, in subjects who are not underweight.

Menstrual irregularities have not only been shown in women with AN, but also in those with BN.[3–5] Amenorrhoea, a feature and diagnostic criterion for active AN, accounts for reduced fertility in women with severe active AN, and has been shown to persist after recovery in some cases of AN. Moreover, amenorrhoea or oligomenorrohea is also present in 60% of women with BN, despite these women being of normal weight.[6,7] Only two studies have investigated eating disorders in women attending fertility clinics, finding a high prevalence of eating disorders (16–20%).[8,9] Fertility problems and difficulties in conceiving have also been shown in women with eating disorders in community and clinical samples.[6,10,11]

Given the menstrual abnormalities present in eating disorders, some authors have suggested that women with eating disorders might underestimate their ability to conceive. In fact two recent studies using large community-based cohorts of pregnant women have shown that women with AN had increased odds of having an unintentional pregnancy.[10,12] A higher prevalence of unplanned pregnancies has also been found amongst women with BN,[13] perhaps secondary to the risk-taking behaviours that are common in BN.

We previously showed that a history of eating disorders was associated with unplanned pregnancies, and negative feelings about these pregnancies, in a large community-based sample of pregnant women.[8] Fertility treatment and multiple births have not been previously investigated in women with eating disorders from community samples.

With the present study we aimed to investigate fertility treatment, twin births, unplanned pregnancies, and feelings towards unplanned pregnancies, in women with recent and past eating disorders who were able to get pregnant. In particular, we aimed to investigate the effect of pre-pregnancy body mass index (BMI) on any associations.

Methods

Study design

Generation R is a prospective general population cohort study based in Rotterdam, the Netherlands, at the Erasmus Medical Centre. Generation R was designed to identify early life risk factors for health and determinants of pre- and post-natal growth in a multi-ethnic sample.[14]

Study population

All pregnant women living in the Rotterdam area were eligible for enrolment if they had a delivery date between April 2002 and January 2006. The study aimed to enrol women at early stages of pregnancy (i.e. before 18 weeks of gestation), but enrolment was possible until birth. The estimated participation rate is ~61% of all eligible live-born children and parents living in the area at the time of recruitment. The characteristics of the sample and details of recruitment are given elsewhere.[14]

In total, 8880 women were recruited during pregnancy. Eligible for the present study were women who completed the questionnaire used to determine exposure for this study (n = 7145, 80.5%). Women with missing items on exposure (n = 817, 11.4%) were excluded, leaving 6328 for analyses.

Outcomes

Fertility and twin births

Information on whether the woman had received fertility treatment to conceive the current pregnancy, and, if so, which type, was obtained from midwives/obstetricians and medical records (from clinical letters and patient registration data). Data on twin births were obtained from obstetric/midwifery records.

Unplanned pregnancies

Upon enrollment women were asked by questionnaire whether the current pregnancy was intentional and, if not, how they felt about the unplanned pregnancy: pleased; mixed feelings initially; still with mixed feelings; or unhappy.

Exposure

Exposure was determined using data from a pregnancy questionnaire completed by the women at ~20 weeks of gestation that asked about history of several psychiatric disorders; a vignette was given in order to clarify what was meant by each specific disorder. All women were asked about having suffered from either AN or BN in the past, and in the previous year: 141 (2.2%) women reported having suffered from AN in the past, and 29 (0.5%) women reported having suffered from AN in the previous year; 191 (3.0%) women reported having suffered from BN in the past, and 74 (1.2%) women reported having suffered from BN in the previous year; and 119 (1.9%) women reported having suffered from both AN and BN in the past, and 11 (0.2%) women reported having suffered from AN and BN in the previous year. Exposure groups were defined as: lifetime (recent or past) AN (n = 170); lifetime BN (n = 265); and lifetime AN and BN (AN + BN, n = 130). Given the relatively small number of women who reported an eating disorder in the previous year, these groups were used for additional descriptive analyses only. The combined/co-morbid AN + BN group was kept as a separate category because of previous evidence of a higher degree of eating disorder severity.[15]

Women who reported having (ever) suffered from depression, anxiety, psychosis, and/or manic episodes constituted the group of other psychiatric disorders (n = 1396,

22.1%) to allow for an assessment of whether any observed associations were specific to eating disorders.

The remaining women in the cohort formed the comparison group: 4367 (69.0%) women.

We validated the self-reported eating disorder diagnosis against interview-based diagnosis using a Dutch subsample (n = 928) from the overall Generation R sample, which was given the Composite International Diagnostic Interview in order to diagnose mental health disorders.[16,17] Self-reported lifetime AN had a sensitivity of 100% and specificity of 96%; self-reported BN had a sensitivity of 94% and specificity of 81%.

Covariates

Information on women's age, education, income, ethnicity, pre-pregnancy weight and height, marital status, and parity was obtained by questionnaire at enrolment. Income was highly collinear with education: therefore, the latter was used in all analyses. Educational level (the highest schooling level attained) was divided into three categories: no education or primary only; secondary education; and university degree or higher. Ethnicity was categorised as white (Dutch or Western origin) or non-white (Indonesian, Asian, Afro-Caribbean, Turkish, Middle Eastern, and other). Parity was categorised as primiparae versus multiparae. Marital status was dichotomised as married/cohabiting versus not married/not cohabiting.

All women were asked whether their menstrual cycle was regular by questionnaire at enrollment.

Pre-pregnancy BMI was derived from self-reported pre-pregnancy weight (in kg) and height (in m) in the enrolment questionnaire, and this was highly correlated with the objective BMI collected at enrollment.[17]

Attrition

Available data varied by outcome: 5% of women had missing data on fertility treatment; 0.2% had missing data on twin births; and 8% had missing data on unplanned pregnancies. There was no evidence of selective attrition by eating disorder group. Missing data on outcomes was predicted by maternal education, age, and marital status.

Statistical analyses

The distribution of covariates according to exposure was assessed using the chi-square test or F-test, depending on the variable type. Mean and standard deviations (SDs) were estimated for all continuous variables, after normality checks. Logistic regression models were used to estimate crude odds ratios (ORs) and 95% confidence intervals (95% CIs).

Potential confounding factors (maternal age, ethnicity, education, parity, and marital status) were subsequently added, one at a time, to produce adjusted OR estimates.

The role of pre-pregnancy BMI in explaining the effect of maternal eating disorders on the outcomes was studied by further including BMI to the models to generate adjusted OR estimates.

Analyses were performed using STATA 11.[18]

Ethical approval

Ethical approval for the main study was given by the Medical Ethical Committee of the Erasmus Medical Centre in Rotterdam (MEC 198.782/2001/31). Further ethical approval for these secondary data analyses was given by the London School of Hygiene and Tropical Medicine (LSHTM) Ethical Committee.

Written consent was obtained from all participants.

Results

Sociodemographic variables

The distribution of sociodemographic variables across exposure groups is shown in Table 1.

Women with AN + BN and those with other psychiatric disorders were less likely to have a partner compared with the comparison group. Women with lifetime BN were more likely to be educated to secondary/higher level (Table 1). Women with AN and with AN + BN reported a lower prevalence of regular menstrual cycles compared with women without psychiatric disorders.

As expected, relative to women without psychiatric disorders, those with lifetime AN and with AN + BN had a lower pre-pregnancy BMI, whereas those with lifetime BN had a higher pre-pregnancy BMI.

Fertility and twin births

About 1.5% of women without psychiatric disorders reported having received fertility treatment to conceive the pregnancy under study (Table 2).

The prevalence of fertility treatment was 3.2% (n = 8) in women with lifetime BN; all eight women had BN in the past (Table 2). Of these, five (2.0%) women were treated with induced ovulation and three (1.2%) women were treated with *in vitro* fertilisation (IVF); women with lifetime BN had a four-fold increased odds of having received induced ovulation compared with women without psychiatric disorders [n = 22 (0.5%); crude OR 3.9, 95% CI 1.4–10.3; P = 0.007].

Women with BN had twice the odds of having received fertility treatment than the comparison group, with this difference persisting after adjusting for potential confounding factors (OR 2.4, 95% CI 1.1–5.4). In contrast, women with other lifetime psychiatric disorders had similar odds to those without lifetime psychiatric disorders. Accounting for the effect of pre-pregnancy BMI did not change the magnitude of these associations (Table 3).

Table 1. Sociodemographic characteristics across exposure groups: numbers, percentages, and means (SDs) in bold

	AN lifetime (*n* = 170)	BN lifetime (*n* = 265)	AN + BN lifetime (*n* = 130)	Other psychiatric (*n* = 1396)	Women without psychiatric disorders (*n* = 4367)	Statistic*
Ethnicity						
White (Dutch, European, of European origin)	118 (69.4%)	180 (67.9%)	85 (65.4%)	854 (61.1%)	2678 (61.3%)	$\chi^2 = 8.3$ $P = 0.08$
Non-white (Indonesian, Asian, Dutch Antilles, Suriname, African, Cape Verdian, Turkish, other)	50 (29.4%)	77 (29.1%)	44 (33.8%)	500 (35.8%)	1552 (35.5%)	
Missing	2 (1.2%)	8 (3.0%)	1 (0.8%)	42 (3.0%)	137 (3.1%)	
Marital status						
Married/cohabiting	144 (84.7%)	224 (84.5%)	103 (79.2%)	1,114 (79.8%)	3659 (83.8%)	χ^2=23.8
No partner	22 (12.9%)	32 (12.1%)	22 (16.9%)	225 (16.1%)	493 (11.3%)	$P < 0.0001$
Missing	4 (2.3%)	9 (3.4%)	5 (3.8%)	57 (4.1%)	215 (4.9%)	
Education						
None or primary only	13 (7.6%)	11 (4.1%)	14 (10.8%)	126 (9.0%)	351 (8.0%)	$\chi^2 = 24.9$
Secondary	84 (49.4%)	118 (44.5%)	58 (44.6%)	656 (47.0%)	1812 (41.5%)	$P = 0.002$
Higher	69 (40.6%)	127 (47.9%)	56 (43.1%)	564 (40.4%)	2002 (45.8%)	
Missing	4 (2.3%)	9 (3.4%)	2 (1.5%)	50 (3.6%)	202 (4.6%)	
Age, mean (SD), years	**30.1 (5.1)**	**30.2 (5.3)**	**29.8 (5.4)**	**30.2 (5.1)**	**30.0 (5.0)**	$F = 0.4$ $P = 0.8$
Parity						
Primiparae	105 (61.7%)	157 (59.2%)	76 (58.5%)	820 (58.7%)	2524 (57.8%)	$\chi^2 = 1.4$
Multiparae	65 (38.2%)	106 (40.0%)	54 (41.5%)	566 (40.5%)	1820 (41.7%)	$P = 0.8$
Missing	0	2 (0.7%)	0	10 (0.7%)	23 (0.5%)	
Pre-pregnancy BMI, mean (SD)	22.3 (3.5)	24.7 (5.5)	22.6 (3.7)	23.6 (4.4)	23.5 (4.1)	$F = 8.7$ $P < 0.0001$
Regular menstrual cycles						
Yes	115 (67.7%)	179 (67.5%)	64 (49.2%)	913 (65.4%)	2887 (66.1%)	$\chi^2 = 15.5$
No	42 (24.7%)	54 (20.4%)	44 (33.9%)	306 (21.9%)	937 (21.5%)	$P = 0.004$
Missing	13 (7.6%)	32 (12.1%)	22 (16.9%)	177 (12.7%)	543 (12.4%)	

*Chi-square or *F* statistic, as appropriate.

Women with lifetime AN had a higher prevalence of twin births compared with those without the disorder (3.5 versus 1%), as did women with BN and women with AN + BN, albeit to a lesser extent (see Table 2).

All eating disorders were associated with increased odds of having twins, with this association being weaker only in women with lifetime AN (OR 2.7, 95% CI 1.0–7.9; $P = 0.06$). These associations persisted after adjustment for potential confounding factors (lifetime AN, OR 2.7, 95% 1.0–8.0; lifetime BN, OR 2.7, 95% CI 1.1–6.4); lifetime AN + BN, OR 3.9, 95% CI 1.3–11.1). Women with other lifetime psychiatric disorders had similar odds as women without psychiatric disorders (Table 3).

When fertility treatment was included in the model the odds ratios for twin births increased slightly for maternal lifetime AN (OR 3.2, 95% CI 1.1–9.3; $P = 0.03$), but reduced for lifetime BN (OR 2.2, 95% CI 0.8–5.7; $P = 0.1$), and remained unchanged for women with AN + BN.

Unplanned pregnancies

The prevalence of unplanned pregnancies was higher across all eating disorder groups (32.3% for women with lifetime AN, 25.3% for women with lifetime BN, and 32.3% for women with lifetime AN + BN) than among women without psychiatric disorders (22.3%). Similarly, women with other lifetime psychiatric disorders also reported more unplanned pregnancies (29.3%; Table 2). Women with AN in the year prior to pregnancy reported the highest prevalence of unplanned pregnancies (55.2%).

The majority of women (>50%) with unplanned pregnancies across all exposure categories reported being pleased about the pregnancy; however, only 30–40% of women with unplanned pregnancies with BN or AN in the

Table 2. Fertility treatment, twin births, and unplanned pregnancies across exposure groups

	Fertility treatment *n* (%)	Twin births *n* (%)	Unplanned pregnancies *n* (%)	Feelings towards unplanned pregnancy *n* (%)			
				Pleased	Mixed initially	Mixed still	Not happy
AN lifetime (n = 170)	1 (0.6%)	6 (3.5%)	55 (32.3%)	31 (53.4%)	21 (36.2%)	5 (8.6%)	1 (1.7%)
In the last year (n = 29)	0	1 (3.5%)	16 (55.2%)	6 (35.3%)	8 (47.1%)	2 (11.8%)	1 (5.9%)
Past (n = 141)	1 (0.7%)	5 (3.6%)	39 (28.9%)	26 (60.5%)	14 (32.6%)	3 (7.0%)	0
BN lifetime (n = 265)	8 (3.2%)	6 (2.3%)	67 (25.3%)	38 (52.8%)	32 (44.4%)	2 (2.8%)	0
In the last year (n = 74)	0	2 (2.7%)	25 (38.5%)	12 (38.7%)	16 (51.6%)	3 (9.7%)	0
Past (n = 191)	8 (4.2%)	4 (2.1%)	42 (23.6%)	28 (57.1%)	20 (40.8%)	1 (2.0%)	0
AN + BN lifetime (n = 130)	2 (1.4%)	4 (3.1%)	42 (32.3%)	16 (53.3%)	11 (36.7%)	3 (10.0%)	0
In the last year (n = 11)	0	0	4 (44.4%)	2 (50.0%)	1 (25.0%)	1 (25.0%)	0
Past (n = 119)	2 (1.7%)	4 (3.4%)	38 (34.9%)	22 (56.4%)	13 (33.3%)	4 (10.3%)	0
Other psychiatric (n = 1396)	18 (1.3%)	14 (1%)	409 (29.3%)	235 (54.1%)	169 (38.9%)	25 (5.8%)	5 (1.1%)
Women without psychiatric disorders (n = 4367)	62 (1.4%)	38 (1%)	974 (22.3%)	672 (62.8%)	363 (33.9%)	29 (2.7%)	6 (0.6%)

last year reported being pleased about the pregnancy. These groups more often reported still having mixed feelings about the pregnancy in the second trimester.

Relative to women without psychiatric disorders the odds of having an unplanned pregnancy were similarly increased for all exposed women, except those with lifetime BN (Table 3). These effects persisted with adjustment for potential confounding factors and upon the inclusion of pre-pregnancy BMI in the model.

After adjustment for potential confounding factors (and pre-pregnancy BMI) women with lifetime BN and those with other psychiatric disorders had increased odds of having initial mixed feelings about the unplanned pregnancy. Women with lifetime AN had a five-fold increased odds of continuing to have mixed feelings about the pregnancy in the second trimester, with the magnitude of this association increasing slightly after adjustment (lifetime AN, OR 5.0, 95% CI 1.7–14.4; Table 3).

Discussion

Main findings

We showed that maternal eating disorders are differentially but significantly associated with fertility treatment, twin births, and unplanned pregnancies in a community sample of pregnant women. Lifetime BN (especially past) was associated with receiving fertility treatment, in particular induced ovulation. Overall, women with all eating disorders were more likely to give birth to twins. Lifetime AN (both in women with AN only and in women with AN + BN) was associated with unplanned pregnancies and mixed feelings about the pregnancy.

Interpretation

Our findings on fertility treatment are in line with previous findings that BN and binge eating are associated with fertility problems.[19] The fact that pre-pregnancy BMI did not modify these associations suggests fertility problems in this group might not be secondary to weight status. Induced ovulation is usually indicated for anovulation resulting from hypothalamic and pituitary dysfunction (including polycystic ovary syndrome, PCOS), amenorrhoea, and oligomenorrhoea.[20] There is evidence that PCOS is associated with BN and binge eating[21]; therefore, it is possible that infertility in women with BN was secondary to PCOS. Induced ovulation can cause multiple pregnancies.[20] In fact, the higher prevalence of twin births in women with BN was mainly explained by having received fertility treatment (the odds ratios for twin births became non-significant when adding fertility treatment as a covariate). Women with lifetime AN did not differ from women without disorders on fertility treatment for the current pregnancy, but had

Table 3. Fertility treatment, twin births, and unplanned pregnancies: comparison of women with eating disorders and women without psychiatric disorders.

	AN lifetime (*n* = 148)	BN lifetime (*n* = 219)	AN + BN lifetime (*n* = 108)	Other psychiatric (*n* = 1143)	Women without psychiatric disorders (*n* = 3552)
Fertility treatment					
Crude OR (95% CI)	–[†]	2.3***(1.1–5.2)	1.3 (0.3–5.5)	0.8 (0.4–1.5)	Ref.
Adjusted OR (95% CI)[a]	–[†]	2.4*** (1.1–5.4)	1.6 (0.4–6.7)	0.8 (0.4–1.4)	Ref.
Full model[a]	–[†]	2.2*** (1.0–5.1)	1.7 (0.4–7.0)	0.8 (0.4–1.4)	Ref.
Twin births					
Crude OR (95% CI)	2.7**** (1.0–7.7)	2.7*** (1.1–6.6)	3.7**(1.3–10.7)	1.0 (0.5–2.0)	Ref.
Adjusted OR (95% CI)[a]	2.7**** (1.0–7.9)	2.7*** (1.1–6.5)	3.8** (1.3–11.1)	0.9 (0.5–2.0)	Ref.
Full model[b]	2.7**** (1.0–8.0)	2.7*** (1.1–6.4)	3.9**(1.3–11.1)	1.0 (0.5–2.0)	Ref.
Full model, additionally adjusted for fertility treatment	3.2*** (1.1–9.3)	2.2 (0.8–5.7)	3.9**(1.3–11.4)	1.1 (0.6–2.2)	Ref.
Unplanned pregnancies					
Crude OR (95% CI)	1.7** (1.2–2.3)	1.1 (0.8–1.6)	1.6** (1.1–2.5)	1.5*(1.3–1.7)	Ref.
Adjusted OR (95% CI)[a]	1.8** (1.2–2.6)	1.2 (0.9–1.7)	1.6*** (1.01–2.4)	1.4* (1.2–1.7)	Ref.
Full model[b]	1.8** (1.2–2.6)	1.2 (0.9–1.7)	1.5** (1.0–2.4)	1.4* (1.2–1.7)	Ref
	(*n* = 55)	(*n* = 69)	(*n* = 38)	(*n* = 382)	(*n* = 921)
Feelings toward unplanned pregnancy[c]					
Pleased	Ref.	Ref.	Ref.	Ref.	Ref.
Mixed initially					
Crude OR	1.2 (0.7–2.2)	1.8*** (1.1–2.9)	0.8 (0.4–1.7)	1.3 (0.9–1.6)	Ref.
Adjusted OR[a]	1.4 (0.8–2.5)	2.0** (1.2–3.3)	0.8 (0.4–1.8)	1.3*** (1.0–1.7)	Ref.
Mixed still					
Crude OR	4.1** (1.5–11.5)	2.2 (0.6–7.5)	3.0 (0.8–10.5)	2.7* (1.5–5.0)	Ref
Adjusted OR[a]	5.0** (1.7–14.4)	2.3 (0.6–7.9)	2.8 (0.8–10.2)	2.5** (1.4–4.6)	Ref

[†]Not possible to calculate odds ratios because of empty cells.
[a]Adjusted for maternal age, ethnicity, education, parity, and marital status.
[b]Model includes maternal age, ethnicity, education, parity, marital status, and pre-pregnancy BMI.
[c]This variable applies only to women who reported and unplanned pregnancy; the 'not happy' category was dropped because of empty cells.
*$P \leq 0.001$;**$P \leq 0.01$; ***$P \leq 0.05$,****$P = 0.06$.

a higher prevalence of multiple births. The causes of multiple births are: ovarian stimulation and assisted reproductive technologies[22]; genetic (family members with twins); older maternal age at conception; parity; and ethnicity.[23] We looked in detail at women with lifetime AN who had twin births and found no evidence that they were older at conception, had higher parity, or were from non-European ethnicity. Several explanations are plausible for this finding, including a spurious finding, a biologically different ovulation process in this group, and higher folate use.[24] Further studies should clarify the biological reasons for this finding.

The only study to date to identify poor fertility outcomes in women with AN ($n = 140$) focused on women previously hospitalised for AN (i.e. women who had severe illness), and was carried out in the 1980s[11]: a very different sample from that under study here.

Unplanned pregnancies were common in women with lifetime eating disorders (~30%), confirming previous findings.[10,12] Strikingly, 55% of women with AN in the year prior to the pregnancy reported an unplanned pregnancy. This suggests unplanned pregnancies might be a consequence of wrongly believing one is not fertile whilst ill with AN.

Lastly, as previously reported,[10] women with eating disorders were more likely to have mixed feelings about pregnancy compared with women without disorders, with a five-fold increased odds of continuing to have mixed feelings about the pregnancy in the second trimester in women with AN. This finding warrants important consideration given the likely need for increased support antenatally for these women.

Contrary to our expectations, pre-pregnancy BMI had little or no effect as a mediator in the studied outcomes.

This might be a result of very few eating disordered women in this study being underweight or overweight/obese pre-pregnancy.

Although women with other psychiatric disorders were similar to those without eating disorders in relation to fertility treatment and twin births (suggesting that fertility problems are specific to eating disorders), they had increased odds of unplanned pregnancies, as previously reported by our group.[10]

Strengths and limitations

The interpretation of the results of this study must take into account its strengths and limitations.

Firstly, in relation to the ascertainment of exposure, this was obtained from self-report and therefore was marginally prone to measurement error; however, validation of self-reported eating disorders in a subsample of Generation R women yielded very high levels of sensitivity and specificity.[17] Previous evidence has highlighted similar results for the diagnostic properties of self-reported eating disorders.[25] A second limitation is the small numbers of women who reported eating disorders in the year prior to pregnancy, which limited our ability to statistically investigate the effect of active/past disorder on risk mechanisms. Thirdly, because of the study design, only women who were able to become pregnant were included, and therefore the study is representative of women with eating disorders who were able to get pregnant (with or without fertility treatment). It is therefore possible that more severe cases of women who might not be able to get pregnant, even after fertility treatment, were not included; if this were the case our estimates of fertility treatment and twin births are likely to be under- rather than over-estimates. Lastly, because of the nature of the study detailed information on whether women received fertility treatment prior to the current pregnancy was not available.

The study has several strengths, including relying on a population-based, multi-ethnic cohort of pregnant women. Generation R is well suited to investigate hypotheses related to uncommon exposures and outcomes, and to extend previous findings in the field, which mostly relied on samples of white women of predominantly high socio-economic status. Another important strength is the availability of objectively measured outcomes for fertility and twin births. These are unlikely to have been affected by information bias. Overall, fewer than 5% of women had missing data, and therefore this is unlikely to have substantially biased our results; moreover, the strongest predictors for missingness were included in all models.

Conclusion

Past or recent eating disorders are associated with fertility treatment, twin births, and unplanned pregnancies. Unplanned pregnancies have been associated with perinatal depression, anxiety, and negative psychosocial maternal outcomes.[26] It is therefore essential for mental health care providers to educate women with eating disorders about their fertility, and about the need for contraception even in the presence of amenorrhoea. An awareness of eating disorders in the antenatal care setting should be strongly emphasised, because of the potentially increased need of support for this patient group. There is evidence of under-detection of women with eating disorders presenting to infertility clinics,[9] and fertility treatment providers should be aware that women presenting for treatment might not just be underweight women with past or active AN, but may also include women with BN. Further research aimed at clarifying the mechanisms for: (1) the observed increase in multiple births in women with AN, and (2) the biological mechanisms that might be responsible for infertility in women with BN, is important in order to adequately inform healthcare providers and sufferers.

Disclosure of interests

None of the authors have a conflict of interest.

Contribution to authorship

NM had the original idea for this study, analysed the data, and wrote the article. HT provided supervision and advice on the data available, data analyses, and interpretation of the results. ISS and BDS provided supervision and guidance on data analyses and interpretation of the results. JSD contributed to data cleaning and preparation. HT, BDS, ISS, VWVJ, EAPS, AH, and FCV contributed to writing up the study and revised the article critically.

Details of ethics approval

Ethical approval for the main study was given by the Medical Ethical Committee of the Erasmus Medical Centre in Rotterdam (MEC 198.782/2001/31) in 2001. Further ethical approval for this secondary data analyses was given by the London School of Hygiene and Tropical Medicine (LSHTM) Ethical Committee in March 2011. Written consent was obtained from all participating mothers.

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Are women with eating disorders more responsive to fertility treatment?

Mini commentary on 'Fertility treatment, twin births, and unplanned pregnancies in women with eating disorders: findings from a population-based birth cohort'

Eating disorders, including anorexia nervosa (AN) and bulimia nervosa (BN), are under-recognised in both primary care and in fertility clinics, but have a substantial impact on a variety of health outcomes. This study is a welcome addition to the limited data we have on the relationships between eating disorders and reproductive outcomes, as examined in a population-based pregnancy cohort from the Netherlands. Strengths of the study include the population-based sampling, the high sensitivity and specificity of the questionnaire instrument for detecting eating disorders, and the objective determination of outcomes from clinical records. Some findings from this study confirm prior findings, whereas others are novel and unexpected, and require further confirmation. Key to our consideration of the findings is that the data are limited to pregnant women.

As displayed in table 2, authors found a current (i.e. previous year) prevalence in this cohort of any eating disorder of 1.8% (n = 114), and a lifetime prevalence of 8.9% (n = 565). Both prevalence figures are considerably higher than were reported in population-based data for women in the Netherlands a few years earlier: namely 0.6 and 1.3%, respectively (Bijl et al. *Soc Psychiatry Psychiatr Epidemiol* 1998;**33:**587–595). Other research reviewed by the authors suggests that women with eating disorders may have reduced fecundity. So why might eating disorders be over-represented among pregnant women? Women with eating disorders might not be as consistent with the use of family planning (consistent with the higher rate of unplanned pregnancy found in this and earlier studies), might be more likely to seek treatment when trying to conceive, or might be more likely to respond to fertility treatment than women who receive fertility treatment for other reasons. These latter possibilities would be consistent with the increased level of fertility treatment found among women with a history of eating disorders in this cohort. Here it should also be noted that the proportion of pregnancies associated with fertility treatment in the women without eating disorders seems to be low compared with treatment registries, e.g. a reported national prevalence of IVF-related births of 2.6% in the Netherlands in 2009 (Ferraretti et al. *Hum Reprod* 2013;**28:**2318–2331).

This brings us to the most counterintuitive finding of this study: namely that a history of eating disorders was associated with twins, an outcome ordinarily associated with high fecundity. (It should be noted again that the prevalence of twin gestation seems low in the women without eating disorders.) This is also consistent with a hypothesis of a more robust response to fertility treatment among women with history of eating disorders, as compared with women receiving fertility treatment for other reasons.

Although further research will be needed to unpack all of the underlying reasons for these findings, these results still have immediate clinical relevance in reminding all clinicians of the high impact of eating disorders on fecundity and pregnancy. Finally, one of the most interesting findings of this study for clinicians is that a lifetime history of an eating disorder may have as much relevance and impact as a currently active eating disorder.

Disclosure of interests

I have no competing interests to disclose. ■

JB Stanford
Office of Cooperative Reproductive Health, Department of Family and Preventive Medicine,
University of Utah, Salt Lake City, UT 84108, USA