

## Risk of major adverse perinatal outcomes in women with eating disorders

NADIA MICALI, EMILY SIMONOFF and JANET TREASURE

**Background** Low birth weight, prematurity and higher miscarriage rates have previously been reported in women with eating disorders.

**Aims** To determine whether women with a history of eating disorders are at higher risk of major adverse perinatal outcomes.

**Methods** Adjusted birth weight, preterm delivery and miscarriage history were compared in those with a history of eating disorders (anorexia nervosa ( $n=171$ ), bulimia nervosa ( $n=199$ ) and both ( $n=82$ )) and those with other ( $n=1166$ ) and no psychiatric disorders ( $n=10\ 636$ ) in a longitudinal cohort study.

**Results** The group with bulimia nervosa had significantly higher rates of past miscarriages (relative risk ratio 2.0,  $P=0.01$ ) and the group with anorexia nervosa delivered babies of significantly lower birth weight than the general population ( $P=0.01$ ), which was mainly explained by lower pre-pregnancy body mass index. Preterm delivery rates were comparable across groups.

**Conclusions** Women with a history of eating disorders are at higher risk of major adverse obstetric outcomes. Antenatal services should be aware of this higher risk.

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Eating disorders are a common source of psychiatric morbidity in women of child-bearing age (Van Hoeken *et al*, 2003). Previous studies on clinical samples have reported that women with anorexia nervosa, bulimia nervosa and women hospitalised for an eating disorder deliver lower birth weight and more preterm babies (Stewart *et al*, 1987; Brinch *et al*, 1988; Bulik *et al*, 1999; Waugh & Bulik, 1999; Sollid *et al*, 2004). Higher miscarriage rates have also been reported in women with eating disorders, especially those with bulimia nervosa (Mitchell *et al*, 1991; Abraham, 1998; Bulik *et al*, 1999; Blais *et al*, 2000).

No studies to date have determined, in an epidemiologically representative sample, whether the effect on adverse pregnancy outcomes is specific to the eating disorders and their symptoms, rather than to any severe psychiatric disorder. Moreover, most studies on women with eating disorders have not taken into account the effect of other mediating factors that may affect perinatal outcomes. In this study we investigated the effect of a history of eating disorders on the outcome of pregnancy in a representative sample of the British population.

### METHOD

#### Sample

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a longitudinal, prospective study of women and pregnancy (Golding *et al*, 2001). All pregnant women living in the geographical area of Avon, UK, who were expected to deliver their baby between 1 April 1991 and 31 December 1992 were recruited. All women gave informed and written consent. It was estimated that 85–90% of those eligible took part. The sample has been shown to be representative of the British population.

There were 14 663 women enrolled at the 9th week of pregnancy. Data were obtained on 14 472 women via postal

questionnaires. Women were excluded from the current study if they had not answered the questionnaire sent at approximately 12 weeks (2019). We only included singleton births in the study (12 254), as babies from multiple pregnancies have different patterns of foetal growth and gestational length. At 12 weeks women were also asked whether they had any recent or past history of psychiatric problems, including depression, schizophrenia, alcoholism, anorexia nervosa, bulimia nervosa or any other psychiatric disorder. Their pre-pregnancy weight and height were also obtained. Socio-demographic data were obtained during pregnancy. At 18 weeks of gestation information was obtained on vomiting and the use of laxatives for weight loss prior to and during pregnancy. Data on smoking and alcohol intake before and during the first and second trimesters of pregnancy were obtained at two time-points during pregnancy. Body mass index (BMI) was calculated as pre-pregnancy weight/height squared.

#### Outcomes

Birth weight, outcome of pregnancy (live or stillbirth), gender of the baby and gestational age at birth were obtained from obstetric records. Birth weights were corrected for gestational age and gender. Preterm delivery was defined as birth before 37 weeks of gestation. Only pregnancies where clinical estimates of length of gestation based on ultrasonography agreed with mothers' dates (plus or minus 2 weeks) were included. Women were asked at 18 weeks about any previous miscarriages. The data were then categorised as none, one and two or more.

#### Data analysis

Parametric (one-way analysis of variance) and non-parametric tests were used as appropriate for group comparisons, after testing for normality. Bivariate linear regression models were used to test for predictors of continuous outcomes. Multinomial and binary logistic regression models examined predictors of categorical and binary outcomes respectively.

Potential covariates likely to influence outcomes were first tested in bivariate models and included in multivariate models when significant. The final model accounted for the main effects of each covariate. Factors considered to be possible mediators (Kraemer *et al*, 2001) of main effects were included in the multivariate

model at a second stage. All analyses were performed using Stata version 8 for Windows. All statistical tests presented are two-tailed. Statistical significance was defined as  $P < 0.05$ .

Although our sample was relatively big, the sizes of groups with eating disorders were variable and some groups were small (anorexia nervosa plus bulimia nervosa in particular) in relation to the 'general population' control sample. We were therefore concerned that differences in rarer outcomes might not be detectable when comparing groups with eating disorders and the reference group. Hence we carried out a power calculation and found that effect sizes of 0.3 in continuous outcomes could be detected with a power of 75–93% at the 5% significance level. Group differences in proportions for common outcomes could be detected with 92–99% power and group differences in proportions for uncommon outcomes (such as prematurity) could be detected with 63–99% power at the 5% significance level.

### Ethical approval

The study was approved by the ethics committees of the Institute of Psychiatry and ALSPAC.

## RESULTS

Women who were included in the current study ( $n=12254$ ) were divided into five groups: (a) 171 (1.4%) who only endorsed the question 'Have you ever had anorexia nervosa?' (7 of these reported a recent episode); (b) 199 (1.6%) who only endorsed

the question 'Have you ever had bulimia nervosa?' (51 of these reported a recent episode); (c) 82 (0.7%) who endorsed both questions; (d) 1166 (9.5%) who reported having had schizophrenia, severe depression or other psychiatric disorders (including drug addiction and alcoholism) and formed the 'other psychiatric disorders' group; (e) 10 636 who formed the 'general population' comparison group.

### Socio-demographic data

Maternal age at delivery and ethnicity did not differ across the five groups (see Table 2). Women with other psychiatric disorders were less likely to be in full-time or part-time employment, or full-time education or training and were more likely to be multiparous than the general population sample. Women in the three eating disorder groups did not differ from the general population sample on parity or employment status. Women with a history of anorexia nervosa, anorexia nervosa plus bulimia nervosa and other psychiatric disorders were significantly more likely to have smoked during the first trimester of pregnancy. Women with other psychiatric disorders were significantly more likely to have smoked during the second trimester of pregnancy and drunk alcohol during the first trimester. All four clinical groups were less likely to be living with a partner than the 'general population' group.

### Eating disorders and related symptoms

We compared BMI across the five groups and the proportions of women reporting

past vomiting and laxative use for weight loss (Table 2). Women in the three eating disorder groups were significantly more likely to have used laxatives and self-induced vomiting. Women with a history of anorexia nervosa and anorexia nervosa plus bulimia nervosa had a significantly lower mean BMI than the other groups (Table 2).

### Pregnancy outcomes

Foetal deaths ( $n=66$ ) were excluded from these analyses. Women with a history of anorexia nervosa had 2 foetal deaths (1.2%), those with bulimia nervosa and those with anorexia nervosa plus bulimia nervosa had none, those with other psychiatric disorders had 7 (0.6%) and general population controls had 57 (0.7%). Differences were not statistically significant.

### Birth weight

We excluded 67 women who developed gestational diabetes because of high rates of macrosomia in this group. Rates of gestational diabetes were significantly higher in the group with anorexia nervosa plus bulimia nervosa (2 positive, 2.4%, Fisher's exact= $17.9$ ,  $P=0.01$ ) and that with other psychiatric disorders (16 positive, 1.4%) compared with the general population (48 positive, 0.5%). Data were missing on birth weight for 148 babies.

Mean birth weights corrected for gender and gestational age were calculated for 11 973 babies. The mean birth weight for babies born to women with a history of anorexia nervosa was 3340 g (95% CI

**Table 1** Socio-demographic data

	Anorexia nervosa $n=171$	Bulimia nervosa $n=199$	Anorexia nervosa plus bulimia nervosa $n=82$	Other psychiatric disorders $n=1166$	General population $n=10\ 636$
Age at delivery, years: mean (s.d.)	28.9 (5.2)	28.2 (4.6)	29.2 (4.6)	28 (5.5)	28.2 (4.8)
Multiparity, % (OR, 95% CI)	52.5 (0.9, 0.6–1.2)	51.6 (0.9, 0.7–1.2)	53.3 (0.9, 0.6–1.5)	59.1 (1.2, 1.0–1.3)***	54.9
White ethnicity, % (OR, 95% CI)	96.2 (0.6, 0.3–1.4)	97.4 (0.9, 0.4–2.2)	98.8 (1.9, 0.3–13.8)	98 (1.2, 0.8–1.9)	97.6
Employment, % (OR, 95% CI) <sup>1</sup>	49.0 (1.0, 0.7–1.4)	48.9 (1.0, 0.7–1.3)	42.7 (0.8, 0.5–1.2)	32.8 (0.6, 0.6–0.7)***	49.1
Any smoking in first trimester, % (OR, 95% CI)	27.8 (1.4, 1.0–2.0)*	26.2 (1.3, 0.9–1.8)	39.5 (2.4, 1.5–3.8)***	40.2 (2.5, 2.2–2.8)***	21.4
Any smoking in second trimester, % (OR, 95% CI)	20.2 (1.3, 0.9–1.9)	20.6 (1.3, 0.9–1.8)	23.5 (1.6, 0.9–2.6)	32.6 (2.5, 2.2–2.8)***	16.3
Has a partner, % (OR, 95% CI)	95.2 (0.4, 0.2–0.8)*	95.6 (0.4, 0.2–0.9)*	90.5 (0.2, 0.1–0.3)***	94.6 (0.4, 0.3–0.5)***	98.1
Any alcohol use in first trimester, % (OR, 95% CI)	11.6 (0.7, 0.4–1.2)	18.8 (1.3, 0.9–1.9)	24.7 (1.8, 1.1–3.0)*	19.3 (1.3, 1.1–1.6)*	15.2

1. Percentage in full-time/part-time employment or full-time education/training v. unemployed, housewives or retired.  
\* $P < 0.05$ , \*\*\* $P < 0.001$  v. general population.

**Table 2** Lifetime weight control behaviours and pre-pregnancy body mass index

	Anorexia nervosa n=175	Bulimia nervosa n=199	Anorexia nervosa plus bulimia nervosa n=82	Other psychiatric disorders n=1166	General population n=10 636
Self-induced vomiting for weight control, %	23.4***	56.3***	62.2***	4.0	3.6
Laxative use for weight control, %	25***	29.1***	55***	4.5	3.2
Body mass index pre-pregnancy: mean (s.d.)	21.5 (3.2)**	23.1 (4.3)	21.5 (3.0)*	23.1 (4.2)	22.9 (3.8)

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , v. general population.

**Table 3** Linear regression analysis of birth weight after stepwise adjustment for relevant covariates

	Anorexia nervosa n=159	Bulimia nervosa n=195	Anorexia nervosa plus bulimia nervosa n=78	Other psychiatric disorders n=1101
<i>B</i> (95% CI) $\beta$				
Birth-weight <sup>1</sup>	−83.9 (−151.9 to −15.9) −0.018*	14.3 (−48.7 to 77.4) 0.003	−2.6 (−101.7 to 96.5) 0.000	−33.5 (−60.9/ −6.1) −0.018*
Birth weight <sup>1</sup> adjusted for maternal factors	−75.1 (−143.6 to −6.5) −0.016*	20.5 (−42.4/83.5) 0.004	−2.6 (−101.7 to 96.5) −0.000	−36.4 (−64.0 to −8.8) −0.019**
Birth weight <sup>1</sup> adjusted for maternal factors and smoking in the second trimester	−64.5 (−132.3/3.3) −0.013 <sup>2</sup>	27.6 (−34.5 to 89.7) 0.006	8.8 (−90.2 to 107.9) 0.001	−4.4 (−31.9 to 23.2) −0.002
Birth-weight <sup>1</sup> adjusted for maternal factors, smoking in the second trimester and BMI	−40.7 (−109.1 to 27.8) −0.009	11.5 (−52.6 to 75.5) 0.003	23.9 (−78.8 to 126.6) 0.003	−2.7 (−31.0 to 25.5) −0.001

BMI, body mass index.

\* $P < 0.05$ , \*\* $P < 0.01$ .

1. Adjusted for gestational age and gender of the baby.

2.  $P=0.06$  v. general population.

3272–3407); to women with bulimia nervosa 3439 g (3377–3502); to women with anorexia nervosa plus bulimia nervosa 3422 g (3323–3521); to women with other psychiatric disorders 3392 g (3366–3413); and to the general population sample 3425 g (3416–3433). Babies of women with anorexia nervosa were significantly lighter than babies of control women, as were babies of women with other psychiatric disorders (overall  $F(6, 11966)=918.8$ ,  $P < 0.05$ ) (Table 3).

We studied the role of covariates known to influence birth weight, including maternal factors such as parity, maternal age, employment status, whether women had a partner and alcohol intake (a factor relating to the studied pregnancy). Alcohol intake, relationship status and employment status were not significantly related to the outcome and were not included in the final model.

Smoking in the first and second trimester, pre-pregnancy BMI, laxative use and self-induced vomiting in pregnancy were investigated as possible mediators of effect.

Laxative use and self-induced vomiting in pregnancy were not significantly related to birth weight in bivariate analyses. When maternal covariates (parity, maternal age) were included in the model, babies born to women with a lifetime history of anorexia nervosa were still significantly lighter than babies of control women ( $B=-75.1$ ,  $\beta=-0.016$ ,  $P=0.03$ ) (Table 3). When smoking in the second trimester was included in the model, a marginal difference remained for babies of women with anorexia nervosa compared with general population controls ( $B=-63.5$ ,  $\beta=-0.013$ ,  $P=0.06$ ). When BMI pre-pregnancy was included in the model, the effect of maternal history of anorexia nervosa on birth weight disappeared.

#### Preterm delivery

Data for evaluation of preterm delivery were available on 12 188 births. The rates of preterm delivery were: anorexia nervosa 6.5%; bulimia nervosa 5.0%; anorexia nervosa plus bulimia nervosa 4.9%; other psychiatric disorders 5.8%; general population

4.8%; with no group differences on logistic regression analysis. After controlling for ethnicity, maternal age, and parity, the group with other psychiatric disorders had significantly higher rates of preterm delivery compared with the general population (odds ratio 1.3, 95% CI 1.0–1.8,  $P=0.03$ ).

#### Previous miscarriages

Data on previous miscarriages were analysed in 11 700 women. An initial multinomial logistic regression showed that women with bulimia nervosa, those with anorexia nervosa plus bulimia nervosa and those with other psychiatric disorders were significantly more likely to report previous miscarriages (Table 4). When adjusted for relevant covariates (lifetime smoking and alcohol use, age, parity), only women with a history of bulimia nervosa and of other psychiatric disorders remained significantly more likely to have a history of previous miscarriages than the general population. A trend remained for women with anorexia nervosa plus bulimia nervosa.

**Table 4** History of miscarriages

	Anorexia nervosa n=159	Bulimia nervosa n=195	Anorexia nervosa plus bulimia nervosa n=79	Other psychiatric disorders n=1100
<b>Any previous miscarriages</b>				
Unadjusted OR (95% CI)	1.2 (0.9–1.8)	1.4* (1.1–1.9)	1.7* (1.1–2.7)	1.7*** (1.5–1.9)
Adjusted <sup>1</sup> OR (95% CI)	1.0 (0.7–1.6)	1.4* (1.1–2.0)	1.4 (0.9–2.4)	1.6*** (1.4–1.8)
<b>Number of miscarriages</b>				
One, unadjusted OR (95% CI)	1.0 (0.7–1.6)	1.2 (0.8–1.8)	1.2 (0.6–2.2)	1.5*** (1.3–1.7)
Two or more unadjusted, OR (95% CI)	1.5 (0.8–2.8)	2.0** (1.2–3.3)	3.2*** (1.6–6.3)	2.5*** (2.0–3.1)
One, adjusted <sup>1</sup> OR (95% CI)	0.9 (0.6–1.5)	1.2 (0.8–1.8)	1.0 (0.6–2.0)	1.4*** (1.2–1.7)
Two or more, adjusted <sup>1</sup> RRR (95% CI)	1.4 (0.7–2.7)	2.1** (1.2–3.6)	2.8** (1.4–5.8)	2.2*** (1.7–2.8)

OR, odds ratio; RRR, relative risk ratio.

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  v. general population.

1. Adjusted for maternal age, parity, lifetime alcohol use (more than 1 glass of alcohol/week), lifetime smoking.

The same three groups of women were significantly more likely to have had two or more miscarriages compared with the general population. The difference remained after controlling for relevant covariates (Table 4).

## DISCUSSION

### Main findings

Women with a history of bulimia nervosa (with or without a history of anorexia nervosa) had an increased rate of lifetime miscarriages, as did women with a history of other psychiatric disorders. This persisted after controlling for potential covariates. Women with a history of anorexia nervosa were more likely to deliver babies of lower birth weight than control women, although weights were comparable to babies of women with other psychiatric disorders.

### Miscarriages

Higher rates of miscarriage in women with bulimia nervosa have been reported previously (Mitchell *et al*, 1991; Morgan *et al*, 2006). A higher risk of miscarriage for women with current and past bulimia nervosa was reported in two studies (Abraham, 1998; Blais *et al*, 2000). Our results confirm these findings. Possible hypotheses include polycystic ovary syndrome and leptin abnormalities (Morgan *et al*, 2006). Future research will need to address the issue of direct cause of miscarriages in women with bulimia nervosa and the exact physiology.

### Birth weight

Previous studies have shown that women with current or past eating disorders have a higher risk of delivering lower birth

weight babies (Stewart *et al*, 1987; Bulik *et al*, 1999; Sollid *et al*, 2004) and our study confirms this finding. However, we found that the lower birth weight of babies born to women with anorexia nervosa may be mediated by lower pre-pregnancy BMI and to a lesser extent by smoking in the second trimester of pregnancy. None of the previous studies has investigated the effect of either variable in a population with eating disorders. However, the effect of maternal weight pre-pregnancy on birth weight of offspring has been documented in population studies; low maternal weight at conception or delivery has been found to have a significant impact on perinatal outcomes, mainly birth weight and preterm delivery (Kaminsky *et al*, 1973; Wolfe *et al*, 1991; Cnattingius *et al*, 1998; Ehrenberg *et al*, 2003). It is likely that a low pre-pregnancy BMI is an indicator of poor maternal nutritional status during pregnancy, but we were not able to evaluate this in this study.

Previous studies have highlighted an increased risk for adverse perinatal outcomes in women with severe mental illness (Jablensky *et al*, 2005), but no previous study has compared women with eating disorders with women with other severe psychiatric disorders. In our study, smoking during the second trimester seemed to be mainly responsible for the low birth weight in women with other psychiatric disorders. This suggests that the mechanism for low birth weight might be different in women with other severe psychiatric disorders compared with women with anorexia nervosa.

### Preterm delivery

Two previous studies of clinical samples have shown higher rates of prematurity in

babies of women with eating disorders (Bulik *et al*, 1999, Sollid *et al*, 2004). Bulik *et al* (1999) relied on a small sample and self-report of premature birth. The study of Sollid *et al* (2004), although larger, was register-based and included only women who had been hospitalised for an eating disorder, which was likely to be severe. Recall and sampling differences might therefore partly explain the disparity of these findings with those of our study. Our study is in line with that of Franko *et al* (2001) who found no difference in rates of prematurity when comparing women with anorexia and bulimia nervosa. There is the possibility that this finding might be a result of a low power to detect differences in our sample. This finding needs replication.

### Strengths and limitations

The strengths of the study include the use of data from a large longitudinal prospective community cohort. We were able to include a comparison group of women with psychiatric disorders other than eating disorders in addition to a general population control group. We were also able to take into account the role of several covariates relevant to the outcomes.

The main weakness of this study is that women were classified according to self-report of lifetime anorexia nervosa or bulimia nervosa or both. It is uncertain how accurate this classification is in terms of psychiatric classificatory systems. However, the availability of rates of lifetime eating disorder behaviours and BMI pre-pregnancy lends weight to self-reported diagnoses. The prevalence of eating disorders in this sample was 3.7%. According to estimates of the prevalence of eating disorders in women of child-bearing age



(Striegel-Moore *et al*, 2006), the prevalence of anorexia nervosa is between 0 and 1.5% and that of full-syndrome bulimia nervosa between is 0.4 and 0.8%. When partial syndromes are included the prevalence rate of eating disorders reaches about 5%. The prevalence of anorexia nervosa in our sample is 1.4% and that of bulimia nervosa 1.6%. It is therefore likely that a proportion in these two groups might have had an eating disorder not otherwise specified or a milder eating disorder compared with clinical samples. The current study is therefore likely to have underestimated rather than overestimated the rates of adverse perinatal outcomes in women with eating disorders.

Another limitation of the study is that weights and heights pre-pregnancy were also obtained by self-report. Moreover, we were not able to determine the temporal relationship between previous miscarriages and the course of bulimia nervosa. The sample did not have sufficient power to determine whether rare complications such as foetal deaths were more common in women with anorexia nervosa, although there was a trend in this direction.

## Implications

Our results, together with previous reports in the literature, suggest that maternal eating disorders are associated with higher risk of some obstetric complications. This is extremely relevant to the prevention of adverse foetal outcomes. Moreover, the extent to which perinatal complications are predictors of later psychiatric disorders is still unclear. We found that women with eating disorders have similar rates of major adverse perinatal outcomes to women with other psychiatric disorders, although some of the causal factors implicated might differ. Women with bulimia nervosa are at higher risk of miscarriage. Future research will need to clarify the exact mechanism.

Women with a history of anorexia nervosa should be informed when planning a pregnancy that good general health includes having a healthy BMI as well as smoking cessation. Previous studies suggest that the association of smoking with high levels of body image distortion, and the role of smoking in weight control are relevant to women with and without eating disorders (George & Waller, 2005; John *et al*, 2006). If this is so, the link with body image and weight control may need to be considered when counselling women about smoking cessation in pregnancy.

NADIA MICALI, MD, MRCPsych, Department of Child and Adolescent Psychiatry and Eating Disorders Research Unit, Institute of Psychiatry, King's College London; EMILY SIMONOFF, MD, FRCPsych, Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London; JANET TREASURE, PhD, FRCP, FRCPsych, Eating Disorders Research Unit, Department of Academic Psychiatry (Guy's Hospital), King's College London and ALSPAC, Department of Pediatric and Perinatal Epidemiology, University of Bristol, Bristol, UK

Correspondence: Dr Nadia Micali, Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London, Box 085, De Crespigny Park, London SE5 8AF, UK. Email: N.Micali@iop.kcl.ac.uk

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Experts agree that women should be counselled to delay pregnancy until the eating disorder is in complete remission (Sollid *et al*, 2004). Advising women with eating disorders on possible effects of the disorder on fertility and the possibility of adverse outcomes in their offspring could be important for motivating women to implement changes in their behaviour.

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