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Maternal Eating Disorders and Perinatal Outcomes: A Three-Generation Study in the Norwegian Mother and Child Cohort Study

Hunna J. Watson, PhD[1,2,3], Stephanie Zerwas, PhD[1], Leila Torgersen, PhD[4], Kristin Gustavson, PhD[4,5], Elizabeth W. Diemer, BA[6] Gun Peggy Knudsen, PhD[4], Ted Reichborn-Kjennerud, MD, PhD[7,8], and Cynthia M. Bulik, PhD[1,9,10]

[1] Department of Psychiatry, University of North Carolina at Chapel Hill, United States
[2] School of Paediatrics and Child Health, The University of Western Australia, Perth, Australia
[3] School of Psychology and Speech Pathology, Curtin University, Perth, Australia
[4] Division of Mental Health, Norwegian Institute of Public Health, Oslo, Norway
[5] Department of Psychology, University of Oslo, Oslo, Norway
[6] Harvard T. H. Chan School of Public Health, Harvard University, United States
[7] Division of Mental Health Services, Akershus University Hospital, Oslo, Norway
[8] Institute of Clinical Medicine, University of Oslo, Norway
[9] Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, United States
[10] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

Corresponding author: Dr Hunna Watson, Department of Psychiatry, University of North Carolina at Chapel Hill, CB #7160, Chapel Hill, North Carolina 27599-7160. Voice: (919) 966 4410. Fax: (919) 843 8802. E-mail: hunna_watson@med.unc.edu

Abstract

Previous research suggests that maternal eating disorders are associated with adverse pregnancy, delivery, and neonatal outcomes. In turn, adverse perinatal outcomes have been associated with subsequent eating disorder risk in adult offspring, possibly reflecting a transgenerational cycle of risk. Previous studies of the relationship between maternal eating disorders and adverse perinatal outcomes have failed to control for familial transmission of perinatal event phenotypes, which may confound the association. In a unique design afforded by the Norwegian Mother and Child Cohort Study (MoBa) and Medical Birth Registry of Norway, we linked three generations through birth register records and maternal-reported survey data. The aim was to determine if maternal eating disorders increase risk after parsing out the contribution of familial transmission of perinatal events. The samples were 70,881 pregnancies in grandmother-mother-child triads for analyses concerning eating disorder exposure during pregnancy and 52,348 for analyses concerning lifetime maternal eating disorder exposure. As hypothesized, eating disorders predicted a higher incidence of perinatal complications even after adjusting for grandmaternal perinatal events. For example, anorexia nervosa immediately prior to pregnancy was associated with smaller birth length (relative risk = 1.62, 95% confidence interval = 1.20, 2.14), bulimia nervosa with induced labor (1.21; 1.07, 1.36), and binge-eating disorder with several delivery complications, larger birth length (1.25; 1.17, 1.34), and large-for-gestational-age (1.04; 1.01, 1.06). Maternal pregravid body mass index and gestational weight mediated most associations. Our results support the contention that exposure to eating disorders increases the risk for negative health outcomes in pregnant women and their babies.

Keywords: anorexia nervosa, birth outcomes, binge-eating disorder, bulimia nervosa, eating disorder, MoBa, pregnancy

General Scientific Summary

This study found that pregnant women with acute or a lifetime history of anorexia nervosa, bulimia nervosa, binge-eating disorder, or purging disorder are more likely than pregnant women without previous eating disorders to experience poorer pregnancy, delivery, and offspring health outcomes, even after statistically adjusting for problems at the mothers' own birth. This supports the notion that exposure to maternal eating disorders can increase the risk of birth complications. Evidence emerged for full and partial mediation through the pathways of pregravid body mass index and gestational weight gain.

Maternal Eating Disorders and Perinatal Outcomes: A Three-Generation Study in the Norwegian Mother and Child Cohort Study

Eating disorders, such as anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED), involve serious disturbances in eating and body image and carry increased risk of psychological and medical morbidity and mortality (Arcelus, Mitchell, Wales, & Nielsen, 2011; Fichter & Quadflieg, 2016; Hudson, Hiripi, Pope, & Kessler, 2007). The lifetime prevalence of eating disorders in European samples is 0.5% for AN, 0.5% for BN, and 1% for BED and they tend to exhbit a chronic, or remitting and relapsing, natural course (Preti et al., 2009).

Maternal Eating Disorders and the Associated Risks for Mother and Baby During Pregnancy

Eating disorders are associated with a greater risk of health problems among pregnant women as compared with pregnant controls, such as pregnancy-related vomiting and hyperemesis, maternal anemia, and infections (Bansil et al., 2008; Kouba, Hällström, Lindholm, & Hirschberg, 2005; Linna et al., 2014; Torgersen et al., 2008). BED, characterized by loss-of-control overeating, is associated with gestational hypertension (Linna, et al., 2014). Eating disorders are associated with an increased risk of problems at labor and delivery, including higher risk of caesarian delivery (Bansil, et al., 2008; Bulik et al., 1999; Bulik et al., 2009; Eagles, Lee, Raja, Millar, & Bhattacharya, 2012; Ekeus, Lindberg, Lindblad, & Hjern, 2006; Micali et al., 2012; Pasternak et al., 2012), fetal distress (Micali, et al., 2012), resuscitation (Linna, et al., 2014), low Apgar scores in newborns (Linna, et al., 2014), and even perinatal

death (Linna, et al., 2014). Negative outcomes for neonates, especially on nutrition- and growth-related outcomes, have been reported. Maternal AN, which involves extreme underweight and dietary restriction, has been associated with intrauterine growth restriction, small-for-gestational-age, and low birth weight in offspring (Bansil, et al., 2008; Eagles, et al., 2012; Pasternak, et al., 2012; Solmi, Sallis, Stahl, Treasure, & Micali, 2013), and maternal BED with large-for-gestational-age (Bulik, et al., 2009; Linna, et al., 2014).

The association between maternal eating disorders and perinatal outcomes appears to be stronger in clinical and patient register samples rather than in community-ascertained samples (Bulik, et al., 2009; Solmi, et al., 2013). Most studies have focused on the presence of eating disorders at any point in life, because of the unfeasibility of recruiting a large sample of pregnant women with active eating disorders, but associations have been demonstrated in studies of both acutely ill mothers and lifetime history studies (Linna, et al., 2014; Pasternak, et al., 2012). The reasons for the associations between lifetime eating disorders and perinatal complications are unclear, but could involve under- or over-nourishment, higher stress reactivity, residual symptoms, relapse in women at varying stages of recovery, or unmeasured third variables that influence both risk for eating disorders and perinatal complications (Eagles, et al., 2012; Franko et al., 2001; Kouba, et al., 2005). Thus, it is expected that similar perinatal complications would be observed in samples of pregnant women with an acute or lifetime history.

Are Maternal Eating Disorders Specific Determinants of Perinatal Complications?

A large body of evidence suggests that maternal eating disorders are associated with complications during pregnancy and delivery and with neonatal complications. Does being exposed to an eating disorder increase risk, or alternatively is the association an epiphenomenon

of upstream generational factors? Several pregnancy and neonatal outcomes are heritable (i.e., pre-eclampsia, gestational hypertension, birth weight, length, gestational age), and others could be epigenetically transmitted to the second and/or third generations through stressors or illnesses that occur during the grandmother's pregnancy (Lunde, Melve, Gjessing, Skjærven, & Irgens, 2007; Nilsson, Salonen Ros, Cnattingius, & Lichtenstein, 2004; Wilcox, Skjærven, & Lie, 2008). In studies using retrospective recall and register-based methodology, infants who are exposed to a high number of perinatal complications (i.e., cephalhematoma, preterm birth) are at increased risk for AN during their adolescence and young adulthood (Cnattingius, Hultman, Dahl, & Sparén, 1999; Favaro, Tenconi, & Santonastaso, 2006; Foley, Thacker, Aggen, Neale, & Kendler, 2001; Wade, Treloar, Martin, Statham, & Heath, 2004). Perinatal phenotypes may give rise to eating disorders in offspring (Krug, Taborelli, Sallis, Treasure, & Micali, 2013; Raevuori, Linna, & Keski-Rahkonen, 2014). Thus in this model, perinatal complications run in families and perinatal complications increase risk for later eating disorders, but eating disorders, themselves, would not directly increase risk for perinatal complications.

Addressing this question requires multi-generational data. By examining the patterns of perinatal risk and eating disorders across grandmothers (generation 1), mothers (generation 2), and children (generation 3), we investigate the association between maternal eating disorder exposure and adverse perinatal outcomes in the context of grandmaternal perinatal factors.

Background to the Present Study

The present study uses the Mother and Child Cohort Study (MoBa) and Norwegian birth record data, to disaggregate the influence of maternal eating disorder exposure on perinatal adversity from familial transmission of perinatal outcomes. The ability to link three generations

of grandmothers, mothers, and offspring presents a distinct opportunity. Results from a previous study of maternal eating disorders and perinatal outcomes in the MoBa cohort approximately halfway into recruitment found that BED was associated with various adverse birth outcomes, but AN, BN, and purging disorder (PD) were not (Bulik, et al., 2009). The absence of a positive association for some eating disorders may reflect a lower severity of illness in community-based samples or insufficient statistical power. At the time of that study, the MoBa cohort had not been linked to Medical Birth Registry of Norway multigeneration data and recruitment was still underway. Both the linkage and recruitment are now complete.

Aims and Hypotheses

Because of the clear influence of eating disorders on medical morbidity and nutritional status (Micali, et al., 2012; Siega-Riz et al., 2011) we predicted that associations between maternal eating disorders and perinatal complications would remain significant after adjusting for grandmaternal factors. We hypothesized that we would observe positive associations between maternal AN and lower birth weight, small birth length, preterm birth, and small-for-gestational-age, as well as between maternal BED and birth weight and large-for-gestational-age. Other tests were exploratory. We anticipated the discovery of a greater range of significant exposure-outcome associations for all eating disorder subtypes than in Bulik et al. (2009) due to the increased statistical power afforded by the fully recruited MoBa sample.

Pre-pregnancy body mass index (BMI) and gestational weight gain have been suggested as mediating pathways. A previous study found that risk of large-for-gestational-age with maternal BED was attenuated after adjusting for both variables (Bulik, et al., 2009). A causal chain is possible since eating disorders can affect weight and pregnancy weight gain (Micali, et

al., 2012; Zerwas et al., 2014), and in turn these factors can affect health outcomes in pregnant women and their babies (Abenhaim, Kinch, Morin, Benjamin, & Usher, 2007).We hypothesized mediation effects on the basis of previous research (Bulik, et al., 2009).

Method

Participants

This study is based on the MoBa study conducted by the Norwegian Institute of Public Health (www.fhi.no/morogbarn) (Magnus et al., 2006). MoBa participants were recruited throughout Norway from 1999-2008, via a postal invitation in connection with a routine ultrasound examination offered to all pregnant women in Norway at 17-18 weeks gestation. The women consented to participation in 40.6% of the pregnancies. The cohort now includes 114,500 children, 95,200 mothers and 75,200 fathers. Follow-up surveys occur at regular intervals and linkage to national health registries including the Medical Birth Registry of Norway (Irgens, 2000) is possible. Informed consent was obtained from each MoBa participant upon recruitment. The study was approved by The Regional Committee for Medical Research Ethics, the Norwegian Data Inspectorate, and the Institutional Review Board at the University of North Carolina at Chapel Hill.

The current study is based on version 8 of the quality-assured data files released for research in 2015 and data span three generations: maternal grandmothers, MoBa-enrolled mothers, and MoBa offspring. To assist in gaining maximum sample sizes for analyses, two study populations were compiled: a dataset for analyses pertaining to maternal eating disorders exposure during pregnancy which was established with MoBa Questionnaire 1 (wave: 17-18 weeks gestation) and Medical Birth Registry of Norway data (“Dataset 1”) and a dataset

pertaining to lifetime maternal eating disorder exposure which was established with MoBa Questionnaire 5 (wave: 18 months postpartum) and Medical Birth Registry of Norway data ("Dataset 2"). Participant flow through the study and inclusion and exclusion criteria are shown in Figure 1. The exclusion criteria applied were selected to minimize bias and since more complications accompany non-singleton births. The unit of observation in each dataset was the grandmother-mother-child triad.

[Figure 1]

Measures

The present study uses MoBa Questionnaire 1, 5, and Medical Birth Registry of Norway data. Broadly, Questionnaire 1 assesses maternal health and psychosocial wellbeing, socioeconomic factors, and various environmental risk factors during the pregnancy and prior to conception. Questionnaire 5 assesses infant food intake, health, and general development, as well as maternal mental and physical health over the lifetime and since the birth of the child. The Medical Birth Registry of Norway contains information on perinatal risks and birth outcomes for births from 1967 (Irgens, 2000).

Eating disorders. Eating disorder diagnostic algorithms were constructed in accordance with the Diagnostic and Statistical Manual (DSM-5) eating disorder criteria (American Psychiatric Association, 2013). Questionnaire 1 assessed eating disorder status in the six months before and/or during pregnancy (henceforth, for simplicity, referred to as "eating disorders during pregnancy"); though AN was only assessed in the six months before pregnancy, due to difficulties in confirming the weight criterion in the presence of pregnancy-related weight gain.

AN was operationalized as low body weight, severe body image disturbance, and a persistent fear of weight gain. We used a BMI < 18.5 kg/m^2 as the cut-off for low body weight, consistent with the World Health Organization's threshold for 'underweight' (World Health Organization, 2000) and as a more lenient criterion given the community-based sample. BN was operationalized as weekly or more frequent objective binge eating and purging (self-induced vomiting, laxatives) or non-purging (fasting, excessive exercise) compensatory behaviors, and self-evaluation unduly influenced by shape or weight. BED was operationalized as weekly or more frequent objective binge-eating episodes in the absence of purging. PD was operationalized as weekly or more frequent purging without objective binge eating, plus the criterion of overvaluation of weight or shape was added. Individuals who did not meet criteria for AN, BN, BED, or PD were classified as having no eating disorder during pregnancy. Assignment to a category, including no eating disorder, was made only when all responses were available to ensure accurate classification. The variable denoting eating disorders during pregnancy was a multicategory variable coded as 1 = AN during pregnancy, 2 = BN during pregnancy, 3 = BED during pregnancy, 4 = PD during pregnancy, and 5 = no eating disorder during pregnancy.

Questionnaire 5 assessed lifetime eating disorders, specifically BN, BED, and PD (AN was not assessed). BN was defined as recurrent objective binge eating and purging and undue influence of shape and weight on self-evaluation. BED was defined as recurrent objective binge eating in the absence of purging. PD was defined as recurrent purging behaviors in the absence of objective binge eating, and overvaluation of weight and shape. A threshold of "at least twice weekly" for recurrent objective binge and purge episodes had to be used for lifetime diagnoses as the DSM-5 threshold ("at least once per week") was not available, and symptoms had to last at least three months. Because Questionnaire 5 presents a list of eating disorder symptoms and asks

the individual to rate symptoms they experienced "for the period that affected them most", individuals were not able to receive lifetime diagnoses per each eating disorder. Individuals who did not meet criteria for BN, BED, or PD were classified as no lifetime eating disorder. Finally, to increase the validity of the no lifetime eating disorder category, participants were removed from this category if they responded affirmatively to a single-item question in Questionnaire 1, "Do you have or have you ever had anorexia/bulimia/other eating disorders" and excluded from analysis (~1.5%). We exclude participants who self-reported a lifetime eating disorder since Questionnaire 5 did not assess lifetime AN. The variable denoting lifetime eating disorders was a multicategorical variable coded as 1 = lifetime BN, 2 = lifetime BED, 3 = lifetime PD, and 4 = no lifetime eating disorder.

Outcomes. Outcome data were obtained from the Medical Birth Registry of Norway for the occasion of the MoBa child's birth. Obstetric and perinatal variables deemed relevant for testing a transgenerational cycle of risk model for eating disorders were chosen. Outcomes were categorized into pregnancy, delivery, and neonatal, and were all dichotomous (0 = absent, 1 = present), except for birth weight.

Pregnancy outcomes in the present study included diabetes (gestational), pre-eclampsia, umbilical cord knot, and bleeding during pregnancy. These were chosen for several reasons. Binge-spectrum eating disorders increase risk for metabolic illnesses (Hudson et al., 2010). The diabetic intrauterine environment leads to increased blood sugar during pregnancy which causes fetal overgrowth, higher birth weight, pre-eclampsia, and preterm birth (Wendland et al., 2012). Overweight and metabolic abnormalities can increase the risk of subsequent eating disorders. Pre-eclampsia, characterized by high blood pressure during pregnancy, predicts low birth weight and can cause lower oxygen, nutrient restriction and maternal oxidative stress to the fetus, which

leads to lower growth (Kulkarni et al., 2010). Umbilical cord complications are associated with preterm birth and fetal growth restriction. Both in turn are associated with possible insults or injury to the newborn brain and later psychiatric illness (Machin, Ackerman, & Gilbert-Barness, 2000). Bleeding during pregnancy is associated with an increased risk of preterm birth and lower birth weight (Williams, Mittendorf, Lieberman, & Monson, 1991).

Delivery outcomes in this study were prolonged labor, instrument-assisted delivery (forceps, vacuum), caesarian delivery, induced delivery, and nonvertex presentation. In the previous MoBa study, maternal eating disorders were associated with a higher risk of induction, and receiving epidural and assistance delivery (Bulik, et al., 2009). Obstetric trauma during delivery can cause permanent neurological sequelae. Delivery complications have been associated with later eating disorder risk in children. The exact mechanism for this putative association is unknown (Favaro, Tenconi, & Santonastaso, 2008).

Neonatal outcomes included birth weight (standardized), birth length for age and sex < 10^{th} percentile, birth length for age and sex > 90^{th} percentile, preterm birth (< 37 weeks), postmature birth (≥ 42 weeks), small-for-gestational-age (birth weight for age and sex < 10^{th} percentile), and large-for-gestational-age (birth weight for age and sex > 90^{th} percentile). Variables defined from percentiles were derived using World Health Organization (WHO) standards, and biologically implausible values defined by WHO were omitted (WHO Multicentre Growth Reference Study Group, 2009). Birth weight and birth length are primary measures of fetal growth and gestational weight status, and are impacted by the nutritional status of the mother. Preterm birth is predicted by lower pregravid BMI (Hendler et al., 2005) and maternal stress and poor psychosocial status (Copper et al., 1996), in turn, preterm birth has been associated with subsequent onset of psychiatric conditions in offspring. Because the brain of

infants born preterm is very vulnerable to injury and may also induce epigenetic changes, being born preterm could lead to increased risk of psychiatric disorders (Nosarti et al., 2012).

Covariates. For the perinatal covariates, the same variables as the 'outcome' measures were used, obtained from the grandmother's Medical Birth Registry of Norway record. For example, if the outcome variable in the analysis was maternal pre-eclampsia then the analysis adjusted for grandmaternal pre-eclampsia at the mother's birth. Maternal covariates of household income, marital status, education, smoking during pregnancy (coded as a dichotomous variable), parity (defined as total number of live births), and age were included to adjust for socioeconomic status and general risks for birth complications.

Mediators. Pregravid BMI and gestational BMI gain were tested as mediator variables. Maternal weight prior to and weight gain over pregnancy are potential mediators as they can be influenced by eating disorders (Siega-Riz, et al., 2011) and may influence birth outcomes (Cedergren, 2006; Hillesund, Bere, Haugen, & Overby, 2014) particularly those related to growth and nutrition.

Statistical Analysis

Two datasets were analyzed: in Dataset 1 the independent variable was maternal eating disorders during pregnancy and in Dataset 2 the independent variable was lifetime maternal eating disorders. To address the primary aim, Poisson regression modeling with robust variance estimation was chosen as it is suitable for rare and non-rare outcome events. A generalized estimating equations approach accounted for clustering since some mothers had multiple enrolments in MoBa due to multiple pregnancies. The relative risk of adverse perinatal outcome at the MoBa offspring birth occasion was estimated, and each outcome was tested in a separate

model. Two sets of nested models were analyzed: the first model adjusted for maternal covariates (i.e., household income, marital status, education, smoking during pregnancy, parity, age). The second model included all the previous covariates and added the perinatal covariate (birth outcome) from the grandmother's Medical Birth Registry of Norway record. During statistical analysis, convergence problems occurred when predicting gestational diabetes due to small cell sizes, these were resolved by substituting a variable denoting the presence of gestational or pregestational diabetes during pregnancy (1 = yes, 0 = no). Both elevate maternal and infant morbidity and mortality in the perinatal period (Shand, Bell, McElduff, Morris, & Roberts, 2008). The "no eating disorder" group was the reference category of the eating disorder predictor. A false discovery rate (FDR)-corrected alpha level of $p < 0.05$ was used to assess statistical significance (Benjamini & Hochberg, 1995).

Maternal eating disorder-perinatal outcome associations that were statistically in the second nested model were evaluated with Preacher and Hayes (2008) approach to determine whether pregravid BMI and gestational BMI gain were mediators. Separate models were constructed for each outcome, and each model included multicategory maternal eating disorder as a predictor with the "no eating disorder" group serving as the reference category, the maternal covariates, the grandmaternal perinatal covariate, and the two mediators. The PROCESS macro with 1000-bootstrapped samples was used (Hayes, 2016, July 22). PROCESS uses an ordinary least squares or logistic regression-based path analytic approach to simultaneously estimate the direct effects of the predictor on the mediator/s (path *a*), the mediator/s on the outcome (path *b*), and the predictor on the outcome (path *c*') and the indirect effects (mediation) of the predictor on the outcome via the mediator/s (path $a \times b$). Confidence intervals of the indirect effect that do not contain zero indicate mediation. As the macro does not give *p* values for all effects, alpha of

0.05 had to be used. A significant direct and indirect path indicates partial mediation, and a significant indirect path in the absence of a significant direct path indicates full mediation. All analyses were done in SAS 9.4.

Results

Dataset and MoBa Mother and Maternal Grandmother Characteristics

[Table 1]

Maternal characteristics of the samples and the frequency of perinatal outcomes are shown in Table 1. Figure 1 shows the study flow, and frequency of eating disorder diagnoses. The samples included 70,881 grandmother-mother-child triads in Dataset 1 (eating disorder status during pregnancy) and 52,348 grandmother-mother-child triads in Dataset 2 (eating disorder status over the lifetime).

Exposure to Maternal Eating Disorders During Pregnancy and the Lifetime and Relative Risk of Adverse Perinatal Outcomes

[Table 2]

[Table 3]

AN-related hypotheses. In the first set of nested models (eating disorder subtype with maternal covariates of household income, marital status, education, smoking during pregnancy, parity, and

age), maternal AN during pregnancy was associated with significantly lower birth weight (26% lower) of babies (0.74; 0.68, 0.82). But, this association did not remain significant when adjusting for maternal birth weight (0.95; 0.92, 0.99), therefore this hypothesis was not supported. The same pattern was seen for small-for-gestational-age. Maternal AN was significantly associated with a 64% greater risk of smaller birth length in the first nested model (1.64; 1.22, 2.19), and remained significant after adjusting for maternal small birth length in the second nested model (1.62; 1.20, 2.14), hence this hypothesis was supported. There was no significant association between maternal AN during pregnancy and preterm birth in either nested model.

BED-related hypotheses. BED during pregnancy was significantly associated with birth weight in the first nested model (1.07; 1.05, 1.10) but not after adjusting for maternal birth weight in the second nested model (0.99; 0.98, 1.01), thus this hypothesis was not supported. The hypothesis regarding large-for-gestational-age was supported; in the first model, babies of mothers with BED during pregnancy had a 19% higher risk of large-for-gestational-age (1.19; 1.14, 1.26) and in the second nested model that adjusted for maternal large-for-gestational-age the babies had a 4% higher risk (1.04; 1.01, 1.06). Maternal BED during the lifetime was significantly associated with babies' birth weight (1.12; 1.09, 1.15) and large-for-gestational-age (1.25; 1.18, 1.33) in the first nested models, but not with babies' birth weight (1.01; 1.00, 1.03) or large-for-gestational-age (1.03; 1.00, 1.06) in the second nested models. Thus, these hypotheses were not supported.

General findings. When considering relations among all eating disorders and perinatal adversity, thus including both hypothesized and exploratory tests, results suggested that maternal AN, BN, and BED at pregnancy, but not PD, were associated with perinatal adversity after adusting for grandmaternal factors, thus supporting the overall study hypothesis. In the first set

of nested models, there were several significant associations between maternal eating disorders and adverse pregnancy, delivery, and neonatal outcomes (FDR *p*s < 0.05; Table 2). In the second set of nested models most of these associations remained significant: AN during pregnancy was associated with a higher risk of caesarian (1.52; 1.10, 2.10) and small birth length (1.62; 1.20, 2.14), and lower risk of prolonged labor (0.80; 0.68, 0.93), large birth length (0.61; 0.46, 0.80), and postmature birth (0.47; 0.33, 0.67); BN during pregnancy was associated with a higher risk of induced delivery (1.21; 1.07, 1.37); and BED during pregnancy was associated with a higher risk of caesarian (1.19; 1.06, 1.35), induced delivery (1.18; 1.09, 1.28), large birth length (1.19; 1.12, 1.26), large-for-gestational-age (1.04; 1.01, 1.06), and lower risk of small birth length (0.72; 0.61, 0.85) after adjustment for grandmaternal perinatal characteristics (FDR *p*s < 0.05; Table 2). Some associations that were significant in the first model were not found after adjusting for grandmaternal factors, specifically AN and smaller birth weight, small-for-gestational-age, and large-for-gestational-age; and BED and birth weight and small-for-gestational-age (FDR *p*s > 0.05).

We found similar results for lifetime eating disorders.The first set of nested models indicated that mothers and offspring exposed to lifetime BN, BED, and PD in the mother had a significantly higher incidence of perinatal adversities than the referent group (Table 3). The majority of significant associations in the first model remained significant in the second nested models that adjusted for grandmaternal perinatal factors. In these, lifetime history of BN was associated with a higher risk of diabetes during pregnancy (1.78; 1.23, 2.57) and induced delivery (1.26; 1.11, 1.42); lifetime BED was associated with diabetes during pregnancy (2.21; 1.70, 2.87), pre-eclampsia (1.32; 1.08, 1.61), prolonged labor (1.08; 1.02, 1.15), caesarian (1.32; 1.14, 1.53), induced delivery (1.17; 1.05, 1.29), and large birth length (1.25; 1.17, 1.34); and

lifetime PD was associated with caesarian delivery (1.65; 1.17, 2.31) (FDR *p*s < 0.05). Some significant associations in the first model did not remain significant in the second model when adjusting for grandmaternal factors, specifically, BED and birth weight and large-for-gestational-age; and PD and small-for-gestational-age (FDR *p*s > 0.05).

In the vast majority of models (87%), the point estimate for the during pregnancy effect fell within the confidence interval of the point estimate for the lifetime effect, suggesting a similar pattern of results for acute and lifetime eating disorders.

Mediators of the Association Between Maternal Eating Disorders and Adverse Perinatal Outcomes

[Table 4]

Table 4 depicts mediation tests of all the models where eating disorders significantly predicted outcomes in the second nested models of Tables 2 and 3. The mediation analyses supported pregravid BMI and gestational BMI gain as mediators (Table 4). Full mediation via pregravid BMI and gestational BMI gain was observed from: AN during pregnancy to prolonged labor and large birth length; BN during pregnancy to induced delivery; BED during pregnancy to diabetes during pregnancy, caesarian, and induced delivery; and BED lifetime to pre-eclampsia, prolonged labor, caesarian, and induced delivery. All other associations shown in Table 4 indicated partial mediation by one or both mediators.

Discussion

The question of whether maternal eating disorders negatively influence perinatal outcomes, or whether this is an artifact of upstream generational factors increasing the risk for both eating disorders and perinatal complications, has been addressed in part through this study. The main finding of this study was that maternal eating disorders pose health risks for mother and child even after accounting for differences in risk predicted by perinatal complications in the prior generation.

Our use of a larger, more statistically powered sample provides new, previously unavailable information concerning pregnancy complications. BN and BED were associated with negative effects for the mother, such as diabetes during pregnancy and pre-eclampsia. Prior studies with smaller samples did not find this effect (Bulik, et al., 2009; Linna, et al., 2014), although Linna et al. (2014) did find increased risk for gestational hypertension, a health outcome that is also affected by maternal weight and nutritional status.

Greater delivery complications, such as prolonged labor, caesarian, and induced delivery, were observed in all eating disorders. In terms of delivery outcomes, only incidence of caesarian delivery has been considered in other eating disorder samples (AN and BN), and studies have produced mixed results, perhaps in part due to study differences and lower power (Bansil, et al., 2008; Bulik, et al., 1999; Eagles, et al., 2012; Ekeus, et al., 2006; Micali, et al., 2012; Pasternak, et al., 2012).

The most compelling evidence prior to this study of a consistent negative perinatal impact of maternal eating disorders has been found for prenatal and neonatal growth outcomes (Bansil, et al., 2008; Bulik, et al., 1999; Bulik, et al., 2009; Conti, Abraham, & Taylor, 1998; Eagles, et al., 2012; Ekeus, et al., 2006; Kouba, et al., 2005; Linna, et al., 2014; Micali, et al., 2012; Micali, Simonoff, & Treasure, 2007; Pasternak, et al., 2012). Offspring weight and length

are strongly heritable (Lunde, et al., 2007) yet can be modified by environmental exposures. In the current study, there was evidence that AN was associated with offspring undernutrition and BED with overnutrition, supporting prior research (Conti, et al., 1998; Eagles, et al., 2012; Linna, et al., 2014; Perrin et al., 2015).

A second main finding of this study is that pregravid BMI and gestational weight gain mediated the associations between maternal eating disorders and perinatal complications. These factors mediated risk of diabetes during pregnancy and pre-eclampsia, consistent with research in non-psychiatric populations (Solomon et al., 1997), and growth outcomes for maternal AN and BED. These factors are unlikely to be causative agents themselves but indicators of other mechanisms (i.e., placental signalling pathways, maternal diet, endocrinolgic and metabolic pathology) that increase perinatal risk. Prior research in the MoBa cohort showed that compared with referrent women, women with BED had a higher saturated fat and energy intake during pregnancy (Siega-Riz et al., 2008).

No studies known to us, with the exception of Bulik et al. (1999), have reported on perinatal risks with lifetime and acute assessments of eating disorders in the same individuals. Bulik et al. compared women with AN, women recovered from AN, and healthy controls and reported descriptively that smaller birth weight and caesarian risk were similar and more common in the AN groups. Most studies supporting an association among eating disorders and perinatal risks have used lifetime assessments (Eagles, et al., 2012; Kouba, et al., 2005; Linna, et al., 2014; Micali, et al., 2012; Micali, et al., 2007). Consistent with former work, this study suggests that both lifetime and acute episodes modify health outcomes for the pregnant woman and baby as it develops in the womb. Although there was no strong evidence for differential effects by acute versus lifetime status, inferences are limited by differences in the binge eating

and purging thresholds available in the study measures. Future studies may wish to elaborate on this line of research by comparing outcomes among recovered and acutely ill pregnant women with eating disorders.

There has been a critical need to understand the influence of maternal eating disorders on perinatal complications in light of familially transmitted perinatal phenotypes, for two reasons. First, an exposure-outcome association needs to be robust to confounding effects to be regarded as plausible. Second, a transgenerational cycle of risk model explaining the perpetuation of eating disorders across generations needs further investigation (Cnattingius, Villamor, Lagerros, Wikström, & Granath, 2012). A study testing a transgenerational cycle of risk model for obesity found that individuals born large-for-gestational-age had a higher rate of adult obesity and risk of large-for-gestational-age offspring (Cnattingius, et al., 2012). A similarly inspired but relatively unstudied cycle of risk model for eating disorders has been articulated in that maternal eating disorders may influence perinatal outcomes, which in turn may increase the risk for eating disorder onset in offspring as they mature (Bulik, Reba, Siega-Riz, & Reichborn-Kjennerud, 2005). A step toward empirically validating (or refuting) this cycle of risk model is to interrogate the robustness of the association between maternal eating disorders and perinatal outcomes. The present research supports these associations, and encourages future elaboration and testing of an eating disorder cycle of risk model. In the meantime, from a clinical perspective, patients dealing with all eating disorders should be informed that a lifetime history of an eating disorder or the presence of an active eating disorder could increase the relative risk for perinatal complications and adverse outcomes. Obviously, women with active eating disorders require close monitoring and care during pregnancy. But these results suggest that women with lifetime histories of eating disorders should receive additional nutritional guidance and support above and beyond the

current standard of care during pregnancy to ensure that they are meeting their unique dietary and psychological needs.

Strengths of this study include a prospective design, which allowed maternal eating disorders during pregnancy to be measured without retrospective bias, large sample size, population-based recruitment, and use of register data to capture birth outcomes across generations. However, there are several study limitations that also need to be considered. The participation rate was 40.5%, which means that the study population may not be representative of all pregnant women in Norway. Self-selection bias has been suggested to affect prevalence estimates, but not exposure-outcome associations in MoBa (Nilsen et al., 2009). Lifetime eating disorders were measured retrospectively at 18 months postpartum and we could not rule out that some cases may have commenced during the postpartum period. However, this is unlikely given the typical age of onset for eating disorders (Hudson, et al., 2007). The AN subtype was defined with a BMI < 18.5 kg/m^2, since fewer mothers met the AN criteria when a more conservative BMI (< 17.5 kg/m^2) was used, and may not represent very unwell individuals with AN. The mutually exclusive categories for lifetime diagnosis are likely to underestimate lifetime prevalence. The lifetime prevalence of BED was lower than prevalence during pregnancy, which may have been caused by differences in the binge frequency threshold available in Questionnaire 1 and 5, selective attrition from Questionnaire 1 to 5, or could suggest a pregnancy-specific presentation of BED requiring further exploration. Unmeasured confounding factors may also account in full or in part for the exposure-outcome associations observed. We may be observing a perpetuation of the association between eating disorders and perinatal outcomes across generations if grandmothers had an eating disorder, but grandmother diagnoses were unavailable.

In the present study, maternal eating disorders were associated with an increased risk of perinatal complications beyond the risk that could be predicted by grandmaternal perinatal history. These findings underscore the obstetric significance of eating disorder history as a risk factor for perinatal complications. Pregnant women with a history of eating disorders should be offered appropriate nutritional, psychological, and medical support.

Disclosures

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Table 1
Selected Study Characteristics

Characteristic	During pregnancy *N* = 70,881 % (*n*) or *M* (*SD*)	Lifetime *N* = 52,348 % (*n*) or *M* (*SD*)
Maternal characteristics		
Household income		
0-200k NOK	8 (5,762)	7 (3,849)
>200k-500k NOK	48 (33,962)	47 (24,756)
>500k-700k NOK	28 (20,070)	29 (15,298)
>700k NOK	16 (11,087)	16 (8,445)
Married or de facto	96 (68,086)	96 (50,517)
Education		
<3 year high school	7 (4,747)	5 (2,830)
Vocational high school	13 (9,326)	12 (6,541)
3-year high school general studies, junior college	15 (10,883)	15 (7,704)
Regional technical college/4-year university degree	42 (29,642)	43 (22,751)
University, technical college, more than 4 years	23 (16,283)	24 (12,522)
Smoking during pregnancy	8 (5,743)	7 (3,537)
Parity	0.71 (0.81)	0.69 (0.80)
Age	29.69 (4.20)	29.88 (4.11)
Pregnancy outcomes		
Diabetes	1 (962)	1 (701)
Pregestational	1 (374)	1 (288)
Gestational	1 (534)	1 (371)
Antidiabetic medication use with no further information	<1 (54)	<1 (42)
Pre-eclampsia	4 (2,570)	4 (1,875)
Umbilical cord knot	1 (956)	1 (691)
Bleeding during pregnancy	5 (3,468)	5 (2,497)
Delivery outcomes		
Prolonged labor	31 (21,938)	31 (16,432)
Instrument-assisted	9 (6,627)	10 (5,084)
Caesarian	6 (4,515)	6 (3,210)

Induced	13 (9,249)	13 (6,701)
Nonvertex	8 (5,929)	8 (4,358)
Neonatal outcomes		
Birth weight (kg)	3.61 (0.54)	3.62 (0.53)
Small birth length	5 (3,796)	5 (2,712)
Large birth length	22 (15,211)	22 (11,347)
Preterm	4 (2,607)	3 (1,707)
Postmature	15 (10,394)	15 (7,921)
Small-for-gestational-age	4 (2,916)	4 (2,005)
Large-for-gestational-age	28 (19,506)	28 (14,546)

Note. NOK = Norwegian Krone. The unit of observation is pregnancy (some MoBa mothers were enrolled in MoBa more than once). There were 60,852 unique mothers in Dataset 1 (during pregnancy) and 45,689 unique mothers in Dataset 2 (lifetime). Means and standard deviations are given for parity, age, and birth weight.

Table 2

Association Between Maternal Eating Disorder Exposure During Pregnancy and Perinatal Outcomes (N=70,881)

	AN		BN	
	1	2	1	2
Outcome	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Pregnancy				
Diabetes	0.97 (0.40, 2.32)	0.97 (0.41, 2.37)	1.59 (1.11, 2.29)	1.57 (1.09, 2.26)
Pre-eclampsia	0.37 (0.17, 0.82)	0.38 (0.17, 0.84)	1.04 (0.80, 1.35)	1.03 (0.79, 1.35)
Umbilical cord knot	1.19 (0.53, 2.64)	1.19 (0.53, 2.64)	1.17 (0.77, 1.76)	1.17 (0.77, 1.76)
Bleeding	1.13 (0.74, 1.72)	1.13 (0.74, 1.72)	1.16 (0.94, 1.44)	1.16 (0.94, 1.44)
Delivery				
Prolonged labor	**0.80 (0.69, 0.93)****	**0.80 (0.68, 0.93)****	1.03 (0.95, 1.10)	1.03 (0.96, 1.11)
Instrument-assisted	0.81 (0.59, 1.11)	0.81 (0.59, 1.11)	0.89 (0.75, 1.05)	0.89 (0.75, 1.05)
Caesarian	**1.52 (1.11, 2.10)****	**1.52 (1.10, 2.10)***	1.23 (1.02, 1.47)	1.22 (1.02, 1.47)
Induced	0.80 (0.60, 1.06)	0.80 (0.60, 1.06)	**1.21 (1.07, 1.36)****	**1.21 (1.07, 1.37)****
Nonvertex	1.06 (0.78, 1.44)	1.06 (0.78, 1.44)	1.19 (1.02, 1.40)	1.19 (1.02, 1.40)
Neonatal				
Birth weight	**0.74 (0.68, 0.82)*****	0.95 (0.92, 0.99)	1.00 (0.96, 1.04)	1.01 (0.98, 1.03)
Small birth length	**1.64 (1.22, 2.19)****	**1.62 (1.20, 2.14)****	0.92 (0.73, 1.16)	0.91 (0.73, 1.15)
Large birth length	**0.58 (0.44, 0.77)*****	**0.61 (0.46, 0.80)*****	1.03 (0.93, 1.14)	1.03 (0.93, 1.14)
Preterm	1.39 (0.93, 2.07)	1.40 (0.94, 2.10)	0.79 (0.59, 1.08)	0.79 (0.59, 1.08)
Postmature	**0.47 (0.33, 0.67)*****	**0.47 (0.33, 0.67)*****	1.02 (0.90, 1.15)	1.01 (0.90, 1.15)
Small-for-gestational-age	**1.54 (1.09, 2.17)***	1.06 (0.93, 1.21)	0.90 (0.69, 1.17)	0.99 (0.89, 1.09)
Large-for-gestational-age	**0.36 (0.27, 0.50)*****	0.93 (0.80, 1.09)	1.01 (0.93, 1.10)	1.02 (0.98, 1.06)

Note. AN = anorexia nervosa; BED = binge-eating disorder; BN = bulimia nervosa; CI = confidence interval; FDR = false discovery rate; PD = purging disorder; RR = relative risk. *FDR $p < 0.05$ **FDR $p < 0.01$ ***FDR $p < 0.001$. Two nested models were fitted: Model 1 restricted the covariates to maternal characteristics of household income, marital status, education, smoking during pregnancy, parity, and age; Model 2 added the grandmaternal pregnancy covariate of interest. The referent group is pregnant women without eating disorders. A significant result in Model 1 indicates that maternal eating disorder exposure during pregnancy is associated with the outcome. A significant result in Model 2 indicates that the association between maternal eating disorder exposure during pregnancy and the outcomes is robust when controlling (i.e., statistically adjusting) for familial transmission of perinatal phenotypes.

Table 2 continued…

	BED		PD	
	1	2	1	2
Outcome	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Pregnancy				
Diabetes	**1.53 (1.20, 1.94)*****	**1.52 (1.19, 1.94)***	0.98 (0.14, 6.70)	0.99 (0.14, 6.75)
Pre-eclampsia	1.15 (0.97, 1.36)	1.16 (0.98, 1.37)	1.11 (0.37, 3.35)	1.08 (0.36, 3.21)
Umbilical cord knot	0.99 (0.74, 1.32)	0.99 (0.74, 1.32)	2.86 (0.96, 8.49)	2.88 (0.97, 8.55)
Bleeding	0.96 (0.83, 1.13)	0.96 (0.83, 1.13)	1.45 (0.62, 3.38)	1.45 (0.62, 3.37)
Delivery				
Prolonged labor	1.04 (0.99, 1.09)	1.04 (0.99, 1.09)	1.05 (0.75, 1.46)	1.06 (0.76, 1.47)
Instrument-assisted	0.99 (0.88, 1.10)	0.99 (0.88, 1.10)	1.14 (0.57, 2.29)	1.16 (0.58, 2.33)
Caesarian	**1.19 (1.06, 1.35)***	**1.19 (1.06, 1.35)***	1.35 (0.62, 2.94)	1.34 (0.61, 2.92)
Induced	**1.18 (1.09, 1.28)****	**1.18 (1.09, 1.28)****	1.28 (0.76, 2.14)	1.25 (0.75, 2.07)
Nonvertex	1.04 (0.93, 1.16)	1.04 (0.93, 1.16)	1.54 (0.83, 2.83)	1.54 (0.84, 2.84)
Neonatal				
Birth weight	**1.07 (1.05, 1.10)*****	0.99 (0.98, 1.01)	0.96 (0.82, 1.12)	1.01 (0.96, 1.07)
Small birth length	**0.72 (0.61, 0.85)*****	**0.72 (0.61, 0.85)****	1.05 (0.45, 2.42)	1.02 (0.44, 2.40)
Large birth length	**1.20 (1.13, 1.28)*****	**1.19 (1.12, 1.26)*****	0.65 (0.36, 1.17)	0.65 (0.37, 1.17)
Preterm	0.98 (0.82, 1.17)	0.98 (0.83, 1.17)	0.33 (0.05, 2.36)	0.32 (0.05, 2.30)
Postmature	1.05 (0.97, 1.14)	1.05 (0.97, 1.14)	0.99 (0.56, 1.76)	0.95 (0.54, 1.68)
Small-for-gestational-age	**0.73 (0.60, 0.88)****	0.93 (0.87, 0.99)	1.34 (0.58, 3.11)	1.43 (0.75, 2.74)
Large-for-gestational-age	**1.19 (1.14, 1.26)*****	**1.04 (1.01, 1.06)****	0.91 (0.60, 1.37)	0.89 (0.69, 1.14)

Table 3

*Association Between Lifetime Maternal Eating Disorder Exposure and Perinatal Outcomes (*N=*52,348)*

	BN		BED	
	1	2	1	2
Outcome	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Pregnancy				
Diabetes	**1.78 (1.23, 2.57)****	**1.78 (1.23, 2.57)****	**2.25 (1.74, 2.92)*****	**2.21 (1.70, 2.87)*****
Pre-eclampsia	1.14 (0.87, 1.49)	1.13 (0.87, 1.48)	**1.31 (1.08, 1.60)***	**1.32 (1.08, 1.61)***
Umbilical cord knot	1.33 (0.89, 1.99)	1.33 (0.89, 1.99)	1.20 (0.86, 1.67)	1.19 (0.86, 1.67)
Bleeding	0.96 (0.75, 1.22)	0.96 (0.75, 1.22)	0.97 (0.79, 1.18)	0.97 (0.79, 1.18)
Delivery				
Prolonged labor	0.95 (0.88, 1.03)	0.95 (0.88, 1.03)	**1.08 (1.02, 1.15)***	**1.08 (1.02, 1.15)***
Instrument-assisted	0.84 (0.71, 1.00)	0.85 (0.71, 1.01)	0.96 (0.83, 1.10)	0.96 (0.84, 1.10)
Caesarian	1.19 (0.99, 1.44)	1.19 (0.98, 1.44)	**1.32 (1.14, 1.53)***	**1.32 (1.14, 1.53)***
Induced	**1.26 (1.11, 1.43)****	**1.26 (1.11, 1.42)****	**1.17 (1.05, 1.29)***	**1.17 (1.05, 1.29)***
Nonvertex	1.05 (0.88, 1.25)	1.05 (0.88, 1.25)	0.97 (0.84, 1.12)	0.97 (0.84, 1.12)
Neonatal				
Birth weight	0.99 (0.95, 1.03)	0.98 (0.96, 1.00)	**1.12 (1.09, 1.15)*****	1.01 (1.00, 1.03)
Small birth length	0.90 (0.71, 1.15)	0.90 (0.71, 1.15)	0.91 (0.75, 1.11)	0.91 (0.75, 1.10)
Large birth length	0.87 (0.78, 0.97)	0.87 (0.78, 0.97)	**1.25 (1.17, 1.35)*****	**1.25 (1.17, 1.34)*****
Preterm	1.00 (0.74, 1.34)	0.99 (0.74, 1.33)	1.13 (0.90, 1.40)	1.13 (0.90, 1.40)
Postmature	0.94 (0.83, 1.08)	0.95 (0.83, 1.08)	1.06 (0.96, 1.17)	1.06 (0.96, 1.17)
Small-for-gestational-age	0.88 (0.66, 1.16)	1.02 (0.90, 1.15)	0.88 (0.70, 1.11)	1.00 (0.91, 1.09)
Large-for-gestational-age	0.96 (0.88, 1.05)	1.00 (0.96, 1.04)	**1.25 (1.18, 1.33)*****	1.03 (1.00, 1.06)

Note. BED = binge-eating disorder; BN = bulimia nervosa; CI = confidence interval; FDR = false discovery rate; PD = purging disorder; RR = relative risk. *FDR $p < 0.05$ **FDR $p < 0.01$ ***FDR $p < 0.001$. Two nested models were fitted: Model 1 restricted the covariates to maternal characteristics of household income, marital status, education, smoking during pregnancy, parity, and age; Model 2 added the grandmaternal pregnancy covariate of interest. The referent group is pregnant women without a lifetime history of eating disorders. Significant results in Model 1 indicate that maternal eating disorder exposure during pregnancy is associated with adverse outcomes. Significant results in Model 2 indicate that the association between maternal eating disorder exposure during pregnancy and adverse outcomes is robust when controlling (i.e., statistically adjusting) for familial transmission of perinatal phenotypes.

Table 3 continued…

	PD	
	1	2
Outcome	RR (95% CI)	RR (95% CI)
Pregnancy		
Diabetes	0.71 (0.23, 2.18)	0.71 (0.23, 2.20)
Pre-eclampsia	0.81 (0.44, 1.50)	0.82 (0.45, 1.52)
Umbilical cord knot	0.91 (0.34, 2.40)	0.91 (0.34, 2.40)
Bleeding	1.07 (0.67, 1.71)	1.07 (0.67, 1.71)
Delivery		
Prolonged labor	0.99 (0.85, 1.15)	0.99 (0.85, 1.15)
Instrument-assisted	0.81 (0.57, 1.16)	0.82 (0.57, 1.17)
Caesarian	**1.65 (1.18, 2.32)***	**1.65 (1.17, 2.31)***
Induced	1.18 (0.91, 1.53)	1.18 (0.91, 1.53)
Nonvertex	1.41 (1.04, 1.90)	1.40 (1.03, 1.89)
Neonatal		
Birth weight	1.01 (0.94, 1.09)	1.02 (0.99, 1.05)
Small birth length	1.33 (0.90, 1.95)	1.34 (0.91, 1.98)
Large birth length	0.97 (0.79, 1.20)	0.97 (0.79, 1.20)
Preterm	1.53 (0.93, 2.51)	1.51 (0.92, 2.48)
Postmature	0.98 (0.75, 1.27)	0.98 (0.75, 1.27)
Small-for-gestational-age	**1.80 (1.22, 2.66)***	1.19 (0.98, 1.45)
Large-for-gestational-age	0.98 (0.82, 1.16)	1.00 (0.91, 1.09)

Table 4.

Pregravid BMI and Gestational Weight Gain as Mediators of the Statistically Significant Associations Between Maternal Eating Disorders and Adverse Perinatal Outcomes

Maternal eating disorder		Outcome	Maternal eating disorder → pregravid BMI (Path a_1)	Maternal eating disorder → gestational BMI gain (Path a_2)	Pregravid BMI → outcome (Path b_1)	Gestational BMI gain → outcome (Path b_2)
			b (95% CI)	*b* (95% CI)	OR (95% CI)	OR (95% CI)
During pregnancy	AN	Prolonged labor	**-6.15 (-6.56, -5.75)*****	**0.53 (0.42, 0.64)*****	**1.03 (1.02, 1.03)** ***	**1.08 (1.06, 1.09)*****
		Caesarian	**-6.14 (-6.55, -5.73)** ***	**0.53 (0.42, 0.64)*****	**1.05 (1.04, 1.06)** ***	**1.05 (1.03, 1.08)*****
		Small birth length	**-6.15 (-6.57, -5.74)*****	**0.55 (0.44, 0.66)*****	**0.96 (0.95, 0.97)*****	**0.91 (0.89, 0.94)*****
		Large birth length	**-6.14 (-6.55, -5.72)*****	**0.55 (0.44, 0.66)*****	**1.06 (1.05, 1.06)*****	**1.10 (1.08, 1.12)*****
		Postmature	**-6.14 (-6.55, -5.74)*****	**0.53 (0.42, 0.64)*****	**1.02 (1.02, 1.03)*****	**1.05 (1.04, 1.08)*****
	BN	Induced	**1.21 (0.99, 1.43)*****	**0.26 (0.20, 0.31)**	**1.07 (1.06, 1.07)*****	**1.07 (1.05, 1.09)*****
	BED	Diabetes	**2.97 (1.82, 2.11)*****	**0.17 (0.14, 0.21)** ***	**1.14 (1.13, 1.15)*****	**1.16 (1.11, 1.21)*****
		Caesarian	**1.97 (1.82, 2.11)*****	**0.17 (0.14, 0.21)*****	**1.05 (1.04, 1.06)*****	**1.05 (1.03, 1.08)*****
		Induced	**1.97 (1.82, 2.11)*****	**0.17 (0.14, 0.21)*****	**1.07 (1.06, 1.07)*****	**1.07 (1.05, 1.09)*****
		Small birth length	**1.93 (1.79, 2.08)*****	**0.18 (0.14, 0.22)*****	**0.96 (0.95, 0.97)*****	**0.91 (0.88, 0.94)*****
		Large birth length	**1.93 (1.78, 2.08)*****	**0.18 (0.14, 0.22)*****	**1.06 (1.05, 1.06)*****	**1.10 (1.08, 1.12)*****
		Large-for-gestational-age	**1.94 (1.79, 2.08)*****	**0.18 (0.14, 0.22)*****	**1.08 (1.08, 1.09)*****	**1.15 (1.13, 1.17)*****
Lifetime	BN	Diabetes	0.12 (-0.10, 0.34)	**0.18 (0.12, 0.24)*****	**1.13 (1.12, 1.15)*****	**1.16 (1.09, 1.22)*****
		Induced	0.12 (-0.10, 0.34)	**0.18 (0.12, 0.24)*****	**1.07 (1.06, 1.07)*****	**1.07 (1.04, 1.09)*****
	BED	Diabetes	**3.25 (3.07, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.13 (1.12, 1.15)*****	**1.16 (1.09, 1.22)*****
		Pre-eclampsia	**3.25 (3.08, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.10 (1.09, 1.11)*****	**1.10 (1.05, 1.14)*****
		Prolonged labor	**3.25 (3.07, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.03 (1.03, 1.03)*****	**1.07 (1.05, 1.09)*****
		Caesarian	**3.25 (3.08, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.04 (1.04, 1.04)*****	**1.06 (1.03, 1.09)*****
		Induced	**3.25 (3.08, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.07 (1.06, 1.07)*****	**1.07 (1.04, 1.09)*****
		Large birth length	**3.25 (3.07, 3.43)*****	**-0.08 (-0.13, -0.03)*****	**1.06 (1.05, 1.06)*****	**1.10 (1.08, 1.12)*****
	PD	Caesarian	-0.39 (-0.83, 0.06)	**0.17 (0.06, 0.29)*****	**1.04 (1.04, 1.04)*****	**1.06 (1.03, 1.09)*****

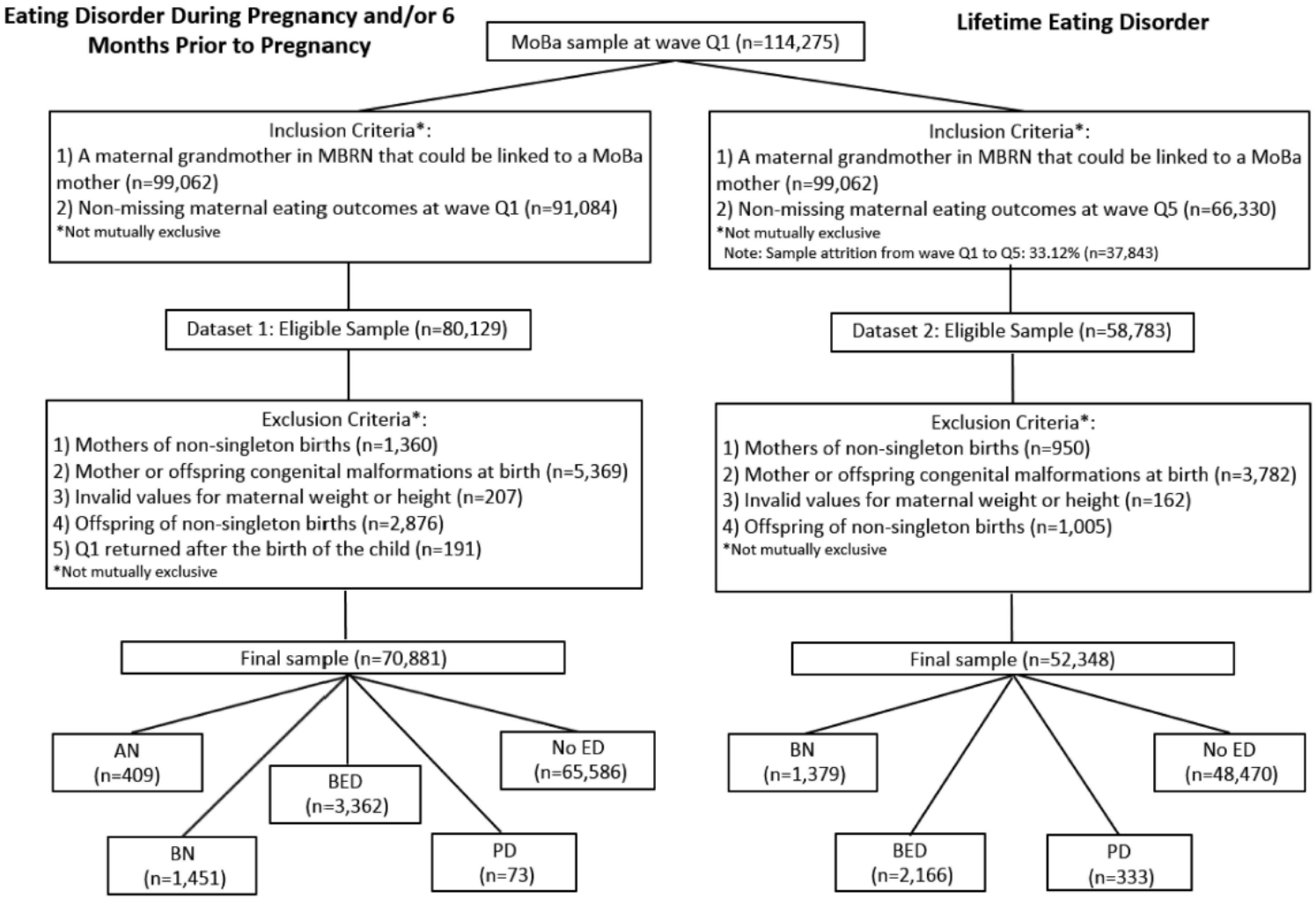
Note. AN = anorexia nervosa; BED = binge-eating disorder; BN = bulimia nervosa; CI = confidence interval; FDR = false discovery rate; PD = purging disorder; RR = relative risk. $^{*}p < 0.05$ $^{**}p < 0.01$ $^{***}p < 0.001$. N=70,881 pregnancies for during pregnancy analyses and N=52,348 pregnancies for lifetime analyses. Path a_1: association between exposure and mediator 1 (i.e., maternal ED →

pregravid BMI). Path a_2: association between exposure and mediator 2 (i.e., maternal eating disorder→ gestational weight gain). Path b_1: association between mediator 1 and outcome (i.e., pregravid BMI → perinatal outcome). Path b_2: association between mediator 2 and outcome (i.e., gestational BMI gain → perinatal outcome). Path *c*': the difference between Path *c* ('total effect') and the indirect effects (Path $a_1 \times b_1$ and Path $a_2 \times b_2$). Each model includes the multicategory eating disorder predictor variable, maternal covariates of household income, marital status, education, smoking during pregnancy, parity, and age, a grandmaternal perinatal covariate, and the mediators. †The PROCESS macro does not output a *t* statistic or *p* value for the indirect effect, just a bootstrapped confidence interval, so only significance at the 0.05 level (i.e., *) can be determined.

Table 4 continued…

Maternal eating disorder		Outcome	Maternal eating disorder → Outcome (Path *c*')	Indirect effect via pregravid BMI (Path $a_1 \times b_1$)†	Indirect effect via gestational BMI gain (Path $a_2 \times b_2$)†
			OR (95% CI)	*b* (95% CI)	*b* (95% CI)
During pregnancy	AN	Prolonged labor	0.81 (0.64, 1.01)	**-0.17 (-0.20, -0.15)***	**0.04 (0.03, 0.05)***
		Caesarian	**2.07 (1.46, 2.95)*****	**-0.29 (-0.33, -0.24)***	**0.03 (0.02, 0.05)***
		Small birth length	**1.44 (1.04, 2.01)***	**0.23 (0.14, 0.27)***	**-0.05 (-0.07, -0.03)***
		Large birth length	0.74 (0.54, 1.01)	**-0.34 (-0.36, -0.32)***	**0.05 (0.04, 0.07)***
		Postmature	**0.49 (0.33, 0.73)*****	**-0.17 (-0.20, -0.14)***	**0.03 (0.02, 0.04)***
	BN	Induced	1.13 (0.98, 1.30)	**0.08 (0.06, 0.09)***	**0.02 (0.01, 0.03)***
	BED	Diabetes	1.09 (0.85, 1.40)	**0.26 (0.22, 0.29)***	**0.02 (0.02, 0.04)***
		Caesarian	1.09 (0.95, 1.24)	**0.09 (0.08, 0.11)***	**0.01 (<0.01, 0.02)***
		Induced	1.05 (0.95, 1.16)	**0.13 (0.11, 0.14)***	**0.01 (0.01, 0.02)***
		Small birth length	**0.77 (0.64, 0.91)****	**-0.07 (-0.09, -0.05)***	**-0.02 (-0.02, -0.01)***
		Large birth length	**1.12 (1.03, 1.22)****	**0.11 (0.09, 0.12)***	**0.02 (0.01, 0.02)***
		Large-for-gestational-age	**1.09 (1.01, 1.18)***	**0.15 (0.14, 0.17)***	**0.02 (0.02, 0.04)***
Lifetime	BN	Diabetes	**1.65 (1.14, 2.40)****	0.02 (-0.02, 0.04)	**0.03 (0.01, 0.04)***
		Induced	**1.28 (1.10, 1.49)****	0.01 (-0.01, 0.02)	**0.01 (0.01, 0.02)***
	BED	Diabetes	**1.43 (1.09, 1.88)****	**0.41 (0.36, 0.46)***	**-0.01 (-0.01, -0.01)***
		Pre-eclampsia	0.96 (0.78, 1.18)	**0.31 (0.26, 0.35)***	**-0.01 (-0.01, -0.01)***
		Prolonged labor	1.03 (0.93, 1.14)	**0.10 (0.09, 0.12)***	**-0.01 (-0.01, -0.01)***
		Caesarian	1.17 (0.99, 1.37)	**0.14 (0.12, 0.18)***	**-0.01 (-0.01, -0.01)***
		Induced	0.96 (0.84, 1.09)	**0.22 (0.20, 0.24)***	**-0.01 (-0.01, -0.01)***
		Large birth length	**1.14 (1.03, 1.27)****	**0.18 (0.16, 0.20)***	**-0.01 (-0.01, -0.01)***
	PD	Caesarian	**1.75 (1.21, 2.53)****	-0.02 (-0.04, 0.01)	**0.01 (0.01, 0.02)***

Figure 1. Description of participant flow through the study.



Note: The unit of observation (n) is grandmother-mother-child triad.