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Paternal and maternal birthweight and offspring risk of macrosomia at term gestations: A nationwide population study

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Abstract

Background: There is a paucity of data on whether parents' macrosomia (birthweight ≥4500 g) status influences the risk of macrosomia in the offspring. The role of maternal overweight in the generational effect of macrosomia is not known.

Objective: To estimate the risk of macrosomia by parental birthweight at term and evaluate if this risk varied with maternal body mass index (BMI, kg/m^2) early in pregnancy.

Methods: We used data from the Medical Birth Registry of Norway on all singleton term births (37–42 gestational weeks) during 1967–2017. The primary exposure was parental macrosomia, and the outcome was macrosomia in the second generation. The secondary exposure was maternal BMI. We used binomial regression to calculate relative risk (RR) with a 95% confidence interval. We assessed potential unmeasured confounding and selection bias using a probabilistic bias analysis and performed analyses with and without imputation for variables with missing values.

Results: The data included 647,957 singleton parent-offspring trios born at term. The prevalence of macrosomia was 3.2% (n = 41,396) in the parental generation and 4.0% (n = 25,673) in the offspring generation. Macrosomia in parents was associated with an increased risk of macrosomia in offspring, with the RR for both parents were born macrosomic being 6.53 (95% confidence interval [CI] 5.31, 8.05), only mother macrosomic 3.37 (95% CI 3.17, 3.57) and only father macrosomic RR 2.22 (95% CI 2.12, 2.33). These risks increased by maternal BMI in early pregnancy: if both parents were born macrosomic, 17% of infants were macrosomic among mothers with normal BMI. If both parents were macrosomic and the mothers were obese, 31% of offspring were macrosomic. Macrosomia-related adverse outcomes did not differ with parental macrosomia status.

Conclusions: Parents' weight at birth and maternal BMI appear to be strongly associated with macrosomia in the offspring delivered at term gestations.

KEYWORDS
foetal macrosomia, generational, birthweight, pregnancy, risk factors, shoulder dystocia

1 | BACKGROUND

Macrosomia, often defined as birthweight of ≥4500 g, is an important risk factor for delivery complications such as shoulder dystocia, labour dystocia, and postpartum haemorrhage.[1–3] Large foetal size may be challenging to assess before delivery, especially in primiparas.[4] Known risk factors include a previous macrosomic offspring, maternal overweight, diabetes mellitus, and post-term delivery.[5]

High maternal birthweight has been associated with high offspring birthweight,[6,7] but whether high birthweight in both parents contributes to the risk of macrosomia is still unclear. Maternal overweight and obesity are strong risk factors for macrosomia,[3] and maternal overweight and obesity hamper our precision in the clinical judgement of fetal size.[8] It is not known if maternal overweight plays a role in the transgenerational aggregation of macrosomia.

Recall of own birthweight has been found to be quite reliable, and precise enough to be of value in risk assessment or judging expected birthweight in the next generation.[9] The validity of the birthweight variable in the Medical Birth Registry of Norway (MBRN) has been shown to be high,[10] and information on parents' birthweight may be an underutilised opportunity to identify the risk of macrosomia. In Norway, all who are born after 1966 can access their own birth record in the MBRN by using their smartphone or personal computer and find their registered birthweight.[11] Our objective was to estimate the risk of macrosomia (here defined as birthweight ≥4500 g), based on paternal and maternal birthweight and evaluate if this risk varied with maternal body mass index (BMI, kg/m^2) in early pregnancy.

Synopsis

Study question

Can information on parents' birthweight and maternal BMI be helpful for identifying pregnancies at high risk of macrosomia at term gestation?

What is already known

Offspring birthweight is correlated with maternal birthweight, and to a lesser degree paternal birthweight. Maternal overweight and obesity are associated with high birthweight in the offspring.

What this study adds

Information on parents' birthweight and maternal prepregnancy BMI helps to identify pregnancies with a high risk of macrosomia at term gestation.

2 | METHODS

2.1 | Study population and data sources

This nationwide population-based cohort included all singleton births with gestational age between 259 (37) and 300 days (<43 weeks), registered in the MBRN from 1983 to 2017 to parents (first generation) who were born in Norway between 1967 and 2002. Exclusion and inclusions in the study population are shown in Figure 1. The data included 647,957 singleton parent-offspring trios. We restricted the generational files to the first three births to the same parents in the second generation. The MBRN was established in 1967 and collects information on birth outcomes, including birthweight, in addition to maternal background characteristics and health in all births in Norway.[12]

Statistics Norway[13] collects mandatorily reported administrative data, including years and level of education. A personal identification number (PIN) is issued to all residents in Norway at birth or immigration. This PIN is used in all public registers and health care and enables linkages of individual-level information across different registries.

2.1.1 | Exposure

The primary exposure was parental macrosomia, defined as a birthweight ≥4500 g and the secondary exposure was maternal BMI (Figure S1).

2.1.2 | Outcome

The outcome was macrosomia in the second generation. In secondary analyses, we assessed the risk of foetal macrosomia-related complications defined as shoulder dystocia, transfer to neonatal care unit, or low 5-min Apgar score (<4) and maternal macrosomia-related complications defined as labour dystocia, post-partum haemorrhage >1500 mL or blood transfusion, and perineal laceration (third or fourth degree), or uterine atonic bleeding combined into one fetal and one maternal composite adverse outcome (yes/no).

2.1.3 | Covariates

The determination of confounders was based on a directed acyclic graph (Figure S1). Possible confounders were considered apriori for the association between parental macrosomia and macrosomic offspring. These included factors that tend to aggregate across generations or have a potential underlying heritable susceptibility. For the delivery in the second generation, we obtained information on maternal and paternal age, as well as birth order (1, 2, or ≥3), gestational age at delivery, diabetes mellitus (any), other medical conditions (chronic hypertension, rheumatoid arthritis, epilepsy, and asthma),

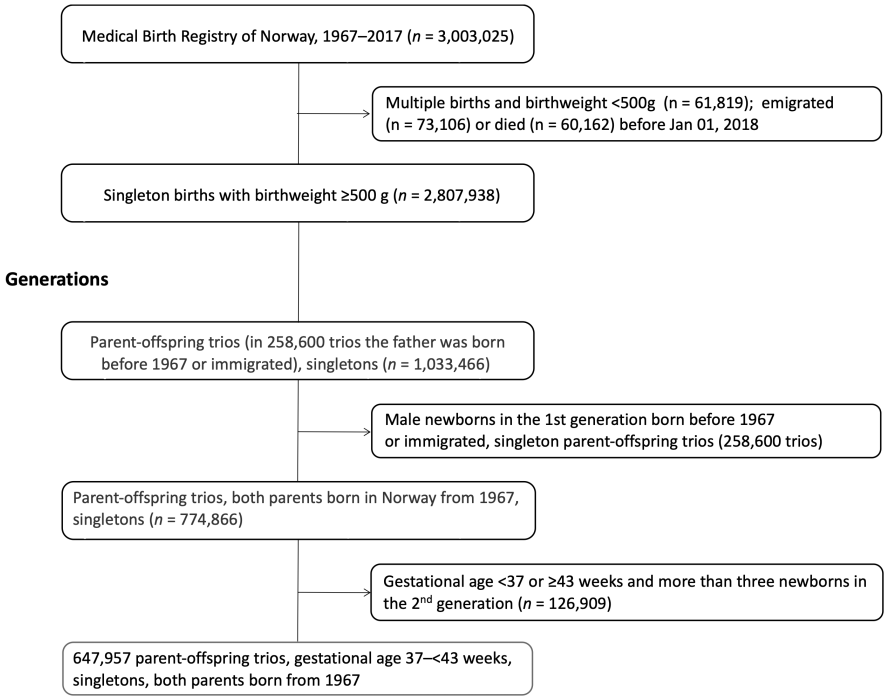

FIGURE 1 Flow diagram of the study sample from the Medical Birth Registry of Norway 1967–2017.

and year of birth (1983–2005, 2006–2011, 2012–2017). After 1999, the MBRN collected information on maternal smoking at the beginning of pregnancy (no, sometimes, daily, or "declines to give information about smoking habits") and after 2006, on maternal BMI in the first trimester. From Statistics Norway,[13] we obtained information on the highest maternal and paternal educational levels until 2013 (categorised as ≤13, 14–17, and ≥18 years).

2.2 | Statistical analysis

We calculated the proportion of infants in the second generation who were macrosomic (birthweight ≥4500 g) within strata of parental birthweight categories: (i) both parents' birthweight <4500 g (reference); (ii) mother <4500 g and father ≥4500 g; (iii) mother ≥4500 g and father <4500 g; and (iv) both parents ≥4500 g.

We fit a multilevel log-binomial regression model from which we derived the relative risk (RR) for a macrosomic offspring by the 4-level parental macrosomia (described above). To account for the hierarchical nature of the family data and to avoid underestimation of standard errors, the data were organised into three levels in the multilevel regression analyses: current delivery (level 1), parent in the second generation (level 2), and grandparent (parent in the first generation (level 3).

We present unadjusted estimates and estimates adjusted for parity, marital status, diabetes mellitus, other medical conditions in pregnancy, maternal and paternal age, and year of birth (1983–2005, 2006–2011, 2012–2017). In supplementary analyses, we also adjusted for the educational attainment of mother and father, smoking, and BMI at the start of pregnancy in the subsample of the second generation born after 2006 when this information became available. We also compared intergenerational aggregation with and without multiple imputed data for the covariates maternal BMI and smoking at the start of pregnancy. We calculated the proportions with macrosomia by parental birthweight within strata of maternal pre-pregnancy BMI; <18.5, 18.5–24.9, 25–29.9, and ≥30.

In secondary analyses, we assessed the risk of macrosomia-related adverse outcomes in macrosomic deliveries in the second generation by parental birthweight groups.

Statistical analyses were conducted using SPSS (version 27), MLwiN (version 3.05), and R package *episensr* version 1.1.0.[14]

2.3 | Missing data

For most variables, there were no missing data, as those with no recorded characteristics were coded as "no" (Table 1). Among births after 1999, when reports of smoking were added to the birth record, the missing proportion was 13% (71,534 of 559,242) for smoking at the start of pregnancy. For births after 2006, when maternal height and weight were added to the birth record, this was not recorded at all clinics in the first years, and the proportion of missing data on BMI in early pregnancy was 49% (188,480 of 382,774). We used multiple imputations with the Markov Chain Monte Carlo method to impute missing data on maternal BMI and smoking.[15] We generated 60 imputation datasets based on 95 variables (family structure variables: grandparent-, parent- and offspring ID number, demographic information, and perinatal complications and characteristics in both generations). We also compared intergenerational aggregation of macrosomia and without multiple imputed data for the covariates maternal BMI and smoking at the start of pregnancy.

TABLE 1 Characteristics of the study population (the number of births included in the second generation is 647,957): Medical Birth Registry of Norway, 1967–2017; singleton births 37–42 weeks of gestation.

Characteristic	No parent macrosomic[d] (*n* = 607,171)	Father macrosomic (*n* = 27,287)	Mother macrosomic (*n* = 12,889)	Both macrosomic (*n* = 610)
Maternal age (years) at birth, No. (%)				
<25	150,419 (24.8)	6314 (23.1)	3140 (24.4)	170 (27.9)
25–29	225,938 (37.2)	10,455 (38.3)	4851 (37.6)	237 (38.9)
30–34	172,463 (28.4)	7900 (29.0)	3658 (28.4)	148 (24.3)
35–39	52,948 (8.7)	2351 (8.6)	1139 (8.8)	52 (8.5)
≥40	5403 (0.9)	267 (1.0)	101 (0.8)	3 (0.5)
Paternal age (years) at birth, No. (%)				
<25	86,508 (14.2)	3897 (14.3)	1738 (13.5)	95 (15.6)
25–29	196,461 (32.4)	9131 (33.5)	4020 (31.2)	199 (32.6)
30–34	205,662 (33.9)	9209 (33.7)	4454 (34.6)	218 (35.7)
35–39	94,398 (15.5)	4094 (15.0)	2066 (16.0)	71 (11.6)
≥40	24,142 (4.0)	956 (3.5)	611 (4.7)	27 (4.4)
Birth order, no (%)				
1	289,266 (47.6)	12,824 (47.0)	6214 (48.2)	290 (47.5)
2	227,753 (37.5)	10,232 (37.5)	4764 (37.0)	236 (38.7)
≥3	90,152 (14.8)	4231 (15.5)	1911 (14.8)	84 (13.8)
Maternal educational (years) No. (%)				
<14	281,420 (46.3)	12,182 (44.6)	5833 (45.3)	262 (43.0)
14–17	259,002 (42.7)	12,013 (44.0)	5690 (44.1)	295 (48.4)
≥18	65,935 (10.9)	3054 (11.2)	1344 (10.4)	53 (8.7)
Unknown/not recorded	814 (0.1)	38 (0.1)	22 (0.2)	0
Paternal educational level (years) No. (%)				
<14	359,428 (59.2)	15,841 (58.1)	7624 (59.2)	364 (59.7)
14–17	176,625 (29.1)	8149 (29.9)	3905 (30.3)	188 (30.8)
≥18	699,15 (11.5)	3252 (11.9)	1324 (10.3)	57 (9.3)
Unknown/not recorded	1203 (0.2)	45 (0.2)	36 (0.3)	1 (0.2)
Maternal diabetes, No. (%)	12,262 (2.0)	565 (2.1)	311 (2.4)	15 (2.5)
Other medical conditions, No. (%)[a]	41,623 (6.9)	1835 (6.7)	846 (6.6)	28 (4.6)
Maternal BMI at start of pregnancy (kg/m^2), No.[b] (%)				
<18.5	6041 (1.7)	314 (1.9)	62 (0.8)	1 (0.3)
18.5–24.9	111,573 (31.2)	5201 (31.2)	2350 (29.1)	114 (30.2)
25.0–29.9	40,583 (11.4)	1945 (11.4)	1148 (14.2)	45 (11.9)
≥30.0	22,951 (6.4)	1069 (6.4)	703 (8.7)	39 (10.3)
Unknown/not recorded	176,207 (49.3)	8150 (48.9)	3799 (47.1)	179 (47.4)
Gestational age in days, median (IQR)	283 (276–289)	283 (276–289)	284 (278–290)	284 (277–289)
Marital status, No. (%)				
Married	219,345 (36.1)	10,549 (38.7)	4811 (37.3)	255 (41.8)
Cohabiting	342,267 (56.4)	14,959 (54.8)	7206 (55.9)	317 (52.0)
Other	45,559 (7.5)	1779 (6.5)	872 (6.8)	38 (6.2)
Maternal smoking at start of pregnancy, No. (%)[c]				
No	391,941 (74.9)	18,318 (76.9)	8746 (76.7)	432 (80.3)
Sometimes	8189 (1.6)	351 (1.5)	193 (1.7)	7 (1.3)

TABLE 1 (Continued)

Characteristic	No parent macrosomic[d] (n = 607,171)	Father macrosomic (n = 27,287)	Mother macrosomic (n = 12,889)	Both macrosomic (n = 610)
Daily	56,232 (10.7)	2186 (9.2)	1073 (9.4)	40 (7.4)
Declined to provide information	67,110 (12.8)	2970 (12.5)	1395 (12.2)	59 (11.0)
Offspring sex, No. (%)				
Male	310,933 (51.2)	14,125 (51.8)	6625 (51.4)	300 (49.2)
Female	296,238 (48.8)	13,162 (48.2)	6264 (48.6)	310 (50.8)
Year of birth second generation, No. (%)				
1983–2005	24,9816 (41.1)	10,608 (38.9)	4827 (37.5)	232 (38.0)
2006–2011	18,4210 (30.3)	8401 (30.8)	3953 (30.7)	197 (32.3)
2012–2017	17,3145 (28.5)	8278 (30.3)	4109 (31.9)	181 (29.7)

[a]The following maternal conditions were included as a composite variable: Chronic hypertension, rheumatoid arthritis, epilepsy and asthma.
[b]Recorded from 2006 onwards.
[c]Recorded from 1999 onwards.
[d]Macrosomia: Birthweight ≥4500 g.

2.4 | Probabilistic bias analyses

Our database lacks information on maternal weight gain, which has been associated with birthweight independently of maternal BMI at the start of pregnancy, although BMI may modify the effect of weight gain.[16] It cannot be ruled out that the groups with both parents born in Norway from 1967 onwards (774,866 parent-offspring trios) and the subgroup with complete data on maternal BMI (194,139 trios) are not representative of the general population (1,033,466 trios). To address potential unmeasured confounding and selection biases, we performed a probabilistic bias analysis for the simulation of summary-level data with 100,000 simulations.[17]

2.4.1 | Unmeasured confounding

Our database contains several possible confounders but lacks information on maternal weight gain during pregnancy, which has been associated with birthweight independently of maternal BMI at the start of pregnancy, although BMI may modify the effect of weight gain.[16] We, therefore, wanted to quantify the effect of unmeasured confounding by maternal weight gain on an intergenerational aggregation of macrosomia on the maternal side, using probabilistic bias analysis.

In the confounding bias analyses, we assumed a triangular probability distribution function with the following bias parameters: Proportions of excessive weight gain among exposed (≥4500 g in the first generation), of 0.3171, 0.5235, and 0.4167 (minimum, maximum, and mode, respectively), and correspondingly 0.2289, 0.2679, and 0.2479 among unexposed (<4500 g)[18] and a risk ratio for a confounder-outcome association of 2.86 (95% CI 2.22, 3.68) in the same birth.[19] To adapt this risk ratio from the literature to have its exposure in the preceding generation, we assumed a reduced ln(risk ratio) to between 20 and 50%, corresponding to scenarios with risk ratios between 1.23 (1.17, 1.30) and 1.69 (1.49, 1.92).

2.4.2 | Selection bias

Although our study was population-based, it cannot be ruled out that the selections from the total study group with 1,033,466 parent-offspring trios (Figure 1) to the main study group with both parents born in Norway from 1967 onwards (647,957 trios) and the group with complete data on maternal BMI (194,139 trios) resulted in differential exposure-outcome relations. To quantify the impact of selection bias, we used a triangular distribution in the probabilistic bias analyses.

We specified the following selection bias parameters: For the selection of the main study group with 647,957 trios, the selection RR calculated from the data was 0.98. We then varied minimum and maximum values with scenarios between 0.93–1.13 and 0.63–1.43, respectively.

For the selection from the total study group (1,033,466 trios) to the group with complete maternal BMI data with 194,139 trios, the selection RR was near 1 (1.01). We varied minimum and maximum values between 0.99–1.03 and 0.60–1.40, respectively.

2.5 | Sensitivity analysis

We performed a sensitivity analysis using a complete-case series including only births in the second generation with available information on maternal BMI and presented unadjusted and adjusted results for the following covariates: marital status, birth order, diabetes mellitus, other medical conditions in pregnancy, period of birth, maternal, and paternal age.

2.6 | Ethics approval

The study was approved by The Regional Committee for Medical and Health Ethics of Western Norway (2013/reference number

1484), which waived the need for consent from participants in this registry-based study.

3 | RESULTS

There were 647,957 second-generation singleton term births in the study period with information on both parents' own birthweight (Figure 1). Characteristics of the study population and number of births with available information are presented in Table 1. The prevalence of macrosomia was 3.2% ($n = 41,396$) in the parental generation and 4.0% ($n = 25,673$) in the offspring generation.

Macrosomia in parents was associated with a substantially increased risk of macrosomia in their offspring (Figure 2 and Table 2) (including up to three births in the second generation). Restricting the analysis to the first offspring in the second generation, the corresponding RRs were 8.06 (95% CI 6.20, 10.49) when both parents were macrosomic, 3.84 (95% CI 3.53, 4.19) when only the mother was macrosomic, and 2.34 (95% CI 2.17, 2.53) when only the father was macrosomic (Table S1).

In analyses restricted to complete cases of births in the second generation with available information on maternal BMI results were similar (Table S2). Adjustments for marital status, birth order, diabetes mellitus, other medical conditions in pregnancy, period of birth, maternal and paternal age, maternal and paternal education, and maternal pre-pregnancy BMI had a small influence on the RRs. Adding imputed covariates did not change the estimates substantially (Table S3).

The risk of macrosomia in the second generation given macrosomia in the first increased with maternal BMI at the beginning of pregnancy, shown using a combination variable between parental macrosomia and maternal BMI (Figure 3 and Table 3). If both parents were born macrosomic, 17% of infants were macrosomic among mothers with normal BMI, whereas if both parents were born macrosomic and the mothers were obese, 31% of offspring were macrosomic. If neither parent was macrosomic at birth, 6% of the offspring of obese mothers were macrosomic, while 2% of the offspring of nonobese mothers were macrosomic (Figure 3 and Table 3).

The RR of maternal and fetal macrosomia-related adverse outcomes did not differ with parental macrosomia status (Tables S4 and S5). However, the "No parent macrosomic group" had marginally increased relative risks of fetal complications compared with the "Mother macrosomic group" (Table S5).

For the selections of the main study group with 774,866 trios and the group with complete BMI data (194,139 trios), the probabilistic bias analysis showed little evidence of selection bias. The probabilistic bias analysis for confounding indicated that our data were robust for confounding by maternal weight gain or selection bias (Table 2 and Table S6).

With different scenarios in strengths of unmeasured confounding by maternal weight gain during pregnancy (accounting for both systematic and random error) differences in effects of confounding bias were small (Table S6) and were not different from the unadjusted RRs.

Varying the bias parameters in the selection to the main study group with 774,866 trios had small effects on the bias-adjusted RRs of macrosomia in the second generation and were not different from the unadjusted effects (Table S6).

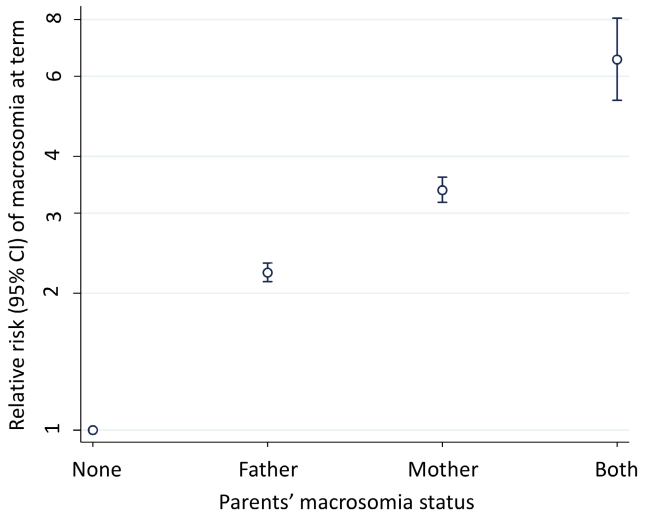

FIGURE 2 Relative risk of offspring macrosomia at term by parental macrosomia status at birth.

3.1 | Comment

3.1.1 | Principal findings

We found a strong paternal and maternal aggregation of macrosomia between generations, and the risk of macrosomia in the second generation increased with maternal BMI at the beginning of pregnancy.

3.1.2 | Strengths of the study

The longitudinal population-based design with prospective birth registry data across two generations excluded potential selection and recall bias. Several variables in the MBRN have been validated, including birthweight.[10] Due to the unique PIN, the record linkage between generations was almost complete. Loss to follow-up was low due to the relatively low emigration and death rates in the birth population (Figure 1). Our probabilistic bias analyses did not indicate selection bias or unmeasured confounding. This was not unexpected as effects of a confounder in the association between macrosomia in both generations, which must be associated with the first generational exposure as well as the outcome in the second generation, are likely to be limited (Figure S1), and adjusted results may not be more informative than the unadjusted. Our study had excellent power for analysis of subgroups even though the prevalence of the main exposure and outcome (birthweight ≥4500 g in the parental and offspring generation)

TABLE 2 Risk of macrosomia in the second generation based on parents' macrosomia status (number of births included in the second generation is 647,957): Medical Birth Registry of Norway, 1967–2017; singleton births 37–42 weeks of gestation.

	Total births	Macrosomia: *n* (%)	Unadjusted	Adjusted[a]	Bias adjusted RR[b]	Bias adjusted RR[c]
Both parents not macrosomic	607,171	21,755 (3.6)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Father macrosomic	27,287	2181 (8.0)	2.22 (2.12, 2.33)	2.23 (2.13, 2.34)	2.01 (1.89, 2.13)	2.21 (2.00, 2.40
Mother macrosomic	12,889	1594 (12.4)	3.37 (3.17, 3.57)	3.44 (3.25, 3.65)	3.28 (3.06, 3.50)	3.43 (2.57, 4.85)
Both parents macrosomic	610	143 (23.4)	6.53 (5.31, 8.05)	6.76 (5.52, 8.29)	7.44 (6.14, 9.00)	6.51 (4.63, 9.58)

[a]Adjusted for maternal age, birth order, marital status, diabetes mellitus, other medical conditions in pregnancy, paternal age, and period of birth.

[b]Relative risk adjusted for unmeasured confounding using probabilistic bias analysis. Scenario with risk ratio for confounder-outcome association = 1.400 (minimum: 1.691, maximum: 1.918).

[c]Selection bias adjusted relative risk using probabilistic bias analysis. Scenario with selection bias relative risk = 0.98 (minimum: 0.63, maximum: 1.43).

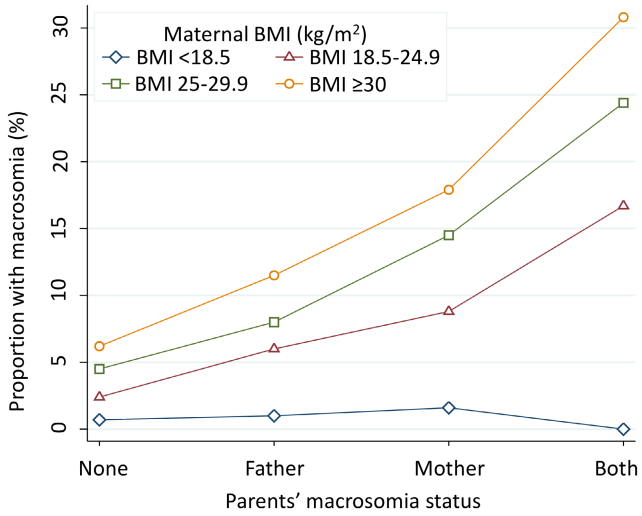

FIGURE 3 Proportion of infants with macrosomia by parental macrosomia status at term birth and maternal BMI in early pregnancy.

was 3.2% and 4.0%, respectively. However, for analysis of extreme macrosomia (birthweight ≥5000 g), with a prevalence in the offspring generation of 0.4%, the numbers were too small for analysis.

3.1.3 | Limitations of the data

As we could only link births from the second generation with parents who were registered in the MBRN with their own births, all parents were born in Norway. This could potentially limit the generalisability to less homogeneous populations, but our probabilistic bias analyses indicated that the selection of the group without fathers who had immigrated to Norway (Figure 1) was not biased. Maternal BMI was only available for births in the second generation after 2006, but our sensitivity analyses indicated that this did not introduce bias in our analyses and that births with BMI available are representative of the total birth population. Information on education was available only until 2013, so pregnancies from 2014 to the end of the study period (2017) may have been registered with a shorter education than attained.

3.1.4 | Interpretation

Our findings suggest that there is an underlying predisposition for being macrosomic at birth which is transferred to the next generation. Being born macrosomic and giving birth to a macrosomic child may share pathophysiological pathways or a sustained environmental and/or genetic background (Figure S1).

Consistent with our results, it has been reported that offspring birthweight is correlated to both maternal and paternal birthweight.[20,21] The intergenerational aggregation of macrosomia on the paternal side suggests that there may be paternal genetic or environmental influences, e.g., over-nutrition shared by other family members, on an intergenerational aggregation of macrosomia. The intergenerational aggregation on the maternal side was higher than on the paternal side, likely at least in part because paternal genes are limited to the foetoplacental unit and the placental bed (decidua).

The finding that the risk of macrosomia in the second generation, given macrosomia in the first, increased with maternal BMI early in pregnancy suggests that maternal BMI modifies intergenerational aggregation of macrosomia (Figure S1, Figure 3, Table 3). Consistently, epidemiological studies have reported a relationship between fetal growth and BMI attained in later life, which may be ascribed to both environmental and genetic influence.[21] Further, it is well known that maternal obesity is associated with fetal overgrowth and fat deposition, possibly related to mechanisms including increased insulin resistance with high fetal glucose and insulin levels.[22,23]

Our findings that parental macrosomia tends to be passed between generations is also consistent with the hypothesis of the fetal origin of adult disease,[24] which proposes that adult disease occurs in response to the intrauterine environment or fetal nutrition, independent of genetic background. Possible mechanisms supported by animal studies include lasting changes in the ratio of fat to lean body mass, pancreatic function, and central nervous system appetite control.[25]

However, our results also lend support to the hypothesis that genes shared between family members (e.g. those affecting insulin metabolism)[26] may increase the risk of both fetal macrosomia and

TABLE 3 The proportion of macrosomia in second-generation infants by the combination of parental macrosomia status and maternal BMI at the start of pregnancy: Medical Birth Registry of Norway, 1967–2017; singleton births 37–42 weeks of gestation.

	Maternal body-mass index (kg/m^2)							
	<18.5		18.5–24.9		25–29.9		≥30	
Macrosomia status in parents	Total births	Macrosomia No. (%)	Total births	Macrosomia No. (%)	Total births	Macrosomia No. (%)	Total births	Macrosomia No. (%)
Up to 3 births in the second generation[a]								
No parent macrosomic	6041	45 (0.7)	111,573	2639 (2.4)	40,583	1809 (4.5)	22,951	1416 (6.2)
Father macrosomic	314	<5 (1.0)	5201	312 (6.0)	1945	155 (8.0)	1069	123 (11.5)
Mother macrosomic	62	<5 (1.6)	2350	206 (8.8)	1148	166 (14.5)	703	126 (17.9)
Both macrosomic	1	0 (0)	114	19 (16.7)	45	11 (24.4)	39	12 (30.8)
Only first birth in the second generation[b]								
No parent macrosomic	3040	16 (0.5)	51,534	746 (1.5)	17,272	485 (2.8)	9595	368 (3.8)
Father macrosomic	164	<5 (1.8)	2428	98 (4.0)	823	35 (4.3)	457	35 (7.7)
Mother macrosomic	31	0 (0)	1089	71 (6.5)	533	58 (10.9)	303	36 (11.9)
Both macrosomic	0	0 (0)	53	7 (13.2)	23	5 (21.7)	14	2 (14.3)

[a]194,139 three first births in the second generation included.

[b]87,359 first births in the second generation included.

obesity in adulthood. Another possible explanation is that eating and physical activity habits shared by family members may cause both fetal macrosomia and adiposity in adulthood.

With information on maternal obesity and parent's macrosomia, it is possible to identify deliveries at high risk of a macrosomic neonate. Information on parents' own birthweight may be useful when considering interventions to reduce delivery complications. In a UK study, universal ultrasound screening for fetal macrosomia was not found to be cost-effective,[27] but it remains to be studied whether selective ultrasound examination using family history and maternal weight improves detection of macrosomia and targeting of interventions.

Birthweight has minor recall bias,[9] and in Norway, all who are born after 1966 have easy and instantaneous access to data on their own birth, including their birthweight.[11] The results from our study show that the combination of maternal BMI and parental birthweight may be of use for risk estimation for offspring macrosomia in a clinical setting. This could potentially increase the possibility of the prevention of macrosomia and related complications. The finding that parents being born macrosomic carried a risk of macrosomia-related complications with the same magnitude as the background population may be counterintuitive, but as shown in Tables S4 and S5, the confidence intervals are overlapping, meaning that having a macrosomic child, regardless of parents' own macrosomia status at birth, carries the risk of macrosomia related complications.

4 | CONCLUSIONS

Information on parents' birthweight and maternal BMI at the beginning of pregnancy may be helpful in identifying pregnancies with a high risk of macrosomia.

AUTHOR CONTRIBUTIONS

SR and CE initiated the project; SR prepared the analytic database, conducted the analyses and wrote the manuscript in collaboration with LEL, CE, EOC, NHM and SHE. EOC contributed to planning of the analyses, interpretation of the results, preparation of figures and finalization of the manuscript. LEL contributed to preparation of the analytic database, planning of the analyses, interpretation and writing of the manuscript. NHM and SEH contributed to planning of the analyses, interpretation and finalization of the manuscript. CE was responsible for project planning and organization, interpretation of the findings, and drafting and finalization of the manuscript.

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CONFLICT OF INTEREST STATEMENT

None of the authors report conflict of interest.

DATA AVAILABILITY STATEMENT

Legal restrictions do not permit the authors to provide the data that constitutes the basis of this study. The main data utilised are available from the data owner, the Norwegian Institute of Public Health (https://www.fhi.no/en/hd), after obtaining approval from The Regional Committee for Medical Research Ethics (https://rekportalen.no/), for researchers who meet the criteria for access to confidential data. Contact information: The Medical Birth Registry of Norway, University of Bergen, P.O. Box 7804, 5020 Bergen, Norway.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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