Systematic Review

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Maternal and Paternal Body Mass Index and Offspring Obesity: A Systematic Review

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Key Words
Obesity · Overweight · Body mass index · Offspring · Parents · Pregnancy

Abstract
Background/Aims: It has been hypothesized that the intrauterine environment is an independent factor in obesity development. If so, the maternal effect is likely to be a stronger influencing factor ('fetal overnutrition hypothesis'). We aimed to systematically evaluate the associations of offspring body mass index (BMI, or adiposity) with pre-pregnancy BMI (or adiposity) of the mother and the father. ***Methods:*** The Medline, Embase and Cochrane Library databases were searched in March 2012. ***Results:*** Seven cohort studies were eligible for the analysis. Among these, 2 groups of trials presented different data from the same parent-offspring cohorts (the Avon Longitudinal Study of Parents and Children, ALSPAC, and the Mater-University Study of Pregnancy, MUSP). In total, 3 large birth cohorts and 1 additional small study were identified. Three studies provided a direct comparison of parent-offspring associations, with a statistically stronger maternal influence found only in the MUSP cohort. Equivocal results were obtained from all studies describing the ALSPAC cohort. The parental effect (indirectly estimated based on the presented odds ratio) was similar in the Finnish cohort. In 1 additional small study, maternal BMI was found to be a strong predictor of childhood obesity. ***Conclusions:*** There is only limited evidence to support the 'fetal overnutrition hypothesis'.

Background

The prevalence of overweight and obesity has increased dramatically in recent decades. According to the 2010 International Obesity Task Force analysis, globally, approximately 200 million school-aged children are overweight or obese [1]. Obesity in children is well known to be associated with serious health consequences, including hypertension, diabetes type 2, dyslipidemia, cardiovascular disease and osteoarthritis, both in childhood and adulthood [2]. In turn, treating obesity-related diseases contributes to a significant economic burden [3]. Currently, treatment for obesity is often unsatisfactory [4], and therefore, prevention is particularly important.

A variety of influencing factors, such as genes and the environment, are considered to predispose individuals to the development of obesity. The intrauterine environment is proposed to be an important factor that influences the body mass index (BMI) and adiposity in later

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life. This effect could theoretically be explained by the 'fetal overnutrition hypothesis', which assumes that greater maternal adiposity during pregnancy leads to changes in energy metabolism, appetite control and functioning of the fetal endocrine system, resulting in increased risk of obesity in childhood and adult life [5]. However, it has also been proposed that this mother-offspring association is primarily due to genetic and/or lifestyle factors shared between the mother and her offspring, which both mother and father contributed to by a comparable extent.

Comparing the association of both maternal and paternal BMI and/or obesity with obesity in the offspring assessed after adiposity rebound (due to better prediction of adult 'fatness' by the child's BMI after adiposity rebound) [6] is one approach to evaluate the magnitude of the maternal effect. If the intrauterine environment is an additional, independent factor in obesity development, the maternal effect is likely to emerge as a stronger influencing factor.

This question has not been the subject of any previously published review related to childhood obesity.

Therefore, our objective was to conduct a systematic review and, if appropriate, also a meta-analysis to test the following hypothesis: 'Paternal obesity and/or adiposity contributes equally to the obesity and/or adiposity of the offspring assessed after the adiposity rebound period (at the age of ≥5 years) as compared to maternal obesity and/or adiposity assessed before pregnancy or within the first trimester of pregnancy.'

Methods

The review protocol was not registered prior to the review. However, the authors formulated and discussed the written protocol for this review before its execution, and previously established decisions were followed.

Criteria for Considering Studies for This Review

Types of Participants

Studies that assessed parents-offspring trios (and those that reported on all children, not only singleton but also twin pregnancies), were acceptable for inclusion. We excluded studies with offspring participants younger than 5 years. This age limit was determined by the occurrence of adiposity rebound. Studies that exclusively recruited special populations, such as women with gestational diabetes mellitus, preterm or small-for-gestational age infants, were not the subject of this review.

Types of Exposures

We included studies in which maternal BMI and/or adiposity measured before pregnancy or within the first trimester versus paternal BMI and/or adiposity was analyzed in relation to offspring obesity and/or adiposity.

Paternal measurements were acceptable if they were obtained at a different time from maternal measurements (however, not later than up until childbirth). In order to minimize recall bias, we excluded studies with prenatal parental measurements reported at the time of offspring assessment. We accepted different ways of reporting parental and offspring weight and height: direct measurement by the study team, self-reporting, one parent reporting for another, and also comparisons of two different options (e.g., direct maternal measurement versus indirect paternal measurement). However, we agreed that the chosen method is a very important element of quality assessment. If not otherwise stated by the author, we made the assumption that the time of reporting the measurements was the time of these measurements made.

Types of Outcome Measures

The primary outcome measure was the association of offspring BMI and/or adiposity at the age of >5 years in childhood or adulthood with pre-pregnancy (or first-trimester) BMI and/or adiposity of the mother in the index pregnancy, as well as BMI and/or adiposity of the father, and their relative contribution to explaining offspring BMI. Studies that provided data on mother-offspring and father-offspring associations, despite no attempt to compare these associations directly, were also eligible, but only if they provided sufficient data that allowed us to perform such comparisons. The secondary outcomes were as follows: (1) association of infant birth weight with pre-pregnancy or first-trimester BMI and/or adiposity of the mother, as well as BMI and/or adiposity of the father, and their relative contribution to explaining offspring birth weight; and (2) association of infant adiposity with pre-pregnancy or first-trimester BMI of the mother and the father and their relative contribution to explaining offspring birth weight. Studies that did not assess our primary outcome were not included, even if they provided data about secondary outcomes.

Types of Studies

All types of observational studies (longitudinal cohort studies, case-control studies, cross-sectional studies) were considered to meet our inclusion criteria. No restrictions regarding the methodological quality of individual studies were applied.

Search Strategy for Identification of Studies

We independently searched the following electronic databases: Medline through PubMed (A.L., B.Z. and B.P.), Embase (A.L., B.Z.) and the Cochrane Library (A.L., B.Z.). Additionally, we screened 2 trial registries: the ClinicalTrials.gov website (http://www.clinicaltrials.gov) and the EU Clinical Trials Register website (http://www.clinicaltrialsregister.eu). In addition, the abstracts from scientific conferences related to obesity, i.e. meetings organized by the North American Association for the Study of Obesity, the European Association for the Study of Obesity and the European Childhood Obesity Group, published in the last 2 years, were reviewed. The reference lists from identified articles were hand searched. In one case, we contacted the author by email to obtain information regarding the results of an ongoing study. For all involved studies, the time frame of the search was March 2012.

We used a combination of five groups of key words [free text and MeSH (Medical Subject Headings) terms] related to our target population and exposure:

- children OR child * OR offspring OR adolescent OR adolescent * OR son OR daughter;

- BMI OR body mass index OR obesity OR obes * OR overweight OR body fat mass OR body composition OR adiposity OR body weight OR Quetelet index OR Quetelet's Index OR Quetelets Index OR body fat OR nutritional status;
- pregnancy OR prenatal * OR pre-pregnancy OR prepregnancy OR pre pregnancy OR pregnant OR gestation * OR gestation OR conception OR intrauterine period;
- mother OR mother * OR maternal OR parent * OR parental OR parent OR mom;
- father OR father * OR paternal OR dad OR parent * OR parental OR parent.

We used no limits related to study-type index terms (because of inconsistent use of study design labels by authors and their unreliable indexing by databases) [7], but we limited our search to studies with human participation. We did not restrict our search to articles published in a particular language. Reviewers screened all titles and selected abstracts and full-text articles for inclusion.

Data Collection

Three reviewers independently extracted the following data from the selected studies into the electronic data forms: author, year of publication, baseline characteristics of the studies, information necessary for quality assessment of each study, outcome measures (together with their definitions), and the results. Data review and extraction was done in an open manner.

Assessment of Methodological Quality

At present, no single, validated and recommended instrument or scale for quality assessment of nonrandomized studies, especially longitudinal studies, exists. Therefore, we did not use any particular tool for the purpose of quality assessment. Rather, based on STROBE guidelines [8] (however, targeting report quality) and following the checklist for observational studies published as part of the US Agency for Healthcare Research and Quality's 'Systems to rate the strength of scientific evidence' [9], as well as the Center for Reviews and Dissemination guidelines [10], we evaluated in a descriptive manner some important elements of each primary study design that may potentially affect its quality. We mainly focused on methods used to measure exposure and outcomes, methods used to control for confounding factors, and the appropriateness of the statistical analysis. Intentionally, as recommended by the Center for Reviews and Dissemination [10], we avoided the use of a scale with a summary score to grade high- and low-quality studies.

Measures of Effect

We expressed our primary and secondary outcome measures in a variety of ways, depending on the method presented by the authors of an individual study, with no restriction of studies expressing parent-offspring associations in one particular way.

Data Synthesis

Data were analyzed regarding quantitative and qualitative synthesis. Based on the observed methodological and clinical heterogeneity between the studies, we found it inappropriate and impossible (different outcome measures) to pool the data together and perform a meta-analysis. Therefore, a narrative synthesis of the results was undertaken. All disagreements were resolved by discussion between the review team participants.

Results

Of 10,801 initially identified articles, we found 31 publications that required further full-text evaluation. Of these, we were able to select 8 studies that met our inclusion criteria. As one of these was an ongoing study [11] with only baseline data provided, finally, 7 studies [5, 12–17] were eligible for inclusion. Figure 1 shows the process of study identification and selection. We excluded 1 study [18] that answered the question for the review because of the time of reporting pre-pregnancy measurements of the parents.

Among the included studies, we identified two groups of trials that presented different data (time of offspring assessment, different outcome measures) collected from the same cohorts of parent-offspring. The first group – 3 studies [12, 13, 17] – represented a British cohort, The Avon Longitudinal Study of Parents and Children (ALSPAC), and the second group – 2 studies [5, 15] – represented an Australian cohort, the Mater-University Study of Pregnancy (MUSP). All included studies were prospective cohort studies. In the study by Catalano et al. [16], about 40% of a relatively small group of participants (n = 89) were women with gestational diabetes mellitus. In the remaining studies, the populations (large birth cohorts) represented general populations from developed countries. We also decided to include the study by O'Callaghan et al. [15] despite the fact that a small proportion (3.6%) of children were younger than 5 years of age (the majority were 5- and 6-year-old children). Detailed characteristics of the included studies are shown in table 1.

Based on the performed quality assessment of the studies (table 2), we identified some important sources of the potential risk of bias. Most commonly, the indirect method of parental measurements, the role of confounding factors, the issue of nonpaternity and not living with both biological parents (table 3).

Primary Outcome

Only 3 studies [5, 12, 13] provided a direct comparison of the mother-offspring association with the father-offspring association (however, 2 of them described the ALSPAC cohort). All these studies used BMI (either as a continuous variable or BMI class) as the unit of parental measurement. BMI (alternatively obesity/overweight based on BMI) was also the method of choice for offspring measurements in the majority of studies. Only 2 studies [13, 16] used the percentage of body fat determined by dual energy X-ray absorptiometry for that purpose. The statistical method used to express the associa-

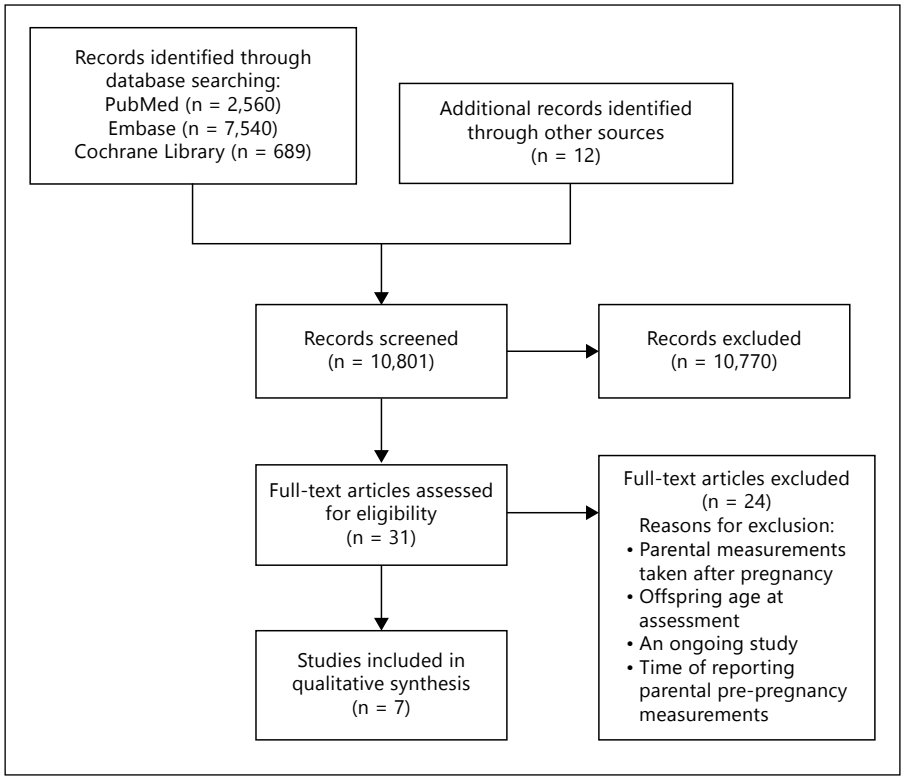

Fig. 1. Flow diagram of the study selection process.

tion of parental BMI with offspring BMI (or overweight, obesity, fat mass) was the correlation coefficient for those studies [5, 12, 13] that aimed to present the difference between maternal and paternal impact. Other studies reported the parent-offspring relation as an odds ratio.

In the study by Catalano et al. [16], the relation of maternal and paternal pregravid BMI with tertiles of percentage body fat of their children at follow-up was presented.

A clear statistical difference in the magnitude of the mother-offspring and father-offspring influence in all confounder-adjusted models tested was found in the MUSP cohort study [5] (all p values <0.0001). The increase (in the fully adjusted model) in standardized offspring BMI for a 1 SD increase in maternal BMI was 0.362 SD [95% confidence interval (95% CI) 0.323–0.402] compared to paternal BMI (0.239 SD; 95% CI 0.197–0.282).

In the study by Smith et al. [12] (ALSPAC cohort), greater maternal influence on offspring BMI was seen in the standardized model, which analyzed z-scores for parental and offspring BMI (p = 0.006). However, it was not persistent when increasing rates (≥6%) of non-paternity were analyzed. Also, no difference was observed when an analysis of offspring BMI age and sex adjusted by the LMS method was performed (in both the unstandardized and standardized model).

In the study by Lawlor et al. [13] (ALSPAC cohort), the maternal association compared to paternal association effect size was stronger in all multivariable models. The mean difference in offspring sex- and age-standardized fat mass z-score per 1 SD BMI was 0.24 (95% CI 0.22–0.26) for maternal BMI compared to 0.13 (95% CI 0.11–0.15) for paternal BMI ($p < 0.001$). Additionally, the authors performed analyses with the use of FTO (fat mass and obesity associated gene) as an instrumental variable for greater maternal adiposity. However, when adjusted for offspring FTO, these analyses showed no association of maternal BMI with offspring fat mass, resulting in the overall author conclusion that the observed associations were similar.

Among other studies – a large Finnish cohort [14], another with ALSPAC [17] and MUSP [15] data – where no direct comparison of parent-offspring associations were performed, an attempt to estimate the effect was based on the presented odds ratios. However, as no formal comparison was performed, provided data (table 1) can only give us an idea about the effect size, but cannot form a basis for any definite conclusions.

In the Finnish cohort [14], as stated by the authors, greater maternal effect was inconsistent and pronounced for male offspring only.

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Table 1. Characteristics of included studies

Reference	Study setting; population	Inclusion/ exclusion criteria	N/n	Offspring age, years	Parental nutritional status assessment time	Outcome measure (primary outcome for the review)	Results (primary outcome for the review)	Comments
Jääskeläinen et al. [14], 2011	Northern Finland Birth Cohort 1986; 99% of births in 2 provinces of Finland	Included if: pregnant, women with an expected delivery date between 1.07.1985 and 30.06.1986 Excluded if: participants refused data usage; missing or incomplete data (age, height, weight); not living with both biological parents at age 16 years	9,479/ 4,788	16	First antenatal visit (12th week gestational age)	Association of maternal and paternal pre-pregnancy BMI class (BMI <25; 25 to <30; ≥30) with offspring overweight Outcome measure: indirect comparison based on presented ORs	Parental pre-pregnancy obesity in prediction of offspring overweight: mother-son: OR 4.36 (95% CI 2.50–7.59); mother-daughter: OR 3.95 (95% CI 2.34–6.68) vs. father-son: OR 3.17 (95% CI 1.70–5.92); father-daughter: OR 5.58 (95% CI 3.09–10.07)	Analysis of parental pre-pregnancy overweight and normal weight in prediction of offspring overweight also available
Catalano et al. [16], 2009	Women obtaining prenatal care at US hospital – both general population and patients with GDM; recruited from 1990 to 1999	Excluded if: multifetal gestation, offspring congenital anomalies, preterm infants, body composition assessment of infant impossible shortly after birth	89/63	6–11 (mean age 8.8)	First prenatal visit for maternal height; other data obtained by history at delivery or by review of antenatal record	Parental BMI in relation to tertiles of offspring percentage body fat at follow-up Outcome measure: indirect comparison of maternal and paternal association with offspring by reviewers	Maternal BMI was significantly greater in children in the upper tertile compared to children in the lower tertile of % body fat ($p < 0.05$) vs. paternal BMI, without significant difference between the 3 tertiles ($p = 0.27$)	The strongest perinatal predictor for a child in the upper tertile for percentage body fat was maternal pregravid BMI
Lawlor et al. [13], 2008	ALSPAC; pregnant women living in 3 health districts in Bristol, England, who had an expected date of delivery between the start of April 1991 and the end of December 1992	Inclusion: only singleton births Exclusion: trios where the mother had reported that her partner was not the biological father of the child and those for whom this information was missing	14,273/ 4,091	9–11	During pregnancy	Associations of parental (maternal vs. paternal) BMI with offspring fat and lean mass Outcome measure: correlation coefficient comparisons	Mean difference in offspring sex- and age-standardized fat mass z-score per 1 SD increase BMI 0.24 (95% CI 0.22–0.26) for maternal BMI vs. 0.13 (95% CI 0.11–0.15) for paternal BMI ($p = 0.001$); the maternal association effect size is stronger in all multivariable models	No association of maternal BMI with offspring fat mass when analysis adjusted for offspring genotype performed (maternal FTO genotype as an instrumental variable for maternal BMI)
Lawlor et al. [5], 2007	MUSP (Australia); women at their first antenatal visit to the Mater Hospital, enrolled between 1981 and 1984 and their offspring	Inclusion: women who delivered a live singleton baby that was not adopted prior to leaving the hospital and completed both initial phases of data collection	7,223/ 3,340	14	First antenatal visit	Associations between maternal pre-pregnancy BMI, in comparison to paternal BMI, with offspring BMI Outcome measure: correlation coefficient comparisons	The increase (in the fully adjusted model) in standardized offspring BMI for a 1 SD increase in maternal BMI was 0.362 SD (95% CI 0.323–0.402) compared to paternal BMI 0.239 SD (95% CI 0.197–0.282; $p < 0.0001$)	Clear statistical difference in the magnitude of the mother-offspring and father-offspring influence in all confounder-adjusted models tested

Table 1 (continued)

Reference	Study setting; population	Inclusion/ exclusion criteria	N/n	Offspring age, years	Parental nutritional status assessment time	Outcome measure (primary outcome for the review)	Results (primary outcome for the review)	Comments
Smith et al. [12], 2007	ALSPAC	Inclusion: women who had a singleton, live-born child Excluded if: partner was not confirmed as being the biological father of the child by the mother, or the partner's age was not recorded	13,822/ 4,654	7.5	During pregnancy	Associations between maternal pre-pregnancy BMI, in comparison to paternal BMI, with offspring BMI Outcome measure: correlation coefficient comparison	Greater maternal influence on offspring BMI in the standardized model (z-scores for parental and offspring BMI analyzed; p = 0.006); no difference when increasing rates (≥6%) of non-paternity were analyzed and when analysis of offspring BMI age and sex adjusted by the LMS method was performed	
Reilly et al. [17], 2005	ALSPAC	Unclear	13,971/ 7,758	7	During pregnancy, obtained from medical records	Associations between parental pre-pregnancy BMI class (>30) with offspring obesity Outcome measure: indirect comparison based on presented ORs	Final model adjusted OR for offspring obesity: father's BMI >30 2.54 (95% CI 1.72–3.75) vs. mother's BMI >30 4.25 (95% CI 2.86–6.32)	
O'Callaghan et al. [15], 1997	MUSP	Exclusion: patients under the care of private obstetricians and patients often requiring intensive neonatal care, transferred from other hospitals	8,556/ 4,062	4–6 (only 147 children were 4 years old)	First antenatal visit	Association of severe/ moderate obesity in offspring with parental BMI class Outcome measure: indirect comparison based on presented ORs	Adjusted OR for BMI ≥95% 3.9 (95% CI 2.3–6.4) when maternal BMI >95% vs. 2.0 (95% CI 1.1–3.6) when paternal BMI >95%	Analysis for different parental and offspring BMI classes available

N/n = N – the number of subjects (trios) initially included in the cohort, n – the number of subjects (trios) analyzed; OR = odds ratio; GDM = gestational diabetes mellitus; FTO = fat mass and obesity associated gene.

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Table 2. Quality assessment of included studies

Reference	Jääskeläinen et al. [14], 2011	Catalano et al. [16], 2009	Lawlor et al. [13], 2008	Lawlor et al. [5], 2007	Smith et al. [12], 2007	Reilly et al. [17], 2005	O'Callaghan et al. [15], 1997
Study design	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort
Subject demographics described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Parental measurements							
Unit of measurement	BMI class	BMI	BMI	BMI	BMI	BMI class	BMI class
Unit of measurement justification	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable
Methods of measurements	Indirect (self-reporting)	Indirect[1]	Indirect (self-reporting)	Indirect[2]	Indirect (self-reporting)	Indirect (self-reporting)	Indirect[2]
Definitions of obesity and overweight							
Offspring	Adequate	Adequate	N/A	N/A	N/A	Adequate	Inadequate[3]
Parents	Adequate	Adequate	N/A	N/A	N/A	Adequate	Not determined
Offspring measurements							
Choice of the unit of measurement	Overweight based on BMI	Tertiles of CDC weight percentiles and tertiles of % body fat	DXA determined fat mass	BMI	BMI	Obesity based on BMI	BMI class
Unit of measurement justification	Acceptable	Optimal for % body fat; inadequate for weight	Optimal	Acceptable	Acceptable	Acceptable	Acceptable
Methods of measurements	Direct	Direct	Direct	Direct	Direct	Direct	Direct
Statistics							
Sample size calculation	Not described	Not described	Not described	Not described	Not described	Not described	Not described
Data analysis methods	Adequate	Adequate	Adequate	Adequate	Adequate	Adequate	Adequate
Conflict of interest?	No	No	No	No	No	No	No data; funding source described elsewhere
Completeness of FU – loss to FU <20%	No	No (for DXA)	No	No	No	No	No
Controlling for CF	See table 3						
Results							
Unadjusted and adjusted estimates	No, adjusted estimates only	Yes	Yes	Yes	Yes	Yes	Yes
Estimate precision (95% CI and/or p value presented)	Yes	Yes	Yes	Yes	Yes	Yes	Yes

N/A = Not applicable; CDC = Centers for Disease Control; DXA = dual energy X-ray absorptiometry; FU = follow up; CF = confounding factors.
[1] Maternal height – directly measured; maternal weight before pregnancy and paternal height and weight obtained by history.
[2] Maternal height – directly measured; maternal weight before pregnancy and paternal height and weight reported by the mother.
[3] BMI >94 percentile: marked obesity; BMI 85–94 percentile: moderate obesity.

In other studies with ALSPAC and MUSP data, although some trend toward a stronger maternal effect might be noticed, significant difference seems to be questionable.

In the study by Catalano et al. [16], a greater maternal BMI for children in the upper tertiles when compared to those in tertiles 1 and 2 was described. No significant difference was observed between paternal BMI in different tertiles, suggesting pregravid maternal BMI to be a stronger predictor of childhood obesity than paternal BMI.

Secondary Outcomes

Only 1 study [5] provided data on the associations of parental BMI with offspring birth size. The maternal effect was found to be stronger than the paternal effect ($p <$

Table 3. Confounding factors (and its method of control), nonpaternity and not living with both biological parent issues

Study ID	CF considered by the author	Baseline characteristics data regarding CF	Method of CF control applied by the author	Nonpaternity considered by the author	Not living with both biological parents considered by the author
Jääskeläinen et al. [14], 2011	Maternal and paternal age, education level	No	Mulitivariable regression analyses	No	Yes (exclusion criterion)
Catalano et al. [16], 2009	GDM	Yes	Stratification (NGT/GDM)	No	No
	Maternal obstetrical data, paternal anthropometric data, and neonatal birth data	Yes	Mulitvariable regression analyses		
Lawlor et al. [13], 2008	Social class, maternal smoking at time of pregnancy, breast feeding, parental education, parity, offspring pubertal status	No	Mulitivariable regression analyses	Yes (exclusion criterion; sensitivity analysis)	No
Lawlor et al. [5], 2007	Other parents BMI, family income during pregnancy, parental education, maternal age at birth, maternal smoking around pregnancy, parity, birth size, offspring diet and exercise	No	Mulitivariable regression analyses	Yes (sensitivity analysis)	No
	Maternal diabetes	Yes	Sensitivity analysis		
Smith et al. [12], 2007	None			Yes (exclusion criterion; sensitivity analysis)	No
Reilly et al. [17], 2005	Maternal social class, maternal education, energy intake of child	No	Mulitivariable regression analyses	No	No
O'Callaghan et al. [15], 1997	Unclear	Unclear	Mulitivariable regression analyses	No	No

CF = Confounding factor; GDM = gestational diabetes mellitus; NGT = normal glucose tolerance.

0.0001) for all birth size outcomes – birth weight and length, as well as birth weight and length standardized for sex and gestational age.

Discussion

Principal Findings

To our knowledge, this is the first systematic review that has made an attempt to compare the associations of maternal and paternal pre-pregnancy BMI with offspring obesity/adiposity. Findings of our systematic review are not homogeneous. Available evidence, regarding four different populations, does not provide strong support for the fetal overnutrition hypothesis. A specific maternal effect was observed in a large Australian birth cohort (MUSP) and in some analyses of a British cohort (ALSPAC). These studies are the only ones that aimed to directly compare maternal and paternal BMI associations with offspring obesity or adiposity. Pregravid maternal BMI was also found to be a strong predictor of childhood obesity in the study by Catalano et al. [16]; however, the population in this study was not representative of the general population (high rate of participants with gestational diabetes mellitus, and the total number of participants was very small). In another large birth cohort [14] (Finnish parents-offspring trios), the maternal and paternal effect on offspring BMI was similar; therefore, it does not support the fetal overnutrition hypothesis.

Limitations

We are aware of important limitations of this systematic review. First, the measurements of parents (with the exception of mothers' heights in some studies) were self-reported or, regarding the fathers, reported by the mother. This fact raises the risk of bias, as there is evidence

suggesting the underestimating of weight and overestimating of height by self-reporting adults, with the degree of this trend varying between women and men and also between populations [19]. Secondly, the mother's prepregnancy weight was obtained by recall, with no precise frame of time before pregnancy described in any study, although it was reported within a short period of time (during pregnancy).

There is the important issue of dealing with confounding factors, which are a source of heterogeneity between the studies. Moreover, this is a potential source of bias in this review. Some examples of confounding factors and effect modifiers include the child not living with both biological parents considered only in 1 study [14], a lack of information about comorbidities among participants (such as maternal diabetes) in many studies [12–15, 17], or no evaluation of the confounding role of gestational weight gain (as a possible independent risk factor for obesity in offspring) [20]. Finally, we made the assumption that both mother and father contribute to the shared lifestyle between parents and offspring to a comparable extent. However, the role of both parents in contributing to the child's diet, feeding habits or level of exercise may require further evaluation.

Another aspect which concerns us is the rate of prepregnancy overweight/obesity among parents, especially among mothers. In only 1 study (the Finnish cohort) data about the rate of overweight and obese parents were provided (with only 13.3% overweight and 3.5% obese mothers vs. 29.4% overweight and 2.9% obese fathers) [14]. Other reports are limited to mean parental BMI only. Therefore, the lack of any effect or the very small maternal effect might be due to a lack of power (very low rate of obesity), even in large sample sizes.

The majority of authors of the included studies evaluated the association of maternal and paternal BMI with childhood BMI. We realize that BMI is not a reliable estimate of childhood fat mass, and it would be more important to assess offspring adiposity by body compositional analysis.

We made some efforts in our search strategy to avoid missing relevant data for this review (i.e. choosing concepts that are well defined and likely to be found in titles and abstracts, use of both text words and index terms, no use of filters for study design, no language restriction, direct contact with an author). Obviously, we cannot rule out the possibility of missing relevant data, since poor reporting and indexing of observational studies is a common problem [7]. Furthermore, the data of our interest may not be a primary outcome for some publications, which makes relevant data hard to identify.

Although this was not a criterion for inclusion, all identified studies in our review were cohort studies, which are the most reliable among observational studies. A further strength of our review is the exclusion of studies with a high risk of recall bias (i.e. studies in which the prepregnancy BMI was reported after pregnancy). Additionally, with the exception of the study by Catalano et al. [16], all included studies represented a large sample size.

We did not take into account a great number of studies that compared parental-offspring associations based on parental BMI measured at the time of offspring assessment. A careful review of this type of evidence would be a valuable addition in formulating conclusions for our review.

Conclusions

Our findings provide limited evidence to support the tested hypothesis. However, considering many limitations and the quality of the identified studies, also taking into account some evidence for a stronger maternal effect in the analysis performed, this review identifies a gap for further evidence of better quality rather than contradicting a role for the fetal overnutrition hypothesis in the current obesity epidemic. We are looking forward to the results of the ongoing FAMILY study [11] (identified through our search) that, among others, addresses the issue of fetal determinants for adiposity development in childhood. Additionally, recently published data [21] (not covered by this review) from a Norwegian cohort did not show any difference between parental-offspring BMI associations when children were at the age of 3 years.

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