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Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analyses

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Background Despite the current obesity epidemic, maternal underweight remains a common occurrence with potential adverse perinatal outcomes. Our objective was to determine the relationship between maternal underweight and preterm birth (PTB) and low birth weight (LBW) in singleton pregnancies in developing and developed countries.

Methods We followed the MOOSE consensus statement. We searched MEDLINE and EMBASE from their inceptions. We included studies that assessed the effect of maternal underweight compared with normal weight according to body mass index in singleton gestations on our two primary outcomes: PTB (<37 weeks) and LBW (<2500 g). Two assessors independently reviewed citations, extracted data and assessed quality.

Results A total of 78 studies were included involving 1 025 794 women. The overall risk of PTB was increased in the cohort studies of underweight women [adjusted relative risk (RR) 1.29, 95% confidence interval (CI) 1.15–1.46], as were the risks of spontaneous PTB (adjusted RR 1.32, 95% CI 1.10–1.57) and induced PTB (adjusted RR 1.21, 95% CI 1.07–1.36). Underweight women had an increased risk of an LBW infant (adjusted RR 1.64, 95% CI 1.38–1.94). In developed countries, underweight women had an increased risk of PTB (RR 1.22, 95% CI 1.15–1.30) but not in developing countries (RR 0.99, 95% CI 0.67–1.45). In both developed and developing countries, underweight women were at increased risk of having an LBW infant (RR 1.48, 95% CI 1.29–1.68, and RR 1.52, 95% CI 1.25–1.85, respectively).

Conclusions In this systematic review and meta-analyses, we determined that singletons born to underweight women have higher risks of PTB (overall, spontaneous and induced) and LBW than those born to women with normal weight.

Keywords Maternal underweight, body mass index, preterm birth, low birth weight, meta-analysis, developing countries, developed countries

Introduction

Despite the current obesity epidemic, at the other end of the spectrum, maternal underweight is also common. For instance, 4.3% of pregnant women in the UK[1] and 9.0% of women in China[2] are underweight at the first antenatal visit according to the World Health Organization's (WHO's) definition of body mass index (BMI) <18.5 kg/m^2. Moreover, 13.3% of Chilean women had a BMI <21 kg/m^2,[3] and a population-based Swedish study observed that 9.6% of women had a BMI in the range of 15–19.9 kg/m^2.[4]

Whether maternal underweight is associated with increased,[5] decreased[6] or neutral risks[7] of preterm birth (PTB) is debated in the literature. PTB persists as the leading cause of neonatal morbidity and mortality[8] and low birth weight (LBW) is the second most important.[9] In order to accurately risk-stratify a pregnancy at its start as is routinely required, it is important to know the impact of maternal underweight on PTB and LBW. We therefore undertook a systematic, comprehensive and unbiased accumulation and summary of the available evidence from all study designs with a reference group of women with normal weight to determine the direction and magnitude of the effect of maternal underweight on both PTB and LBW in singleton pregnancies in developed and developing countries.

Methods

We performed a systematic review and meta-analyses following the MOOSE consensus statement on the conduct of meta-analysis of observational studies.[10] This study is part of a large constellation of systematic reviews examining determinants of PTB/LBW, and one of a series on maternal anthropometry.[11]

Search strategy

We searched MEDLINE (1950 to 2 January 2009) and EMBASE (1980 to 2 January 2009) with the help of an experienced librarian using individual comprehensive search strategies for each database (Supplementary Data #1 available at *IJE* online). Additional eligible studies were sought by reviewing the reference lists of identified articles.

Study eligibility criteria

Inclusion criteria

For the constellation of systematic reviews examining maternal anthropometry, we included randomized trials (although there were none), cohort studies and case–control studies with a reference group of normal weight women if (i) one or more of the following maternal anthropometry variables were assessed as a predictor variable: body mass index (BMI, assessed before pregnancy, during pregnancy or postpartum), weight (assessed before pregnancy), gestational weight gain, attained weight or height (assessed before pregnancy), and (ii) one or more of the following outcomes: PTB (<37 weeks, 32–36 weeks and <32 weeks), LBW (<2500 g), very LBW (VLBW <1500 g), extremely LBW (ELBW <1000 g). For this particular systematic review of maternal underweight, we included studies with any BMI definition of underweight (as defined by the original study) with a reference group. We included studies that used self-reported BMI, as well as studies in which the participants had objective BMI assessments or in which information was obtained from medical charts or databases.

Exclusion criteria

We excluded duplicate publications and studies published only as abstracts. We excluded studies if they involved less than 10 pregnant women. We excluded studies with twins unless stratification allowed extraction of data for singletons.

Outcome measures

Our primary outcomes were PTB (defined as birth before 37 weeks of gestation) and LBW (birth weight <2500 g) in singletons. Where possible, we then subdivided PTB into spontaneous and induced PTB. Secondary outcomes were:

(i) PTB from 32 to 36 weeks and PTB <32 weeks.
(ii) VLBW (birth weight <1500 g) and ELBW (birth weight <1000 g).

We also reported those studies that met the above inclusion criteria and mentioned the following outcomes.

(iii) Intrauterine growth restriction (IUGR, defined as birth weight <10% for gestational age).
(iv) Birth weight (in grams).
(v) Gestational age at birth (in weeks).

Study selection

Two assessors (two of Z.H., S.D.M. and S.M.) independently reviewed the titles and abstracts of all citations identified in the search. The full-text article was retrieved if either reviewer considered the citation potentially relevant. Each full-text article was independently evaluated by two reviewers (two of Z.H., S.D.M., S.M. and G.L.). Disagreements were settled by discussion and consensus, with a third person available as an adjudicator.

Data collection process and data items

Two reviewers (two of Z.H., S.D.M., S.M. and G.L.) independently extracted the following data from full-text articles: country of origin, time span of the study (years), study design, characteristics of participants, outcomes and information on bias. A pilot data collection form was generated, tested and modified prior to tabulation of the final data. We included information available from the publications. Inconsistencies were checked and resolved through the consensus process described above, with a third person available as an adjudicator.

Data synthesis

The Review Manager software (version 5.0; the Cochrane Collaboration, Oxford, UK) was used for statistical analyses. Meta-analyses were performed from available data. Crude and separately adjusted, dichotomous data from cohort studies were meta-analyzed using relative risks (RRs), whereas crude and separately matched dichotomous data from case–control studies were pooled using odds ratios (ORs). (Please note that for our two primary outcomes, PTB and LBW, both crude and adjusted risks are presented in the body of the manuscript. For all other outcomes, the adjusted risks alone are presented in the article, unless only crude data existed. All results are in the tables.) Continuous data were analyzed with a mean difference. Weighting of the studies in the meta-analyses was calculated based on the inverse variance of the study. The random effects model was chosen because it accounts for both random variability and the variability in effects among the studies as we expected a degree of clinical and statistical heterogeneity among the studies, which were all observational. Crude, matched and adjusted data were initially each pooled separately and then data that were matched and/or adjusted were pooled together. Where required and when the incidence of the outcome was rare, in order to be able to pool data, adjusted RRs were calculated from adjusted ORs.[12] As is typical in meta-analyses, no adjustment for multiple analyses was made. Clinical heterogeneity was evaluated and reported in the table of included studies. We calculated the *I*-squared (I^2) value to measure heterogeneity. An I^2 value represents the percentage of total variation across studies because of heterogeneity rather than chance.[13] I^2 values of 25, 50 and 75% have been regarded as low, moderate and high heterogeneity.[13]

Sensitivity analyses

Sensitivity analyses were performed using a few a priori chosen groups to examine the effects of (i) level of material well-being (developed vs developing countries),[14] (ii) study quality (see Quality Assessment section that follows and Supplementary Data #2 available at *IJE* online), (iii) youth (adolescence vs adult) and (iv) race (black vs white). Several post hoc sensitivity analyses were performed examining the effects of (i) self-reported vs measured BMI, (ii) timing of BMI assessment (before pregnancy, during pregnancy or postpartum) and (iii) using exact cut-offs for BMI with a reference BMI of 20–25 vs cut-offs close to this, and using a BMI cut-off of $\leqslant$20 to define the underweight women.

Quality assessment

Two reviewers (two of Z.H., S.D.M. and S.M.) independently assessed the study quality using a pre-defined checklist of six types of bias: (i) selection, (ii) exposure, (iii) outcome, (iv) confounding, (v) analytic and (vi) attrition. This bias assessment was developed for a group of 40 meta-analyses that our group is undertaking on determinants of PTB/LBW.[11,15] The classification in each category was minimal bias, low risk, moderate risk, high risk of bias and not reported (Supplementary Data #2 available at *IJE* online). If the authors included 'all' or 'consecutive' patients (or a 'random' selection of controls), selection bias was assessed as 'minimal'. Exposure and outcome assessment were 'minimal' bias if from the hospital record or direct questioning. If three or more variables were adjusted for, confounding bias was assessed as 'minimal'. Analytic bias was 'moderate' if no sample size calculation was done and only a subsample studied, and 'high' if inappropriate analyses done. Attrition was 'minimal' if $<$10% were lost to follow-up. Studies with (i) high risk of bias or 'not reported' in three or more domains or (ii) an overall assessment of bias as 'high' were excluded by a sensitivity analysis. Selection bias and confounding were given predominance in the overall assessment of bias because of their importance in this meta-analysis.

In order to address publication bias, we showed results without imputation as well as with imputation (the latter using Duval and Tweedie's trim-and-fill method for estimating and adjusting for the number and outcomes of missing studies in a meta-analysis,[16,17] i.e. to adjust for any observed publication bias). A priori we decided to perform the trim-and-fill analyses for outcomes with $\geqslant$10 studies as there were concerns of reliability for outcomes with fewer studies. The generic inverse variance method was used to calculate study-specific weights. All analyses were performed using the R statistical and programming software, version 2.9.0. (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 6283 non-duplicate titles and abstracts were identified in our searches (Figure 1). Based on our screening process, 503 citations were selected to undergo full-text article review and a further 52 articles were identified from reference lists, yielding a total of 555 full articles reviewed. The most common reasons for exclusion were study design and failure to report any outcomes of interest.

Seventy-eight studies were included: 52 cohort studies[2,5–7,18–65] (of which 48 had data that were pooled) and 26 case–control studies[66–91] (all of which had pooled data), involving a total 1 025 794 women with 174 980 underweight women and 785 697 normal weight women in the cohort studies and 11 879 cases and 52 279 controls in the case–control studies (Tables 1 and 2). The studies originated predominantly from developed countries although developing countries were also represented. The studies assessed BMI by self-report and by measurement, mainly at the first antenatal appointment, and used a variety of BMI cut-offs to define underweight (Tables 1 and 2).

PTB

The overall risk of PTB <37 weeks was increased in underweight women compared with normal weight women [in both crude and adjusted data, RR 1.21, 95% confidence interval (CI) 1.14–1.28, 32 studies, and RR 1.29, 95% CI 1.15–1.46, 14 studies, respectively] (Table 3, Figures 2 and 3). Similarly, there were increased risks of spontaneous PTB <37 weeks (adjusted RR 1.32, 95% CI 1.10–1.57, eight studies) and induced PTB <37 weeks (adjusted RR 1.21, 95% CI 1.07–1.36, four studies) in underweight women compared with normal weight women. Two studies mentioned the reasons for induction: 'severe preeclampsia and intrauterine growth retardation or other signs of fetal compromise'[65] and medically induced PTB was that 'not preceded by spontaneous labour or spontaneous rupture of membranes'.[47] (For outcomes other than our two primary outcomes, PTB overall and LBW, the adjusted risks alone are presented in the article, unless only crude data existed. Complete results for crude and adjusted data are in the tables). Similarly, the risk of PTB from 32 to 36 weeks was increased (adjusted RR 1.25, 95% CI 1.09–1.43, two studies) in underweight women. The risk of PTB <32 weeks was not increased (adjusted RR 1.13, 95% CI 0.92–1.38, four studies).

The above pooled results were generally supported by the findings of three cohort studies, the format of whose data did not permit pooling.[18,26,28,64] Women with normal BMI (20–24.9 kg/m^2) had a lower risk of PTB (33–36 weeks, as well as $\leqslant$32 weeks) than women with low BMI ($\leqslant$19.9), with adjusted OR of 0.8 (0.8–0.9) and 0.8 (0.7–0.9), respectively. Underweight women had increased risks of PTB <37 weeks (adjusted OR 4.9, 95% CI 1.5–15.9),[28] and spontaneous PTB <37 weeks (adjusted OR 1.49, 95% CI 1.17–1.86,[64] and adjusted hazard ratio 1.43, 95% CI 1.30–1.59[26]), although the risk of induced PTB <37 weeks was not increased in one study (adjusted OR 1.02, 95% CI 0.86–1.35).[64]

In the case–control studies, underweight women had an increased risk of overall PTB <37 weeks in the crude but not the matched/adjusted data (crude OR 1.55, 95% CI 1.35–1.77, three studies, and OR 1.41, 95% CI 0.7–2.71, three studies, respectively) (Table 4). Underweight women had an increase in spontaneous PTB in the crude but not the adjusted data (OR 1.77, 95% CI 1.35–2.32, two studies, and OR 1.25, 95% CI 0.41–3.80, two studies, respectively).

LBW

Underweight women had an increased risk delivering an LBW infant (in both crude and adjusted cohort data, RR 1.50, 95% CI 1.34–1.68, for 24 studies and RR 1.64, 95% CI 1.38–1.94, for 9 studies) (Table 3, Figures 4 and 5). Similarly, underweight women had increased risks of having an infant with moderately LBW (1500–2500 g, adjusted RR 2.10, 95% CI 1.59–2.76, one study), VLBW (<1500 g, adjusted RR 1.54, 95% CI 1.22–1.94, one study) and a trend towards an increase in ELBW (<1000 g, adjusted RR 1.48, 95% CI 0.98–2.23, one study).

The results of the above meta-analyses were supported by the results of two cohort studies whose data could not be pooled, with both showing an increased risk of LBW in underweight women (adjusted OR 5.1, 95% CI 2.1–12.0,[38] and adjusted OR 5.5, 95% CI 2.0–14.6[28]).

Similarly, the case–control studies found an increased risk of LBW in underweight women (in both crude data, OR 1.81, 95% CI 1.16–2.84, three studies, and adjusted data, OR 2.02, 95% CI 1.26–3.14, one study) (Table 4).

Other outcomes

In the cohort studies, underweight women had higher risks of having an infant with IUGR (adjusted RR 1.54, 95% CI 1.38–1.72, four studies), lower mean birth weight (by –153 g, –288 to –79 g, eight studies, unadjusted data) and shorter mean gestation (by –0.14 weeks, –0.21 to –0.06 weeks, three studies) (Table 3). None of the case–control studies reported IUGR, birth weight or gestational age at birth.

Quality assessment

Quality assessment (Tables 5 and 6) was based on the evaluation of six types of bias: (i) selection bias was unlikely in most studies as the women with low and normal BMIs were usually drawn from the same population. (ii) Exposure bias was possible in most studies, given that the participants self-reported their weight rather that it being objectively measured.

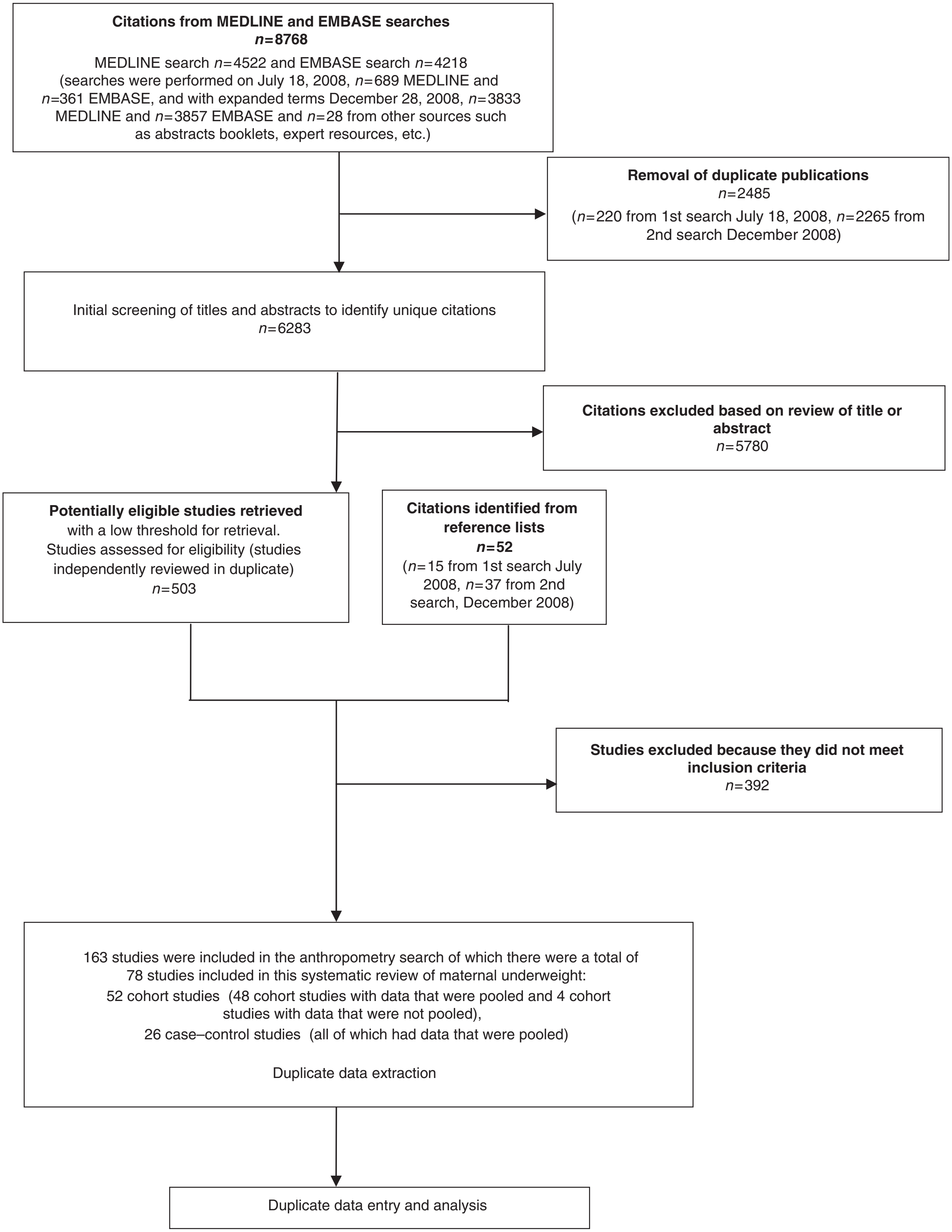

Figure 1 Study process of systematic review and meta-analyses of PTB and LBW in underweight women compared with women with normal weight. Review and selection of articles

Table 1 Characteristics of cohort studies included in systematic review and meta-analyses of PTB and LBW in underweight women compared with normal weight women

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women	
							Exposed	Not exposed (reference)
Adams, 1995[65]	1987–90	Black and white enlisted service women >20 weeks' gestation who delivered a live or stillborn singleton at one of the four largest army medical centres in the USA	Four army medical centres, USA	Medical record	NR	BMI <19.8 (reference 19.8–25.9)	231	1419
Ancel, 1999[64]	1994–97	Exposed included all consecutive single preterm births between 22 and 36 weeks. Unexposed: randomly selected 1 of every 10 consecutive term (>37 weeks) single births. The sample included both stillborn and live-born infants	15 European countries	Measured	NR	BMI <18.3 (reference 18.3–29.8)	665	11 328
Baeten, 2001[5]	1992–96	Nulliparous women (those reporting no previous live births) who delivered live singletons	Washington State, USA	Self-report (chart)	NR	BMI <20 (reference 20.0–24.9)	18 957	50 378
Barros, 1996[7]	18 months	Consecutive women who delivered a live singleton at a level-2 facility or, for the last 4 months of the study, at a level-3 facility (teaching hospital)	Two hospitals: Hospital de Famalicào and Hospital de S. Joao Porto, Portugal	Self-report	Within 48 h of the birth	BMI <20 (reference 20.0–24.9)	625	2158
Barton, 2001[46]	1990–95	Women with mild preeclampsia and proteinuria >1 in an outpatient management programme with singletons at 24–36 weeks of gestation	Matria Healthcare, Marietta, Georgia, USA	Measured	NR	BMI <20 (reference 22–28)	99	99
Berkowitz, 1998[47]	1986–94	Women who delivered singletons; one pregnancy was randomly selected for women who had one or more eligible	Mount Sinai Hospital, New York City, USA	Perinatal database	NR	BMI <20 (reference 20.0–26.0)	712	1668
Bhattacharya, 2007[48]	1976–2005	All primigravid women who delivered singletons >24 gestational weeks in Aberdeen city and district	Aberdeen maternity Neonatal Databank, Aberdeen, UK	Measured	Pre-pregnancy	BMI ⩽20 (reference 20.0–24.9)	2842	14 076
Bondevik, 2001[49]	1994–96	Outpatients at first antenatal visit	Patan Hospital, Kathmandu, Nepal	Self-report	NR	BMI ⩽20 (reference 20–22)	262	661

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women	
							Exposed	Not exposed (reference)
Clausen, 2006[50]	1995–97	Women of Norwegian ancestry who received an appointment for ultrasound screening	Aker Hospital, covered 14 of 23 districts from Oslo, Norway	Medical record	17–19 weeks of gestation	BMI ⩽20 (reference 20–25)	651	2183
Cnattingius, 1998[18,a]	1992–93	Women born in Sweden, Denmark, Norway, Finland or Iceland with information on their pre-pregnancy BMI, who delivered singletons registered in the Swedish Medical Birth Register	NR (five countries, births recorded in the Swedish Medical birth register)	Self-report (chart)	First visit	BMI 20.0–24.9[b] (reference ⩽19.9)	22 634 (BMI ⩽19.9)	101 266 (BMI 20.0–24.9)
De, 2007[43]	1996–2004	Women who initiated prenatal care at <20 weeks of gestation, were ⩾18 years of age, could speak and read English, planned to carry the pregnancy to term and to deliver at either of the two study hospitals	Swedish Medical Center, Seattle and Tacoma General Hospital, Tacoma, Washington, USA	Self-report, hospital record	NR	BMI <20 (reference 20–24.9)	451	1450
Dietz, 2006[20]	1996–2001	Women with singleton births with data in pregnancy risk assessment monitoring system in 21 states	21 states, USA	Self-report (questionnaire)	NR	BMI <19.8 (reference 19.8–26.0)	20 352	59 088
Driul, 2008[51]	2006	Consecutive women with complete baseline maternal clinical information and pertinent outcome data, who delivered singletons	University of Udine, Italy	Maternal database	NR	BMI <18.5 (reference 18.5–24.9)	230	533
Dubois, 2006[52]	1998–2002	Women who delivered in Quebec's public health districts in 1998	Quebec, Canada	Self-report	NR	BMI <18.5 (reference 18.5–24.9)	122	1253
Ehrenberg, 2003[53]	1997–2001	All women with complete baseline information and outcome data who delivered a live infant at >20 weeks of gestation	Metro Health Medical Center, Cleveland, USA	Perinatal database	NR	BMI <19.8 (reference 19.8–26.0)	1978	6988
Frederick, 2008[29,c]	1996–2004	English-speaking women ⩾18 years old and at ⩾20 weeks of gestation who planned to deliver at Swedish Medical Center or Tocoma General Hospital	Swedish Medical Center, Seattle or Tacoma General Hospital, Tacoma, Washington, USA	Self-report	Pre-pregnancy	BMI <19.8 (reference 19.8–26.0)	393	1629
Gardosi, 2000[54]	1988–95	Consecutive women who delivered live singletons	One hospital: at tertiary care centre, Birmingham, UK	Measured (chart)	First visit	BMI ⩽20 (reference 20.1–29.4)	2038	15 946

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women	
							Exposed	Not exposed (reference)
Gilboa, 2008[55]	1981–89	White or black women without pregestational diabetes mellitus who delivered live infants (without birth defects) between 25 and 40 weeks' gestations; one infant was randomly selected from women with >1 eligible births	District of Columbia, North, Virginia, Maryland	Self-report	6 months after birth	BMI <18.5 (reference 18.5–24.9)	321	2218
Haas, 2005[37]	May 2001 to July 2002	Women who delivered singletons, participated in Project Women and Infants Starting Healthy (WISH), and: (i) received prenatal care at one of the practices or clinics associated with one of six delivery hospitals and planned to deliver at one of these hospitals, (ii) were ⩾18-years-old at recruitment, (iii) spoke English, Spanish or Cantonese, (iv) sought prenatal care at <16 weeks of gestation, and (v) could be contacted by telephone	Six delivery hospitals in the San Francisco Bay area, California, USA	Self-report	First visit <20 weeks' gestation	BMI <18.5 (reference 18.5–24.9)	54	863
Hauger, 2008[36]	2003–06	Women with pregnancies ending in a live birth or fetal death, ⩾22 weeks or infant birth weight of >500 g	10 public hospitals in Buenos Aires city and province, Argentina	Self-report and measured	First visit	BMI ⩽18.5 (reference 18.5–24.9)	2628	29 644
Hickey, 1997[56]	1982–86	Low-income women registered for prenatal care	Five clinical centres: California, Illinois, Ohio, Tennessee, Alabama	Self-report (medical record)	Pre-pregnancy	BMI <19.8 (reference 19.8–26.0)	2741	6943
Hulsey, 2005[57]	1998–99	Women who delivered live singletons weighing ⩾500 g	South Carolina–resident women, USA	Self-report	NR	BMI <19.8 (reference 19.8–26.0)	14 141	45 916
Johnson, 1992[41]	1987–89	Women who received prenatal care and delivered live singletons at Shands Hospital at ⩾38 weeks of gestation. Patients with appendicitis, non-haemoglobinopathic anaemia, bone or joint disease, urinary tract infections and asthma were eligible if no fetal anomalies, oligohydramnios or polyhydramnios	Shands Hospital, Gainesville, Florida, USA	Self-report	First visit	BMI <19.8 (reference 19.8–26.0)	755	1621

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women	
							Exposed	Not exposed (reference)
Kim, 2005[30]	2001–04	Women with singleton gestations between 20 and 42 weeks who had been admitted to a collaborating hospital and undergone an obstetric sonogram	Five collaborating institutions in Korea	Self-report	NR	BMI <20 (reference BMI 20.0–24.9)	1362	1112
Lawoyin, 1992[58]	1988	Randomly selected gravid women at first antenatal clinic visit with singleton infants	Random yet fair representation of whole city, Ibadan, Nigeria	Measured	NR	BMI <20 (reference BMI 20.0–24.9)	5	109
Leung, 2008[2]	1995–2005	Ethnically Chinese women with a singleton pregnancy who presented at ⩽20 completed weeks of gestation and gave birth at ⩾24 completed weeks of gestation	A university obstetric unit, Hong Kong, China	Dataset	NR	BMI <18.5 (reference BMI 18.5–25.0)	2629	22 041
Lumme, 1995[59]	1985–86	Women with singleton pregnancies	Northern Finland	Measured	NR	BMI <19 (reference 19.0–24.9)	990	6433
Maddah, 2005[27]	June 2002 to May 2003	Pregnant women at 6 randomly selected (out of 12 in the city) urban health centres in Rasht, with data routinely collected by the centres	Six health centres, Rasht, Iran	Self-report and measured	NR	BMI <19.6 (reference 19.6–26.0)	208	414
Mercer, 1996[34]	1992–94	Women with singletons were recruited at ⩽24 weeks of gestation and followed until delivery. The study population was selected to match the race and parity distribution at each participating centre; all women were required to have an obstetric sonogram before enrollment	10 centres of the Maternal–Fetal Medicine Units Network of the National Institute of Child Health and Human Development, Maryland, USA	Measured	NR	BMI <19.8 (reference ⩾19.8)	568	2361
Merlino, 2006[60]	1996–2004	Women who delivered live or stillborn infants at >20 weeks of gestation	One university medical centre, Cleveland, USA	Measured (chart)	NR	BMI <18.5 (reference 18.5–24.9)	152	1374
Mobasheri, 2007[31]	2004–05	Women who attended the two urban and rural centers for prenatal care	Urban and rural centres for prenatal care in Gorgan, Iran	Self-report	NR	BMI <19.6 (reference 19.6–26.0)	46	161
Monaghan, 2001[61]	1992–95	All pregnant women at two sites with last menstrual period between 25 December 1992 and 23 July 1994	Two hospitals, geographically based in Kyiv Dni prodzerzhinsk, Ukraine	Measured	NR	BMI <20 (reference 20–24)	640	1387

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women: Exposed	Number of women: Not exposed (reference)
Nohr, 2007[19]	1996–2002	Women in the Danish National Birth Cohort study who delivered singletons, accepted the invitation, and signed the consent form	Denmark	Self-report	Early pregnancy	BMI <18.5 (reference 18.5–24.9)	3857	57 923
Ogbonna, 2007[62]	1998–99	Women from surrounding urban centres who delivered at the study hospital and agreed to participate	Harare Maternity Hospital, A university-affiliated hospital in Harare, Zimbabwe	Measured	Postpartum hospital stay	BMI <22.8 (reference 22.8–24.6)	136	117
Ogunyemi, 1998[42]	1990–95	Consecutive black, low-income pregnant women who registered for prenatal care in the first trimester and (i) delivered singletons, (ii) >37 weeks	Western Alabama, USA	Self-report and measured	First visit	BMI <19.8 (reference 19.8–26.0)	78	223
Panahandeh, 2007[32]	2002–03	Women who delivered at >38 weeks of gestation in seven rural local health centres; centres were selected by clustered multistage random sampling among 15 centres	Seven local health centres (rural region), Guilan, Iran	Self-report (chart, prenatal/ obstetrical record)	First visit	BMI <19.8 (reference 19.8–26.0)	38	219
Panaretto, 2006[28,a]	2000–03	All consecutive women who delivered singletons and attended Townsville Aboriginal and Islanders Health Service for antenatal care	The Panaretto Hospital, the tertiary referral centre for North Queensland	Measured	First visit	BMI <20 (reference 20.0–24.9)	Total $n = 456$, not broken down by exposure	
Rasmussen, 1992[33]	1 June 1987 to 31 May 1989	Women in a central patient registry with normal pregnancies and BMI <20.0 (exposed group) or BMI 20.0–24.9 (non-exposed)	Skive Hospital, Skive, Denmark	Chart, obstetrical record	At first visit but do not state if BMI is pre-pregnancy or not	BMI <20 (reference 20.0–24.9)	149	149
Ray, 2001[6]	1993–98	All consecutive women with either pre-gestational or gestational diabetes mellitus, singleton first pregnancy	Women's College Hospital, Toronto, Canada	Antenatal sheet	NR	BMI <20 (reference 20.0–24.9)	43	218
Rode, 2007[35]	November 1996 to October 1998	Women ⩾18 years of age, fluent in Danish, without alcohol or drug abuse, who had singleton, term pregnancies and answered a questionnaire at 12, 18 and 37 weeks	A university hospital in Copenhagen, Denmark	Self-report	12–18 weeks of gestation	BMI <19.8 (reference 19.8–26.0)	385	1531
Ronnenberg, 2003[63]	NR	Newly married nulliparous women aged 20–34 years, who were full-time employed textile workers and had permission to have a child	AnQing, China	Measured	NR	BMI <19.8 (reference 19.8–26.0)	303	272

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women: Exposed	Number of women: Not exposed (reference)
Sahu, 2007[44]	2005–06	Women from all socio-economic levels with singletons	Queen Mary's Hospital, King George's Medical University, Lucknow, India	Self-report	NR	BMI <19.8 (reference 19.9–24.9)	46	205
Savitz, 2005[45]	August 1995 to February 2001	Women with singleton pregnancies who attended the participating clinic <30 weeks, had telephone access, able to communicate in English and planned to continue care and deliver at a study hospital	University of North Carolina Hospitals and Wake County Human Services and Wake Area Health Education Centre in central North Carolina	Self-report	24–29 weeks of gestation	BMI <19.8 (reference 19.8–26.0)	365	1102
Sayers, 1997[38,a]	1987–90	Self-identified aboriginal women living in area who delivered live singletons	The Royal Darwin Hospital, the Darwin Health Region, Northern Territory, Australia	Measured	Postpartum before discharge when they were ambulatory	BMI <18.5 (reference 18.5–25.5)	Total no. of patients only reported, not broken down by exposure; varying models used, included $n = 321$ for maternal BMI and antenatal record attendance, $n = 503$ with substituted data set. ($n = 503$ used in total below)	
Scholl, 1989[39]	NR	White, black and Hispanic adolescents (⩽18 years at entry of care) who delivered live singletons and were registered into Camden County Adolescent Family Life Project	Five hospital and clinics in Camden County (Cooper Hospital/ University Medical Center, Kennedy Hospital/ University Medical Center, Our Lady of Lourdes Hospital, St. John's Prenatal Clinic, West Jersey Health Systems, New Jersey, USA	Self-report	First visit	BMI <19.0 (reference 19.1–24.0)	415	1164
Sebire, 2001[21]	1989–97	Women with singleton pregnancies having data in St Mary's Maternity Information System Database	National Health Service Hospital, Northwest Thames Region, UK	Measured	First visit	BMI <20 (reference 20–25)	38 182	176 923

(continued)

Table 1 Continued

Study	Year study spans	Population	Setting	Self-reported or measured BMI	Period when BMI was measured	BMI definition of exposure (vs reference group BMI)	Number of women	
							Exposed	Not exposed (reference)
Siega-Riz, 1996[22,c]	1983–87	Women at public health clinics undergoing first pregnancy	Public Health Clinics, West Los Angeles, USA	Self-report and measured	NR	BMI <20 (reference 20.0–26.0)	499	2626
Smith, 2006[26,a]	1992–2001	Women from western Scotland undergoing their first-term pregnancy (previous miscarriage was a risk factor) who delivered singletons	Probability-based matching using maternal identifiers to link Scottish Morbidity Record, Scottish Stillbirth and Infant Death Enquiry and prenatal screening database in the Institute of Medical Genetics	Assumed from chart (maternal weight obtained from biochemical database. Maternal height and smoking status obtained from Scottish Morbidity Record)	NR	BMI <20 (reference 20–24)	9573	45 812
Smith, 2007[23]	1991–2001	Women who: (i) had a record in the prenatal screening database, (ii) could be linked to the Scottish Morbidity Record, (iii) gave birth to a singleton infant weighing >400 g and (iv) gave birth between 22 and 43 weeks of gestation	Scotland, UK	Measured	Early pregnancy	BMI <20 (reference 20.0–24.9)	17 968	95 516
Tsukamoto, 2007[24]	2002–03	Women who delivered singletons at 37–42 weeks of gestation	Nagai Clinic, Saitama, Sagamihara Kyoudou, Kanagawa in Japan's Tokyo metropolitan area	Self-report and measured	Pre-pregnancy	BMI <18.5 (reference 18.5–25.0)	493	2301
Yekta, 2006[25]	2002–03	Women who enrolled in public care centres in urban areas at ⩽8 weeks of gestation	Urmia, Iran	Self-report and measured	Early in pregnancy	BMI <19.8 (reference 19.8–26.0)	30	140
Zhou, 1997[40]	1984–87	Women 958 707 with singletons who were enrolled in a community trial from two well-defined geographic areas	Odense, Aalborg, Denmark	Chart	NR	BMI <19.8 (reference 19.8–26.0)	1938	4536
Totals							174 980[d]	785 697[d]
Totals including studies which did not report by exposure								961 636

NRD: no raw data available in the study; NR: not reported in study.
[a]Cohort studies that were not pooled.
[b]Cnattingius 1998 defined reference group as having BMI ⩽19.9 and examined the effect of BMI above this (20.0–24.9 kg/m^2).
[c]Siega-Riz[22] and Frederick[29] are cohort studies. However, in each of their manuscripts, data were also presented in a format that allowed pooling with case–control data but are listed only in the tables with cohort studies.
[d]At least this many participants, because some studies did not report number exposed and not exposed.

Table 2 Characteristics of case–control studies included in systematic review and meta-analyses of PTB and LBW in underweight women compared with women with normal weight

Study	Year study spans	Population	Setting	Measured or self-reported BMI	Time when BMI was measured	Definition of underweight (BMI in kg/m^2)	Outcome and its definition	Number of women	
								Cases	Controls
Al-Eissa, 1994[81]	One-year study, year NR	Cases: women who delivered live preterm infants (⩾20 weeks, <37 weeks' gestation) with birth weight appropriate for GA Controls: women who delivered live infants at term (37–42 weeks' gestation) with birth weight appropriate for GA	King Khalid University Hospital, Riyadh, Saudi Arabia	Measured	Within 24 h after delivery	<23	Spontaneous PTB (20–36 weeks)	118	118
Amin, 1993[66]	1990–91	Cases: all women who delivered infants with LBW Controls: random selection of women who delivered infants with normal (not low) birth weight	Rural village of K.V. Kuppam block, Tamil Nadu, India	Measured	NR	<18.5	LBW (<2500 g)	51	51
Begum, 2003[67]	1995	Cases: women with spontaneous labour who delivered at <37 weeks' gestation Controls: women with spontaneous labour who delivered at >37 weeks' gestation	A tertiary hospital, northern India	Recorded from chart	NR	<19	Spontaneous PTB (<37 weeks)	94	88
Catov, 2007[68]	1997–2001	Cases: all women with uncomplicated pregnancies who delivered preterm (spontaneous onset or PROM) Controls: randomly chosen women with uncomplicated pregnancies and blood sample at <15 weeks' gestation, who delivered at >37 weeks' gestation	USA	Measured	NR	NR	Spontaneous PTB (<37 weeks)	90	199
Chumnijarakij, 1992[86]	12 months, year NR	Cases: all women who delivered LBW (<2500 g) singletons Controls: women from the same study areas with comparable periods of confinement at the same hospitals, who delivered normal weight (2500–4200 g) singletons; 2 controls per case	Five MCH centres, Thailand	Self-reported	NR	<20	LBW (<2500 g)	2000	4095

(continued)

Table 2 Continued

Study	Year study spans	Population	Setting	Measured or self-reported BMI	Time when BMI was measured	Definition of underweight (BMI in kg/m^2)	Outcome and its definition	Number of women: Cases	Number of women: Controls
Conti, 1998[69]	1994–95	Cases: Women who delivered premature infants (<37 weeks' gestation) with LBW (1000–2500 g) Controls: Women who delivered infants >2500 g	A major teaching hospital, Sydney, New South Wales, Australia	Self-reported	During pregnancy	NR	PTB (<37 weeks)	54	86
de Haas, 1991[70]	1988–89	Cases: women with spontaneous labour or rupture of the membrane (without induction for maternal or fetal indications) who delivered live singletons at 20–37 weeks' gestation	Brigham and Women's Hospital, Boston, Massachusetts, USA	Measured	NR	<22.0	Spontaneous PTB (20–37 weeks)	114	232
Delgado-Rodriguez, 1998[71]	1990–93	Cases: women residing in referral area of hospital, who delivered live infants <2500 g	University of Granada Hospital, Granada, Spain	Self-reported (chart)	NR	NR	LBW (<2500 g)	240	374
Deshmukh, 1998[72]	1994	NR	Urban field practice area, Government medical college, Nagpur, Maharashtra, India	Measured	NR	NR	LBW (<2500 g)	61	140
Dhar, 2003[88]	1999	Women who delivered liveborn infants; every third patient of all pregnant women at maternal–child health training institute	One hospital: a public maternity hospital, Dhaka, Bangladesh	Measured	At term Postpartum	NR NR	LBW (<2500 g)	27 41	167 258
Gosselink,1992[73]	1985–90	Women (15- to 45-year-old) who delivered singletons and consented to be interviewed Cases: women who with spontaneous labour and who delivered preterm Controls: women from the same hospital with spontaneous labour and GA >39 weeks	University of Chicago and University of Iowa Hospitals, Chicago and Iowa, Illinois, USA	Self-reported	NR	<20	PTB (<36 weeks)	368	368

(continued)

Table 2 Continued

Study	Year study spans	Population	Setting	Measured or self-reported BMI	Time when BMI was measured	Definition of underweight (BMI in kg/m^2)	Outcome and its definition	Number of women: Cases	Number of women: Controls
Hashim, 2000[74]	NR	Randomly selected Saudi postpartum mothers first 24 h after delivery Cases: women who delivered LBW (<2500 g) infants at >37 weeks Controls: women who delivered infants with normal birth weight (>2500 g) at >37 weeks	One hospital: El-Shemasy Maternity and Children Hospital, Riyadh, Saudi Arabia	Measured	NR	<19.8	LBW (<2500 g)	250	250
Hediger, 1995[89]	October 1990 to November 1993	Every third subject enrolled in the larger study (ongoing study of nutrition and growth in adolescent and older gravidas). All study participants were initially enrolled at entry to prenatal care (under the same protocol) and had a real-time and Doppler ultrasound scan from research purpose at 32 weeks within 1 month of entering care	An urban clinic in Camden, New Jersey, USA	Self-reported	First visit	NR	PTB (⩽32 weeks)	46	2444
Karim, 1997[82]	NR	Women living within the four identified sections of the Mirpur area with no immediate plans to move from their current address, between age 17 and 35 years on the date of interview	One hospital: a mother and child clinic, in the Mirpur area of Dhaka, India	Self-reported	Immediately after birth	<18.5	LBW (<2500 g)	51	196
Lawoyin, 1997[83]	NR	Consecutive maternities for which complete information was available and deliveries at the Armed Forces Hospital Cases: women who delivered infants <2500 g Controls: women who delivered infants >2500 g	One hospital: Armed Forces Hospital, Tabuk, northwest Saudi Arabia	Measured	During pregnancy	NR	LBW (<2500 g)	50	478

(continued)

Table 2 Continued

Study	Year study spans	Population	Setting	Measured or self-reported BMI	Time when BMI was measured	Definition of underweight (BMI in kg/m^2)	Outcome and its definition	Number of women: Cases	Number of women: Controls
Le, 2007[75]	2006	Women with normal mental health, ability to communicate, ⩾20 teeth (study's focus was periodontitis) and willingness to participate in the study, who delivered at the study hospital between July and December 2006 Controls: selected through random sampling	One hospital: Thai Nguyen center General Hospital, Thai Nguyen, Thailand	Self-reported	After birth	NR	Spontaneous PTB (<37 weeks)	130	260
Melamed, 2008[90]	1996–2004	All women with type I or II diabetes mellitus who were followed from conception through delivery Controls: all non-diabetic women who delivered preterm singletons	Rabin Medical Centre, Tel Aviv, Israel	Hospital record	NR	NR	PTB (24–37 weeks)	119	329
Mohsen, 2007[85]	2004–06	Women with normal vaginal deliveries at full term (37–42 weeks' gestation) and without hypertension, diabetes, toxemia of pregnancy, ante-partum haemorrhage or any medical or obstetric problems	One hospital: Al-Mataria Teaching Hospital, Cairo, Egypt	Assumed direct measurement (anthropometric measurements of the mother including weight, height and BMI were recorded)	After delivery	NR	LBW (<2500 g)	24	30
Ngare, 1998[91]	NR	A purposive sample of women studied for 2 years in three sub-locations of Kyeni South location in Embu district; only women who delivered during the study period were included in this study	Three sub-locations of Kyeni South location in Embu district, rural Kenya	Measured	NR	NR	LBW (⩽2500 g)	14	109
Ojha, 2007[76]	2004–05	Women who delivered live infants at term (37–41 weeks) Cases: women who delivered LBW infants Controls: women who delivered infants >2500 g	One hospital: Paropakar Shree Panch Indra Laxmi Devi Maternity Hospital, Thapathali, Nepal	Measured	Post-pregnancy	<18.5	LBW (<2500 g)	154	154

(continued)

Table 2 Continued

Study	Year study spans	Population	Setting	Measured or self-reported BMI	Time when BMI was measured	Definition of underweight (BMI in kg/m^2)	Outcome and its definition	Number of women: Cases	Number of women: Controls
Pitiphat, 2008[77]	1999–2002	Medically insured women who participated in Project Viva and delivered live infants	1 of 8 Harvard Vanguard Medical Associates Centres, eastern Massachusetts, USA	Self-reported	Pre-pregnancy	NR	PTB (<37 weeks)	105	1530
Spinillo, 1998[78]	1988–95	Women who received prenatal care and delivered at the Department of Obstetrics and Gynecology at Pavia University Cases: women with spontaneous preterm (24–35 weeks) deliveries Controls: women who delivered at term	One hospital: Pavia University, Pavia, Italy	Self-reported	NR	<19.5	Spontaneous PTB (24–35 weeks)	230	460
Williams, 1993[87]	1977–80	Women who delivered singletons	One hospital: the Boston Hospital for Women, Boston, Massachusetts, USA	Self-reported	Postpartum	<18	Spontaneous PTB (<37 weeks)	795	795
Xue, 2008[80]	2001–02	Caucasian nurses who were cancer free and whose mother reported their birth weight, lived with spouse, received prenatal care and had singleton pregnancies without pre-eclampsia or eclampsia	Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII), USA	Self-reported	Post-pregnancy	NR	LBW (<2500 g)	1810	30 051
Yogev, 2007[79]	1995–99	Women with GDM first diagnosed in their current pregnancy, who delivered singletons; all were treated at the same centre	One hospital: San Antonio, Texas, USA	Measured	Pre-pregnancy	NR	Spontaneous PTB (24–37 weeks)	163	1363
Zeitlin, 2001[84]	NR	Cases: all women who delivered live and stillborn singletons at 22–36 weeks' gestation Controls: every 10th woman who delivered a live or stillborn singleton at ⩾37 weeks' gestation	Maternity hospitals in 16 European countries	Self-reported, hospital record	NR	<18.3	PTB (22–36 weeks)	4707	7821
Total								11 879	52 279

GA: gestational age; GDM: gestational diabetes mellitus; MCH: maternal–child health; NR: not reported in study; NRD: no raw data available in the study, on adjusted OR; PROM: premature rupture of membranes; NA: no information.

Table 3 Summary table of outcomes in cohort studies of underweight women compared with women with normal weight

	Pooled crude data			Pooled adjusted or matched data		
Outcome	Number of studies	RR (95% CI)[a]	I^2 value (%)	Number of studies	RR (95% CI)[a]	I^2 value (%)
PTB <37 weeks	32	1.21 (1.14 to 1.28)	81	14	1.29 (1.15 to 1.46)	76
Spontaneous PTB <37 weeks	13	1.19 (1.02 to 1.39)	89	8	1.32 (1.10 to 1.57)	64
Induced PTB <37 weeks	6	1.09 (0.89 to 1.34)	68	4	1.21 (1.07 to 1.36)	0
PTB 32–36 weeks	4	1.09 (0.91 to 1.31)	85	2	1.25 (1.09 to 1.43)	0
PTB <32 or 33 weeks	9	1.15 (1.01 to 1.31)	76	4	1.13 (0.92 to 1.38)	47
LBW <2500 g	24	1.50 (1.34 to 1.68)	73	9	1.64 (1.38 to 1.94)	50
Moderately LBW 1500–2500 g	1	1.85 (1.74 to 1.97)	NA	1	2.10 (1.59 to 2.76)	NA
Very LBW <1500 g	2	1.04 (0.59 to 1.83)	91	1	1.54 (1.22 to 1.94)	NA
Extremely LBW <1000 g	1	1.61 (1.21 to 2.13)	NA	1	1.48 (0.98 to 2.23)	NA
IUGR	8	1.58 (1.42 to 1.76)	57	4	1.54 (1.38 to 1.72)	36
Difference in mean birth weight (g)	8	−153 (−288 to −79)	99	0	NA	
Difference in mean gestational age at birth (weeks)	3	−0.14 (−0.21 to −0.06)	0	0	NA	

g: grams; I^2: I squared; NA: not applicable; LBW: low birthweight (<2500 g); IUGR: intrauterine growth restriction (<10% for gestation age).
[a]RR calculated using random effects, inverse variance.

(iii) There was little outcome bias given that our outcomes had standard definitions and were objectively measured; for instance, LBW was always defined as birth weight <2500 g. (iv) Confounding was assessed based on the number of variables that were adjusted for. Confounding variables that might explain part or all of the relationship we detected between maternal underweight and PTB or LBW were incompletely addressed in a variety of ways by the included studies: (a) exclusion, (b) matching, (c) comparison of some variables such as age and BMI and determining that they were not different between the exposed and unexposed women and (d) controlling for some variables that were different between the two groups using multiple regression. Most studies assessed some confounding variables; however, no single study addressed all. (v) Many of the studies did not calculate a sample size or power calculation or use matched analyses when indicated. (vi) Attrition bias was rare given that follow-up occurred within the admission to hospital for delivery.

Trim-and-fill analyses

In order to assess publication bias, a priori we planned trim-and-fill analyses for outcomes with ⩾10 studies. The trim-and-fill analysis of PTB <37 weeks suggested that two studies were 'missing' from the initially meta-analyzed crude RR of 1.21, 95% CI 1.14–1.28; however, when the two studies were imputed yielding a risk based on a total of 34 studies, the risk of PTB <37 weeks in underweight women remained almost identical (RR 1.21, 95% CI 1.14–1.29). The unadjusted risk of spontaneous PTB in underweight women was similar with four additional imputed studies (RR 1.31, 95% CI 1.14–1.50, 17 studies). There were no additional imputed studies for the adjusted risk of PTB <37 weeks or for LBW (with the original studies showing an increased risk in underweight mothers, RR 1.29, 95% CI 1.15–1.46, 14 studies, and RR 1.50, 95% CI 1.34–1.68, 24 studies, respectively) (Supplementary Data #3 available at *IJE* online).

A priori defined sensitivity analyses for PTB

Many of the categories in the sensitivity analyses had few or no studies.

(i) In developed, but not developing, countries, underweight women had an increased risk of PTB compared with normal weight women (RR 1.22, 95% CI 1.15–1.30, 27 studies, and RR 0.99, 95% CI 0.67–1.45, four studies, respectively) (Table 7).
(ii) There were no low-quality studies (see Quality Assessment section).
(iii) There were no increases in PTB in the study that specified underweight adolescents compared with their normal weight peers (RR 0.97, 95% CI 0.75–1.25[39]) nor in the two studies

Study or Subgroup	Below reference Events	Below reference Total	Reference Events	Reference Total	Weight (%)	Risk ratio (95% CI) IV, Random
Adams *et al.*[65]	28	231	159	1419	1.8	1.08 (0.74–1.58)
Ancel *et al.*[64]	282	665	4434	11328	6.0	1.08 (0.99–1.19)
Baeten *et al.*[5]	1208	18551	2642	49321	6.5	1.22 (1.14–1.30)
Barros *et al.*[7]	32	625	105	2158	1.8	1.05 (0.72–1.55)
Berkowitz *et al.*[47]	439	712	1027	1668	6.4	1.00 (0.93–1.07)
Bhattacharya *et al.*[48]	345	2842	1537	14076	5.7	1.11 (1.00–1.24)
Bondevik *et al.*[49]	16	262	40	661	1.0	1.01 (0.58–1.77)
Clausen *et al.*[50]	31	651	87	2183	1.7	1.19 (0.80–1.78)
De *et al.*[43]	28	451	119	1450	1.7	0.76 (0.51–1.13)
Dietz *et al.*[20]	5941	20352	13786	59088	7.0	1.25 (1.22–1.28)
Driul *et al.*[51]	28	230	46	533	1.4	1.41 (0.91–2.20)
Ehrenberg *et al.*[53]	321	1978	1075	6988	5.6	1.05 (0.94–1.18)
Gardosi and Francis[54]	203	2038	1056	15946	5.0	1.50 (1.30–1.74)
Gilboa *et al.*[55]	27	321	114	2218	1.6	1.64 (1.09–2.45)
Haas *et al.*[37]	8	54	58	863	0.7	2.20 (1.11–4.38)
Hauger *et al.*[36]	360	2628	10	99	0.9	1.36 (0.75–2.46)
Hickey *et al.*[56]	294	2741	521	6943	5.1	1.43 (1.25–1.64)
Kim et al.[30]	69	1362	66	1112	2.2	0.85 (0.61–1.18)
Leung *et al.*[2]	195	2629	1392	22041	5.0	1.17 (1.02–1.36)
Lumme *et al.*[59]	51	990	259	6433	2.6	1.28 (0.95–1.71)
Merlino *et al.*[60]	21	152	149	1374	1.5	1.27 (0.83–1.95)
Monaghan *et al.*[61]	32	640	53	1387	1.5	1.31 (0.85–2.01)
Nohr *et al.*[19]	216	3857	2607	57923	5.2	1.24 (1.09–1.42)
Ray *et al.*[6]	3	43	61	218	0.3	0.25 (0.08–0.76)
Ronnenberg *et al.*[63]	22	303	20	272	0.9	0.99 (0.55–1.77)
Sahu *et al.*[44]	1	46	8	205	0.1	0.56 (0.07–4.35)
Savitz *et al.*[45]	52	365	131	1102	2.5	1.20 (0.89–1.62)
Scholl *et al.*[39]	67	415	194	1164	3.1	0.97 (0.75–1.25)
Sebire *et al.*[21]	2745	38182	9819	176923	6.8	1.30 (1.24–1.35)
Siega-Riz *et al.*[22]	40	499	108	2626	2.0	1.95 (1.37–2.77)
Smith *et al.*[23]	1425	17968	4977	95516	6.6	1.52 (1.44–1.61)
Yekta *et al.*[25]	2	30	8	140	0.2	1.17 (0.26–5.22)
Total (95% CI)		122813		545378	100.0	1.21 (1.14–1.28)
Total events	14532		46668			

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 159.98$, df = 31 ($P < 0.00001$); $I^2 = 81\%$

Test for overall effect: $Z = 6.33$ ($P < 0.00001$)

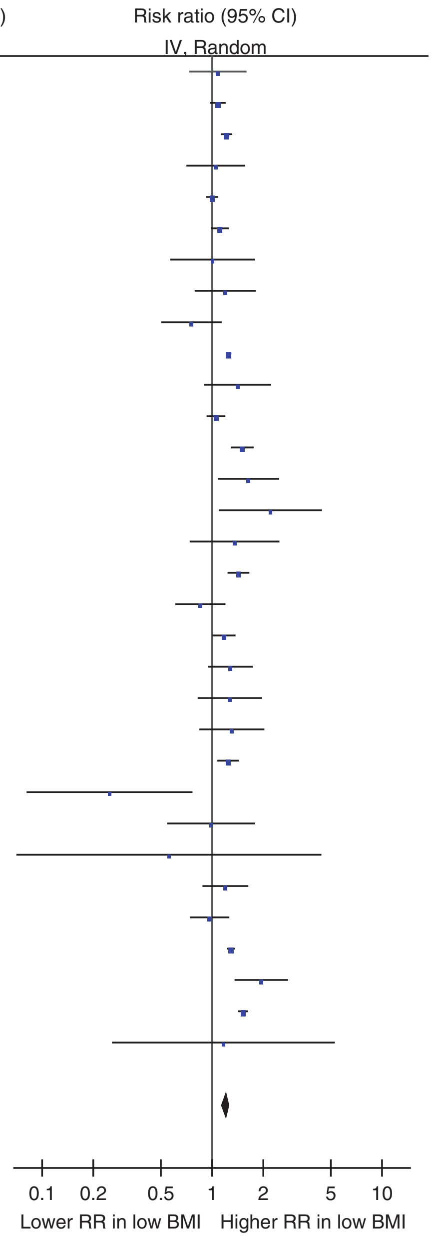

Figure 2 Forest plot of the risk of having a PTB in underweight women compared with women with normal weight in crude data from cohort studies. Preterm birth is defined as birth <37 weeks' gestation. Sizes of data markers indicate the weights of each study in the analysis. Random indicates that the random effects model was used for statistical pooling

that compared underweight adults with their normal weight peers (RR 0.82, 95% CI 0.59–1.14[43,63]).

(iv) The risk of PTB was increased in both black underweight women (RR 1.33, 95% CI 1.10–1.60[56]) and white underweight women (RR 1.53, 95% CI 1.23–1.90[56]) compared with their normal weight peers.

(v) When we excluded the two case–control studies,[70,81] which had a BMI cut-off >20 kg/m^2 to define the underweight women, the risk of PTB in underweight women became significant (matched data, OR 1.78, 95% CI 1.26–2.50, one study), whereas previously with the inclusion of De Haas[70] and Al-Eissa[81] it had not been (OR 1.41, 95% CI 0.73–2.71, three studies).

A priori defined sensitivity analyses for LBW

Many of the categories in the sensitivity analyses had few or no studies.

(i) In both developed and developing countries, underweight women had similarly increased risks of having a singleton with LBW compared with normal weight women (RR 1.48, 95% CI

Study or subgroup	log(Risk ratio)	SE	Weight (%)	Risk ratio (95% CI) IV, Random
Adams *et al.*[65]	0.08	0.26	3.9	1.08 (0.65–1.80)
Barton *et al.*[46]	0.19	0.15	7.5	1.21 (0.90–1.62)
Bhattacharya *et al.*[48]	0	0.08	11.0	1.00 (0.85–1.17)
Gilboa *et al.*[55]	0.34	0.21	5.2	1.40 (0.93–2.12)
Haas *et al.*[37]	0.75	0.38	2.2	2.12 (1.01–4.46)
Hauger *et al.*[36]	0.33	0.06	12.0	1.39 (1.24–1.56)
Kim *et al.*[30]	–0.14	0.21	5.2	0.87 (0.58–1.31)
Leung *et al.*[2]	0.18	0.08	11.0	1.20 (1.02–1.40)
Mercer *et al.*[34]	0.73	0.23	4.7	2.08 (1.32–3.26)
Ronnenberg *et al.*[63]	0.09	0.36	2.4	1.09 (0.54–2.22)
Savitz *et al.*[45]	0.02	0.26	3.9	1.02 (0.61–1.70)
Sebire *et al.*[21]	0.15	0.03	13.1	1.16 (1.10–1.23)
Siega-Riz *et al.*[22]	0.64	0.19	5.9	1.90 (1.31–2.75)
Smith *et al.*[23]	0.5	0.06	12.0	1.65 (1.47–1.85)
Total (95% CI)			**100.0**	**1.29 (1.15–1.46)**

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 54.46$, df = 13 ($P < 0.00001$); $I^2 = 76\%$
Test for overall effect: $Z = 4.20$ ($P < 0.0001$)

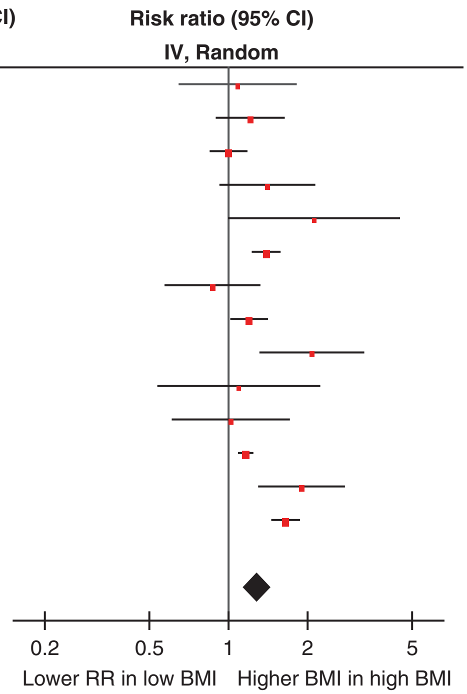

Figure 3 Forest plot of the risk of having a PTB in underweight women compared with women with normal weight in adjusted data from cohort studies. PTB is defined as birth <37 weeks' gestation. Sizes of data markers indicate the weights of each study in the analysis. Random indicates that the random effects model was used for statistical pooling

1.29–1.68, 15 studies, and RR 1.52, 95% CI 1.25–1.85, 9 studies, respectively).

(ii) There were no low-quality studies (see Quality Assessment section).

(iii) Underweight adolescents but not adult women had an increased risk of an LBW infant compared with their normal weight peers (RR 1.62, 95% CI 1.19–2.21,[39] and RR 1.19, 95% CI 0.61–2.33,[63] respectively).

(iv) Compared with their normal weight peers, underweight black women were at increased risk of having an LBW infant in the single study that specified black race (RR 6.13, 95% CI 2.59–14.47[63]). There were no studies that specified a population of white women.

(v) When we excluded the single cohort study,[62] which had a BMI cut-off >20 kg/m^2 to define the underweight women, the pooled risk of LBW was nearly identical (RR 1.49, 95% CI 0.33–1.68) to the previously obtained risk including Ogbonna[62] (RR 1.50, 95% CI 1.34–1.68, 24 studies).

(*Post hoc* sensitivity analyses are in Supplementary Data #4 available at *IJE* online.)

Discussion

In this systematic review and meta-analyses, we determined that singletons born to underweight women have higher risks of overall, spontaneous and induced PTB <37 weeks and LBW <2500 g. PTB and LBW are the two most important determinants of neonatal morbidity and mortality.[8] In addition, underweight women have increased risks of having an infant with moderately LBW 1500–2500 g, VLBW <1500 g, IUGR, lower mean birth weight and shorter mean gestation. These findings were generally supported across the continuum of study design and variations in the definition of maternal underweight, as well as across crude and adjusted data.

The association between maternal underweight and LBW and PTB might be explained directly by a lack of nutrients resulting in diminished fetal growth or duration of gestation or indirectly through other associated factors such as smoking, poor diet or medical illness. In developed countries, underweight women may smoke, which may contribute to both PTB and LBW, but women smoke much less often in developing countries. In developing countries, but less in the developed, there is likely a higher proportion of underweight women in the lower socio-economic classes who are engaged in strenuous manual labour, or possibly have ethnic or genetic predisposition towards thinness.

This is the first complete systematic review and meta-analyses to our knowledge of the association of maternal underweight and PTB or LBW. Two previous studies have addressed a portion of the evidence. Honest *et al.'s* systematic review was limited to spontaneous PTB and found that in seven studies,

Table 4 Summary table of perinatal outcomes in case–control studies of underweight women compared with normal weight women

Outcomes	Total number of studies	Pooled crude data			Pooled adjusted or matched data		
		Number of studies	OR (95% CI)	I^2 value (%)	Number of studies	OR (95% CI)	I^2 value (%)
PTB <37 weeks	6	3	1.55 (1.35–1.77)	0	3	RR 1.41 (0.73–2.71)	81
Spontaneous PTB <37 weeks	4	2	1.77 (1.35–2.32)	0	2	RR 1.25 (0.41–3.80)	86
Induced PTB <37 weeks	0	NA	NA	NA	NA	NA	NA
PTB 32–36 weeks	0	NA	NA	NA	NA	NA	NA
PTB <32 or 33 weeks	0	NA	NA	NA	NA	NA	NA
LBW <2500 g	3	3	1.81 (1.16–2.84)	63	1	2.02 (1.26–3.14)	NA
Moderately LBW 1500–2500 g	0	NA	NA	NA	NA	NA	NA
Very LBW <1500 g	0	NA	NA	NA	NA	NA	NA
Extremely LBW <1000 g	0	NA	NA	NA	NA	NA	NA
IUGR	0	NA	NA	NA	NA	NA	NA
Difference in mean birth weight (g)	0	NA	NA	NA	NA	NA	NA
Difference in mean gestational age at birth (weeks)	0	NA	NA	NA	NA	NA	NA

CI: confidence interval; g: grams; I^2: I squared; IUGR: intrauterine growth restriction (<10% for gestation); NA: not applicable; OR: Odds Ratio calculated using random effect, Mantel-Haenszel; PTB: preterm birth.

maternal BMI <20 kg/m^2 was associated with a positive likelihood ratio ranging from 1.01 (95% CI 0.92–1.10) to 1.75 (95% CI 1.33–2.31).[92] However, there have been a number of large studies published since their literature search ended in 2002. A WHO Collaborative study without the standard literature search that forms the basis of systematic reviews meta-analyzed 25 data sets identified by researchers attending a 1990 conference.[93] They found increased risks of PTB (OR 1.3, 95% CI 1.1–1.4) and LBW (OR 1.8, 95% CI 1.7–2.0) and in women with low BMI (<25% quartile) compared with women with higher BMI (>75% quartile).[93]

Strengths of our meta-analysis include the thoroughness with which the outcomes of PTB and LBW were addressed (including spontaneous and induced PTB as well as varying gestational cut-offs and variations on LBW including <2500, 1500–2500, <1500 and <1000 g). We performed a thorough quality assessment of the included studies and explored heterogeneity with sensitivity analyses. Moreover, we compared the results of crude and matched or adjusted data to try to determine if the perinatal outcomes we found were because of underweight or explained by confounding factors. We undertook a robust analysis of publication bias using trim-and-fill analyses.

Limitations of this systematic review include potential confounding factors (variables besides underweight that might explain the increase in LBW), which were not explored in most of the original studies, such as socio-economic status and smoking. Moreover, none of the studies distinguished between women who were thin but healthy and women who were underweight because they were ill. Presumably most of the women were still able to ovulate, although only one study[47] noted whether reproductive assistance was necessary to conceive. Many studies examining LBW did not either limit to term gestations or stratify term and preterm LBW. Hence, the original studies, and therefore this systematic review, cannot determine if infants who were born preterm and who were LBW were appropriately grown or growth restricted. However, the risk of LBW was higher in underweight women with infants born at term than in studies that did not specify term vs preterm. In many instances, our ability to draw useful information from the sensitivity analyses was limited by the small number of studies in each category, limiting our power to detect significant results. Although many of the studies used self-reported BMI, it has been shown to be very similar to objectively measured BMI in pregnant women. A large study by Schieve[94] observed that the mean difference between measured and reported weight in underweight women was only 0.5 kg (1.1 pounds), and in normal weight women was 1.1 kg (2.5 pounds). Similarly, Lederman[95] observed that pre-pregnancy weight from the clinical record was highly correlated with measured weight as well

Study or subgroup	Below reference Events	Below reference Total	Reference Events	Reference Total	Weight (%)	Risk ratio (95% CI) IV, Random
Baeten *et al.*[5]	1103	18975	2067	50378	10.2	1.42 (1.32–1.52)
Bhattacharya *et al.*[48]	269	2842	980	14076	9.3	1.36 (1.20–1.55)
Bondevik *et al.*[49]	58	262	114	661	6.4	1.28 (0.97–1.70)
Clausen *et al.*[50]	21	651	65	2182	3.6	1.08 (0.67–1.76)
Dubois and Girard[52]	9	122	49	1253	2.2	1.89 (0.95–3.75)
Ehrenberg *et al.*[53]	305	1978	958	6988	9.5	1.12 (1.00–1.27)
Frederick *et al.*[29]	21	393	63	1629	3.6	1.38 (0.85–2.24)
Gilboa *et al.*[55]	11	321	61	2218	2.5	1.25 (0.66–2.34)
Hulsey *et al.*[57]	1630	14141	2984	45916	10.3	1.77 (1.67–1.88)
Johnson *et al.*[41]	36	755	32	1621	3.8	2.42 (1.51–3.86)
Lawoyin and Oyediran[58]	2	5	11	109	0.8	3.96 (1.18–13.30)
Lumme *et al.*[59]	38	990	170	6443	5.3	1.45 (1.03–2.05)
Maddah[27]	18	208	23	414	2.7	1.56 (0.86–2.82)
Mobasheri and Golalipour[31]	2	46	5	161	0.5	1.40 (0.28–6.98)
Ogbonna *et al.*[62]	31	136	16	117	3.0	1.67 (0.96–2.89)
Ogunyemi *et al.*[42]	15	78	7	223	1.5	6.13 (2.59–14.47)
Panahandeh and Purghasemi[32]	7	38	25	219	1.8	1.61 (0.75–3.46)
Rode *et al.*[35]	7	385	17	1531	1.4	1.64 (0.68–3.92)
Ronnenberg *et al.*[63]	21	303	16	272	2.5	1.18 (0.63–2.21)
Sahu *et al.*[44]	11	46	22	205	2.4	2.23 (1.16–4.27)
Scholl *et al.*[39]	56	415	97	1164	5.9	1.62 (1.19–2.21)
Tsukamoto *et al.*[24]	37	493	105	2301	5.1	1.64 (1.15–2.36)
Yekta *et al.*[25]	5	30	15	140	1.3	1.56 (0.61–3.95)
Zhou and Olsen[40]	35	1938	77	4536	4.6	1.06 (0.72–1.58)
Total (95% CI)		**45551**		**144757**	**100.0**	**1.50 (1.34–1.68)**
Total events	3748		7979			

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 85.13$, df = 23 ($P < 0.00001$); $I^2 = 73\%$

Test for overall effect: $Z = 7.03$ ($P < 0.00001$)

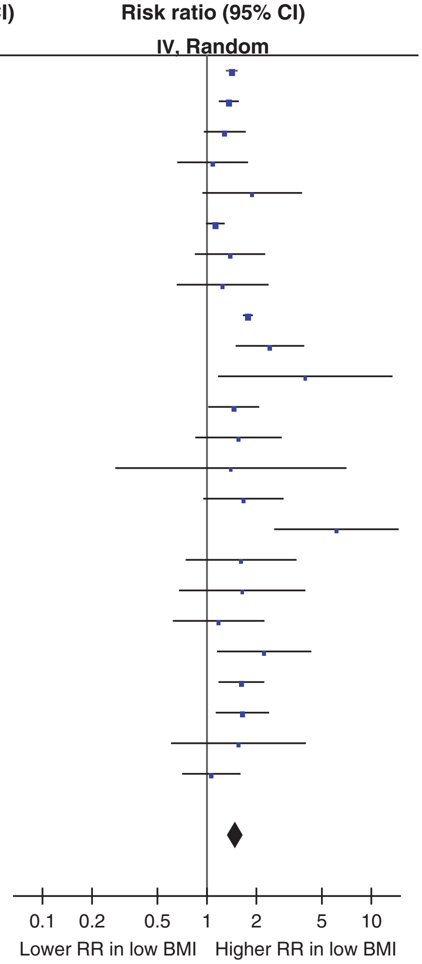

Figure 4 Forest plot of the risk of having an infant with LBW in underweight women compared with women with normal weight in crude data from cohort studies. PTB is defined as birth <37 weeks' gestation. Sizes of data markers indicate the weights of each study in the analysis. Random indicates that the random effects model was used for statistical pooling

Study or subgroup	log(Risk ratio)	SE	Weight (%)	Risk ratio (95% CI) IV, Random
Barton *et al.*[46]	0.05	0.17	12.5	1.05 (0.75–1.47)
Bhattacharya *et al.*[48]	0.48	0.12	16.5	1.62 (1.28–2.04)
Frederick *et al.*[29]	0.43	0.2	10.5	1.54 (1.04–2.28)
Hoa 1996	0.97	0.25	7.9	2.64 (1.62–4.31)
Lumme *et al.*[59]	0.39	0.16	13.2	1.48 (1.08–2.02)
Rasmussen and Borup[33]	1.39	1.11	0.6	4.01 (0.46–35.36)
Ronnenberg *et al.*[63]	0.43	0.2	10.5	1.54 (1.04–2.28)
Tsukamoto *et al.*[24]	0.5	0.18	11.8	1.65 (1.16–2.35)
Wolfe 1991	0.74	0.12	16.5	2.10 (1.66–2.65)
Total (95% CI)			**100.0**	**1.64 (1.38–1.94)**

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 15.93$, df = 8 ($P = 0.04$); $I^2 = 50\%$

Test for overall effect: $Z = 5.75$ ($P < 0.00001$)

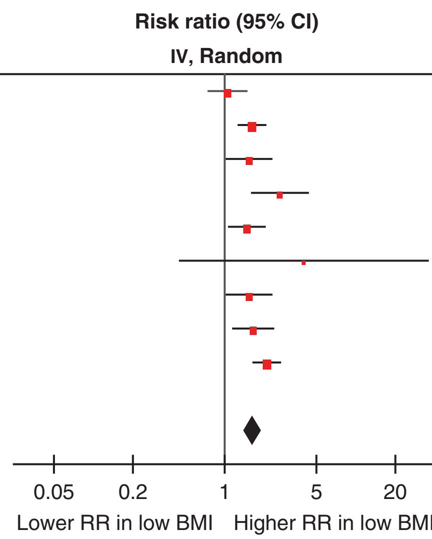

Figure 5 Forest plot of the risk of having an infant with LBW in underweight women compared with women with normal weight in adjusted data from cohort studies. PTB is defined as birth <37 weeks' gestation. Sizes of data markers indicate the weights of each study in the analysis. Random indicates that the random effects model was used for statistical pooling

Table 5 Quality assessment of cohort studies included in systematic review and meta-analyses of PTB and LBW in underweight women compared with normal weight women

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Adams, 1995[65]	Minimal	Medical record	NR	Low	NR	Minimal	Low
				Adjusted for: medical centre			
Ancel, 1999[64]	Minimal	Measured	Minimal	Low	Low	Minimal	Low
				Adjusted for: country of residence			
				Assessed different but not controlled for: age, education, social class, smoking, previous PTB, marital status, previous abortion			
Baeten, 2001[5]	Minimal	Self-reported (chart)	Minimal	Minimal	NR	Minimal	Low
				Adjusted for: age, education, smoking, preeclampsia, insurance, marital status			
Barros, 1996[7]	Low	Self-reported within 48 h of birth	Minimal	N/A (primary exposure not anthropometry)	Low	Minimal	Low
Barton, 2001[46]	Low	Measured	NR	Minimal	Low	Minimal	Low
				Matched for: parity, race, gestational age at diagnosis of mild preeclampsia			
				Assessed for and not different: antihypertensive medications, smoking, low-dose aspirin therapy, height, chronic hypertension, age			
				Assessed different but not controlled for: pre-pregnancy weight			
Berkowitz, 1998[47]	Low	Perinatal database	Low	Low	NR	Low	Low
				Assessed for and not different: IVF			
				Assessed different but not controlled for: DM, hypertension			
Bhattacharya, 2007[48]	Low	Measured pre-pregnancy	Minimal	Minimal	Low	Minimal	Low
				Assessed for and not different: age, husband's social class, DM			
				Assessed different but not controlled for: week of first antenatal visit, height, married or cohabiting, smoking			
Bondevik, 2001[49]	Low	Self-reported	Minimal	N/A (primary exposure not anthropometry)	NR	Minimal	Low
Clausen, 2006[50]	Low	Medical record at 17–19 weeks of gestation	Minimal	Minimal	Low	NR	Low
				Adjusted for:			
				For LBW: age, parity, education, smoking, Oslo east, living alone			
				For PTB: parity, smoking, living alone			

(continued)

Table 5 Continued

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Cnattingius, 1998[18,b]	Minimal	Self-reported during first visit (chart)	Minimal	Minimal Adjusted for: age, parity, education, smoking, total weight gain, height, mother living with father	Low	Minimal	Low
De, 2007[43]	Low	Self-reported, hospital record	Minimal	N/A (primary exposure is not anthropometry)	Low	Minimal	Low
Dietz, 2006[20]	Minimal	Self-reported (questionnaire)	Minimal	Minimal Adjusted for: parity, race, marital status, Medicaid recipient	Low	Minimal	Low
Driul, 2008[51]	Low	Maternal database	Low	Moderate[a] (potential confounders not assessed by the original study)	NR	Minimal	Moderate
Dubois, 2006[52]	Minimal	Self-reported	Minimal	Low Adjusted for: age, gestational age	Low	Low	Low
Ehrenberg, 2003[53]	Low	Perinatal database	Low	Moderate[a] (potential confounders not assessed by the original study)	Low	Minimal	Low
Frederick, 2008[29,c]	Low	Self-reported pre-pregnancy	Minimal	Minimal Adjusted for: age, education, smoking, preeclampsia, GDM, race, marital status, PTB, infant gender	Low	Minimal	Low
Gardosi, 2000[54]	Low	Measured during first visit (chart)	NR	Minimal Adjusted for: age, smoking, weight at first visit, race, history of abortion, alcohol	Low	Minimal	Low
Gilboa, 2008[55]	Low	Self-reported 6 months after birth	Minimal	Minimal Adjusted for: age, parity, education, smoking, preeclampsia, alcohol, infant race, infant sex	Low	Minimal	Low
Haas, 2005[37]	Minimal	Self-reported during first visit before 20 weeks' gestation	Minimal	Minimal Adjusted for: age, country of birth, race/ethnicity, level of education, parity, site of care, BMI, prior to pregnancy: (i) physical function, (ii) depressive symptoms, (iii) chronic health conditions, (iv) level of exercise and (v) smoking status. During pregnancy: (i) smoking status, (ii) physical function, (iii) depressive symptoms, (iv) use of illicit drugs, eclampsia or preeclampsia, GDM, other pregnancy complications and (v) inadequate prenatal care	Low	Minimal	Low
Hauger, 2008[36]	Minimal	Self-reported and measured at first visit	NR	Minimal Adjusted for: age, parity, smoking, preeclampsia, DM, GDM, hypertension, caesarean section, number of prenatal visits	Minimal	Moderate	Low

(continued)

Table 5 Continued

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Hickey, 1997[56]	Minimal	Self-reported pre-pregnancy (medical record)	NR	Minimal Adjusted for: age, parity, education, smoking, previous PTB, last birth, height	Low	Minimal	Low
Hulsey, 2005[57]	Low	Self-reported	Minimal	Minimal Adjusted for: hypertension, ethnicity, DM, prenatal care utilization, WIC (the special supplemental food programme for women, infants and children) participation, intendedness of pregnancy	Low	Minimal	Low
Johnson, 1992[41]	Minimal	Self-reported during first visit	Minimal	Minimal Adjusted for: ethnicity, married, tobacco, alcohol, drugs, parity, fetal sex	Low	Minimal	Low
Kim, 2005[30]	Minimal	Self-reported	Minimal	Minimal Adjusted for: For nulliparous women: income, passive smoking, BMI, vaginal bleeding, coffee drinking, drug abuse For multiparous women: vaginal bleeding, alcohol abuse, prior spontaneous abortion, prior preterm delivery, prior preeclampsia, drug abuse, housework Stratified for: parity	Low	Minimal	Low
Lawoyin, 1992[58]	Minimal	Measured	Minimal	Moderate[a] (potential confounders not assessed by the original study)	Low	Low	Low
Leung, 2008[2]	Low	Dataset	Low	Minimal Adjusted for: age, parity, DM, year delivered, previous caesarean section, gestational age at booking	Low	Minimal	Low
Lumme, 1995[59]	Minimal	Measured	NR	Minimal Adjusted for: age, parity, education, smoking, race	Low	Low	Low
Maddah, 2005[27]	Moderate	Self-reported and measured	NR	Moderate[a] (potential confounders not assessed by the original study)	Moderate	Minimal	Moderate
Mercer, 1996[34]	Minimal	Measured	NR	Minimal Adjusted for: acute or chronic lung disease, vaginal bleeding, paying job during pregnancy, race, previous PTB, contractions, bishop score, poor social environment	Moderate	Moderate	Moderate

(continued)

Table 5 Continued

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Merlino, 2006[60]	Low	Measured (chart)	Low	Minimal Assessed for and not different: previous PTB, gestational age Assessed different but not controlled for: age, gestational age	High	Minimal	Moderate
Mobasheri, 2007[31]	Low	Self-reported	NR	Low Assessed for and not different: working status Assessed different but not controlled for: education	Low	Minimal	Low
Monaghan, 2001[61]	Minimal	Measured	Minimal	Minimal Adjusted for: age, placental complications, pre-existing hypertension, net pregnancy weight gain <10 kg, not married, secondary education or less	NR	Minimal	Low
Nohr, 2007[19]	Minimal	Self-reported early in pregnancy	Low	Minimal Adjusted for: age, parity, social–occupational status, mother's height, alcohol use, smoking	Low	Minimal	Low
Ogbonna, 2007[62]	Low	Measured during postpartum hospital stay	Minimal	Minimal Adjusted for: age, parity, education, marital status, gravidity, HIV, malaria infection, multivitamin use	NR	Minimal	Low
Ogunyemi, 1998[42]	Low	Self-reported and measured during first visit	NR	Minimal Adjusted for: BMI, NICU admission, previous LBW Unclear, but suspect adjustment for: previous cesarean section, previous fetal death, asthma, cesarean, vomiting, preeclampsia, hypertension	Low	Minimal	Low
Panahandeh, 2007[32]	Low	Self-reported (chart, prenatal/ obstetrical record) during first visit	Minimal	Low Adjusted for: For PTB: hypertension, inter-pregnancy interval For LBW: drug use For SGA: drug use, age	Low	Minimal	Low
Panaretto, 2006[28,b]	Low	Measured during first visit	Low	Low Assessed, but not different: For PTB: HTN, inter-pregnancy interval For LBW: drug use For SGA: drug use, age	Low	Minimal	Low

(continued)

Table 5 Continued

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Rasmussen, 1992[33]	Low	Chart, obstetrical record during first visit	Minimal	Low Adjusted for: age, parity	High	Minimal	Moderate
Ray, 2001[6]	Low	Antenatal sheet	Low	Minimal Adjusted for: DM class, age, parity, hypertension, previous PTB, history of prior cesarean section or uterine surgery, history of neonatal death or stillbirth, net weight gain during pregnancy	Low	Minimal	Low
Rode, 2007[35]	Low	Self-reported at 12–18 weeks of gestation	Minimal	Minimal Assessed for and not different: marital status, alcohol intake, caffeine intake, gestational age Assessed different but not controlled for: age, parity, education, smoking, preeclampsia, weight gain	Low	Minimal	Low
Ronnenberg, 2003[63]	Low	Measured	Minimal	Minimal Adjusted for: age, education, infant gender, height, work stress, maternal exposure to dust or noise or passive smoking	Low	NR	Low
Sahu, 2007[44]	Low	Self-reported	NR	Low Assessed for and not different: fetal sex Assessed different but not controlled for: GDM, pregnancy induced hypertension, anaemia	Low	Minimal	Low
Savitz, 2005[45]	Minimal	Self-reported at 24–29 weeks of gestation	NR	Minimal Adjusted for: age, parity, education, smoking, race, previous PTB, marital status, poverty index	Low	Minimal	Low
Sayers, 1997[38,a]	Low	Measured postpartum before discharge	Minimal	Minimal Adjusted for: smoking, male infant, aboriginal ancestor	Moderate	Minimal	Low
Scholl, 1989[39]	Low	Self-reported during first visit	Minimal	Minimal Adjusted for: For LBW, IUGR: age, weight gain adequacy, smoking, ethnicity For PTB: age, weight gain adequacy, previous PTB, adequacy of prenatal care Assessed for and not different: clinical pay status, parity	Low	Minimal	Low

(continued)

Table 5 Continued

Author, year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Sebire, 2001[21]	Minimal	Measured during first visit	Low	Minimal Matched for: age, parity, smoking, pre-eclampsia, DM, GDM, race, hypertension	Moderate	Minimal	Low
Siega-Riz, 1996[22,c]	Low	Self-reported and measured	NR	Moderate Assessed different but not controlled for: education, hypertension, smoking, marital status, race	Low	Minimal	Low
Smith, 2006[26,b]	Minimal	Maternal database	Low	Low Assessed, but not different: age Assessed, different, and not controlled for: (not clearly stated but assumed based on Table 2 in original article) AFP, hCG, smoking, previous miscarriage, marital status, previous therapeutic abortions	Low	Minimal	Low
Smith, 2007[26]	Minimal	Measured early in pregnancy	Minimal	Minimal Adjusted for: age, parity, smoking, marital status, maternal height, deprivation category, previous spontaneous early pregnancy losses and therapeutic	Minimal	Minimal	Low
Tsukamoto, 2007[24]	Minimal	Self-reported and measured pre-pregnancy	Minimal	Minimal Adjusted for: age, parity, maternal weight gain Assessed for and not different: PIH Assessed different but not controlled for: GDM	Low	Minimal	Low
Yekta, 2006[25]	Low	Self-reported and measured early in pregnancy	NR	Minimal Adjusted for: age, parity, education	Low	Minimal	Low
Zhou, 1997[40]	Low	Chart	Minimal	Moderate[a] (potential confounders not assessed by the original study)	Moderate	Low	Moderate

AFP: alpha-fetoprotein; DM: diabetes mellitus; GDM: gestational diabetes mellitus; hCG: human chorionic gonadotropin; HIV: human immunodeficiency virus; IVF: *in vitro* fertilization; NA: not applicable (if the article's primary predictor variable was not anthropometry, but crude data could still be extracted, 'not applicable' was used in the assessment of confounding); NICU: neonatal intensive care unit; NR: not reported in study; PIH: pregnancy-induced hypertension; SGA: small for gestational age; WIC: Women, Infants and Children Nutrition Programme.

[a]Assessment of confounding factor bias was done by evaluation of each studies' assessment of potential confounders by four methods: (i) adjustment with regression, (ii) matching, (iii) assessment of potential confounders on univariate analyses that were found to be not significantly different between groups and (iv) assessment of potential confounders on univariate analyses that were different between groups and not controlled for.

[b]Non-pooled articles.

[c]Siega-Riz[22] and Frederick[29] are cohort studies. However, within the manuscript, data were also presented in a format that allowed pooling with case–control data although they are listed only in the tables with cohort studies.

Table 6 Quality assessment of case–control studies included in systematic review and meta-analyses of PTB and LBW in underweight women compared with normal weight women

Author, Year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Al-Eissa, 1994[81]	Low	Measured after delivery	NR	Minimal Confounders adjusted: age <20 years, previous PTD, previous LBW, mud house, first- or second-degree relatives, non-relatives, prior spontaneous abortion, inadequate prenatal care, antepartum haemorrhage, inter-pregnancy interval <12 months, first- or second-trimester vaginal bleeding	Low	Minimal	Low
Amin, 1993[66]	Low	Measured	NR	Minimal Confounders assessed, but not different: education, caste, type of housing (roof) Confounders assessed, different, and not controlled for: age, gravida	Low	Minimal	Low
Begum, 2003[67]	Minimal	Recorded from chart	NR	Minimal Confounders assessed, but not different: age, parity, previous PTB, gravida, previous abortion Confounders assessed, different, and not controlled for: income, education	Low	Minimal	Low
Catov, 2007[68]	Minimal	Measured	Minimal	Moderate Confounders assessed, but not different: age, parity, education, smoking, preeclampsia, race, hypertension, maternal status, mother's birth weight if <2500 g	Low	Minimal	Low
Chumnijarakij, 1992[86]	Minimal	Self-reported	NR	Minimal Confounders assessed, but not different: age, education, religion Confounders assessed, different and not controlled for: income, occupation, bleeding during early pregnancy, age, parity, no antenatal care, drug addiction, previous abortion, coffee, hypertension, hard work, paternal unemployment/labour, maternal age <19 years, unlawful marriage, second trimester accident, Hct <30%, preeclampsia, education	Low	Minimal	Low
Conti, 1998[69]	Low	Self-reported during pregnancy	Minimal	Minimal Confounders matched: age, parity insurance	Low	Minimal	Low
de Haas, 1991[70]	Low	Measured	Minimal	Minimal Confounders matched: age, delivery date Confounders assessed, different and not controlled for: education, race, marital status	High	Low	Moderate

(continued)

Table 6 Continued

Author, Year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Delgado-Rodriguez, 1998[71]	Low	Self-reported (chart)	Minimal	Minimal	Low	Minimal	Low
				Confounders assessed, but not different: age, parity, smoking			
				Confounders assessed, different and not controlled for: education, race, marital status			
Deshmukh, 1998[72]	Low	Measured	Minimal	Minimal	Minimal	High	Low
				Confounders assessed, but not different: age, birth interval			
				Confounders assessed, different and not controlled for: parity, social class, smoking, anaemia			
Dhar, 2003[88]	Low	Measured	Minimal	Minimal	Low	Minimal	Low
				Confounders adjusted: age, parity, antenatal care, birth to conception interview, sex of new born, gestational age, Hct, BMI after delivery, weight, Hb, mean arm circumference, income, education, father's education, father's occupation			
Gosselink, 1992[73]	Low	Self-reported	NR	Minimal	NR	Minimal	Low
				Confounders matched: age, parity, race			
				Confounders assessed, but not different: age, parity, race			
Hashim, 2000[74]	Low	Measured	Minimal	Minimal	Low	Minimal	Low
				Confounders assessed, but not different: parity, education, social class, antenatal visits, newborn sex, presence of household helper, occupation, consanguinity			
				Confounders assessed, different and not controlled for: age			
Hediger, 1995[89]	Low	Self-reported during first visit	Minimal	Minimal	Low	Minimal	Low
				Confounders assessed, but not different: smoking, maternal height, pregravid BMI, gestational age at delivery, medical recipient, primiparous			
Karim, 1997[82]	Moderate	Self-reported immediately after birth	Minimal	Minimal	Low	Minimal	Moderate
				Confounders adjusted: age, education, income			
				Confounders assessed, but not different: parity, age of last surviving child, husband's occupation, place of delivery			
				Confounders assessed, different and not controlled for: age, income, education, gender of child			
Lawoyin, 1997[83]	Low	Measured during pregnancy	Minimal	Low	Low	Minimal	Low
				Confounders assessed, but not different: Hb			

(continued)

Table 6 Continued

Author, Year	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias[a]	Analytical bias	Attrition bias	Overall likelihood of bias
Le, 2007[75]	Low	Self-reported after birth	Low	NA (article's primary exposure is not anthropometry	Low	Minimal	Low
Melamed, 2008[90]	Low	Hospital record	Minimal	NA (article's primary exposure is not anthropometry)	Low	Minimal	Low
Mohsen, 2007[85]	Low	Measured after delivery	Minimal	Moderate (confounders not assessed)[a]	Low	Minimal	Moderate
Ngare, 1998[91]	Low	Measured	Minimal	Minimal	High	Minimal	Low
				Confounders adjusted: age, parity, education, socio-economic status, BMI, height, weight, Hb, stillbirths, kilocalories consumed, live birth, arm circumference			
				Confounders assessed, different and not controlled for: social and economic status			
Ojha, 2007[76]	Low	Measured post pregnancy	Minimal	Low	NR	Minimal	Low
				Confounders matched: age, parity			
Pitiphat, 2008[77]	Minimal	Self-reported pre-pregnancy	Minimal	NA (primary exposure not anthropometry)	NR	Minimal	Low
Spinillo, 1998[78]	Low	Self-reported	NR	Minimal	Low	NR	Low
				Confounders assessed, but not different: parity, fetal gender			
				Confounders assessed, different and not controlled for: age, social class, smoking			
Williams, 1993[87]	Low	Self-reported postpartum	Minimal	Minimal	Low	Minimal	Low
				Confounders adjusted: age, parity, education, smoking, diabetes mellitus, hypertension, coffee, alcohol, marijuana, previous spontaneous or induced abortion, history of sexually transmitted disease			
Xue, 2008[80]	Low	Self-reported post pregnancy	Minimal	Moderate (confounders not assessed)[a]	NR	Minimal	Moderate
Yogev, 2007[79]	Low	Measured pre-pregnancy	NR	NA (article's primary exposure is not anthropometry)	Low	Minimal	Low
Zeitlin, 2001[84]	Minimal	Self-reported, hospital record	Minimal	Minimal	Low	Minimal	Low
				Confounders adjusted: obstetric history, marital status, BMI <18.3 or $>29.8\,kg/m^2$, smoking in third trimester, age at completion of schooling			

GDM: gestational diabetes mellitus; Hb: haemoglobin; Hct: haematocrit; NA: not applicable (if the article's primary predictor variable was not anthropometry, but crude data could still be extracted, 'not applicable' was used in the assessment of confounding): NR: not reported in study.

[a]Confounding factor bias was done by evaluation of each study's assessment of potential confounders by four methods: (i) adjustment with regression, (ii) matching, (iii) assessment of potential confounders on univariate analyses that were not different and (iv) assessment of potential confounders on univariate analyses that were different and not controlled for.

Table 7 Sensitivity analyses in cohort studies of underweight women compared with normal weight women

Sensitivity analyses	Number of studies	Number of participants	RR (95% CI)	I^2 value (%)
PTB				
Developed countries	27	654 279	**1.22 (1.15–1.30)**	83
Developing countries	4	1919	0.99 (0.67–1.45)	0
Low-quality studies	0		NA	
Remainder of studies	32	668 191	1.21 (1.14–1.28)	81
Adolescents	1	1579	0.97 (0.75–1.25)	NA
Adults	2	2476	0.82 (0.59–1.14)	0
Black women	1	3999	**1.33 (1.10–1.60)**	NA
White women	1	4022	**1.53 (1.23–1.90)**	NA
Self-reported BMI	16	242 488	**1.19 (1.09–1.30)**	78
Measured BMI	7	378 086	**1.28 (1.14–1.44)**	89
BMI assessed prepregnancy	21	252 280	**1.20 (1.11–1.30)**	73
BMI assessed during pregnancy	9	401 135	**1.25 (1.13–1.39)**	86
BMI assessed postpartum	1	11 993	**1.08 (0.99–1.19)**	NA
BMI cut-offs exactly 20–25, <20	5	348 602	**1.26 (1.08–1.46)**	91
BMI cutoffs close to 20–25, <20	15	322 223	**1.19 (1.08–1.30)**	57
BMI cut-offs not close to 20–25, <20	2	27 668	**1.46 (1.33–1.62)**	0
LBW				
Developed countries	15	185 595	**1.48 (1.29–1.68)**	82
Developing countries	9	4713	**1.52 (1.25–1.85)**	0
Low-quality studies	0		NA	
Remainder of studies	24	190 308	1.50 (1.34–1.68)	73
Adolescents	1	1579	**1.62 (1.19–2.21)**	NA
Adults	1	575	1.19 (0.61–2.33)	NA
Black women	1	301	**6.13 (2.59–14.47)**	NA
White women	0		NA	
Self-reported BMI	12	85 254	**1.65 (1.40–1.95)**	38
Measured BMI	4	17 860	**1.43 (1.14–1.79)**	18
BMI assessed pre-pregnancy	20	171 806	**1.58 (1.37–1.82)**	70
BMI assessed during pregnancy	4	20 925	**1.35 (1.19–1.53)**	7
BMI assessed postpartum	1	253	**1.86 (0.96–3.61)**	NA
BMI cut-offs exactly 20–25, <20	4	96 537	**1.43 (1.34–1.52)**	0
BMI cut-offs close to 20–25, <20	20	93 771	**1.65 (1.39–1.96)**	70
BMI cut-offs not close to 20–25, <20	0		NA	
Term LBW	5	7307	**2.14 (1.52–3.00)**	54
LBW of all babies (including term and preterm LBW)	24	190 308	**1.50 (1.34–1.68)**	73

NA: not applicable; all studies: overweight, obese or very obese combined; RR calculated using random effects, inverse variance (crude data), developed and developing countries were assigned according to the Central Intelligence Agency (CIA) criteria and Zeitlin[84] included 16 European countries composed of both developed and developing countries and hence was not included in the sensitivity analyses for developing and developed countries. Significant results are indicated in bold.

as with the self-reported value [with underweight women over-reporting by 1.1 kg (2.4 pounds)]. Another study[96] found self-reported weight during pregnancy to be accurate, within 1.4 kg (3 pounds) of measured. Moreover, we performed a *post hoc* sensitivity analyses examining the effects of (i) self-reported vs measured BMI (Table 7). The risks of PTB were similar in underweight women by self-reported BMI (RR 1.19, 95% CI 1.09–1.30) or measured BMI (RR 1.28, 95% CI 1.14–1.44), as were the risks of LBW with self-reported BMI (RR 1.65, 95% CI 1.40–1.95) and measured BMI (RR 1.43, 95% CI 1.14–1.79).

BMI has a more important influence on outcomes such as PTB and LBW than the amount of weight gained during pregnancy.[97] Although both the Institute of Medicine's 1990 guidelines[98] and the more recent iteration in May 2009[99] advocate higher weight gain for underweight women than normal weight women, risk stratification of the pregnancy is required at the start of the pregnancy, prior to the occurrence of weight gain.

We pooled data based on the original studies' definitions of underweight as has been done in other meta-analyses.[11,93,100] Thus, in the underweight category, BMI ranged from $\leqslant$18.3 to $\leqslant$23 kg/m^2 (but <20 kg/m^2 in all but three studies), and in the reference group BMI ranged from 18.3 to 29.8 kg/m^2, but usually <26 kg/m^2. Using the studies' own definitions overcomes the issue of varying cut-offs between studies for underweight, and moreover, allows the cut-offs to be appropriate to the specific population. Using population-specific BMI cut-offs occurs outside of obstetrics, including for instance, using lower BMI cut-offs for obesity in Asian than Caucasian populations since lower cut-offs have been associated with increased risks of cardiovascular disease.[101]

Further research is required to distinguish outcomes in healthy thin women vs women who are underweight because of illness. More study is need on the impact of race and adolescence.

In conclusion, women who are underweight are at increased risk of PTB in developed countries and of LBW in both developing and developed countries. Underweight women should receive preconception counselling to inform them of their risks. During pregnancy, underweight women may benefit from counselling by a dietician, improved access to nutritious foods or supplements and increased surveillance. There remains considerable work to be done to shift societal values toward normal, healthy weights for women.

Supplementary data

Supplementary data are available at *IJE* online.

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KEY MESSAGES

- In this systematic review, we determined that underweight women have an increased risk of PTB overall (adjusted RR 1.29, 95% CI 1.15–1.46), as well as increases in spontaneous PTB (adjusted RR 1.32, 95% CI 1.10–1.57) and induced PTB (adjusted RR 1.21, 95% CI 1.07–1.36).
- Underweight women had an increased risk of having an LBW infant (adjusted RR 1.64, 95% CI 1.38–1.94). In developed countries, underweight women had an increased risk of PTB (RR 1.22, 95% CI 1.15–1.30) but not in developing countries (RR 0.99, 95% CI 0.67–1.45).
- In both developed and developing countries, underweight women were at increased risk of having an LBW infant (RR 1.48, 95% CI 1.29–1.68, and RR 1.52, 95% CI 1.25–1.85, respectively).

References

1 Heslehurst N, Ells LJ, Simpson H, Batterham A, Wilkinson J, Summerbell CD. Trends in maternal obesity incidence rates, demographic predictors, and health inequalities in 36,821 women over a 15-year period. *BJOG* 2007;**114:**187–94.

2 Leung TY, Leung TN, Sahota DS *et al*. Trends in maternal obesity and associated risks of adverse pregnancy outcomes in a population of Chinese women. *BJOG* 2008; **115:**1529–37.

3 Mardones F, Rosso P. A weight gain chart for pregnant women designed in Chile. *Matern Child Nutr* 2005;**1:**77–90.

4 Rodrigues TC, Canani LH, Gross JL. Metabolic syndrome, insulin resistance and cardiovascular disease in type-1 diabetes mellitus. *Arq Bras Cardiol* 2010;**94:**134–39.

5 Baeten JM, Bukusi EA, Lambe M. Pregnancy complications and outcomes among overweight and obese nulliparous women. *Am J Public Health* 2001;**91:**436–40.

6 Ray JG, Vermeulen MJ, Shapiro JL, Kenshole AB. Maternal and neonatal outcomes in pregestational and

gestational diabetes mellitus, and the influence of maternal obesity and weight gain: the DEPOSIT study. Diabetes Endocrine Pregnancy Outcome Study in Toronto. *QJM* 2001;**94:**347–56.

[7] Barros H, Tavares M, Rodrigues T. Role of prenatal care in preterm birth and low birthweight in Portugal. *J Public Health Med* 1996;**18:**321–28.

[8] Liu S, Allen A, Fraser W. Fetal and infant health outcomes. In: *Preterm Birth Rate. Canadian Perinatal Health Report*. Ottawa, Ontario: Public Health Agency of Canada, 2008, pp. 123–32.

[9] Branum AM, Schoendorf KC. Changing patterns of low birthweight and preterm birth in the United States, 1981–98. *Paediatr Perinat Epidemiol* 2002;**16:**8–15.

[10] Stroup DF, Berlin JA, Morton SC *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;**283:**2008–12.

[11] McDonald SD, Han Z, Mulla S, Lee T, Beyene J. Maternal overweight and obesity and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. *BMJ* 2010;**341:**c3428.

[12] Devereaux PJ, Schunemann HJ, Ravindran N *et al*. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. *JAMA* 2002;**288:**2449–57.

[13] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327:**557–60.

[14] The World Factbook 2008 (CIA). https://www.cia.gov/library/publications/the-world-factbook/index.html (date last accessed January 2009).

[15] McDonald SD, Han Z, Mulla S, Ohlsson A, Beyene J, Murphy KE. Preterm birth and low birth weight among *in vitro* fertilization singletons: a systematic review and meta-analyses. *Eur J Obstet Gynecol Rep Biol* 2009;**146:** 138–48.

[16] Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;**56:**455–63.

[17] Duval S, Tweedie R. A nonparametric ''trim and fill'' method of accounting for publication bias in meta-analysis. *J Am Stat Assoc* 2000;**95:**89–98.

[18] Cnattingius S, Bergstrom R, Lipworth L, Kramer MS. Prepregnancy weight and the risk of adverse pregnancy outcomes [see comment]. *New Engl J Med* 1998;**338:** 147–52.

[19] Nohr EA, Bech BH, Vaeth M, Rasmussen KM, Henriksen TB, Olsen J. Obesity, gestational weight gain and preterm birth: a study within the Danish National Birth Cohort. *Paediatr Perinat Epidemiol* 2007;**21:**5–14.

[20] Dietz PM, Callaghan WM, Cogswell ME, Morrow B, Ferre C, Schieve LA. Combined effects of prepregnancy body mass index and weight gain during pregnancy on the risk of preterm delivery. *Epidemiol* 2006;**17:**170–77.

[21] Sebire NJ, Jolly M, Harris J, Regan L, Robinson S. Is maternal underweight really a risk factor for adverse pregnancy outcome? A population-based study in London. *BJOG* 2001;**108:**61–66.

[22] Siega-Riz AM, Adair LS, Hobel CJ. Maternal underweight status and inadequate rate of weight gain during the third trimester of pregnancy increases the risk of preterm delivery. *J Nutr* 1996;**126:**146–53.

[23] Smith GCS, Shah I, Pell JP, Crossley JA, Dobbie R. Maternal obesity in early pregnancy and risk of spontaneous and elective preterm deliveries: a retrospective cohort study. *Am J Pub Health* 2007;**97:**157–62.

[24] Tsukamoto H, Fukuoka H, Inoue K, Koyasu M, Nagai Y, Takimoto H. Restricting weight gain during pregnancy in Japan: a controversial factor in reducing perinatal complications. *Eur J Obstet Gynecol Reprod Biol* 2007;**133:**53–59.

[25] Yekta Z, Ayatollahi H, Porali R, Farzin A. The effect of pre-pregnancy body mass index and gestational weight gain on pregnancy outcomes in urban care settings in Urmia-Iran. *BMC Preg Childbirth* 2006;**6:**15.

[26] Smith GC, Shah I, White IR, Pell JP, Crossley JA, Dobbie R. Maternal and biochemical predictors of spontaneous preterm birth among nulliparous women: a systematic analysis in relation to the degree of prematurity. *Int J Epidemiol* 2006;**35:**1169–77.

[27] Maddah M. Pregnancy weight gain in Iranian women attending a cross-sectional study of public health centres in Rasht. *Midwifery* 2005;**21:**365–70.

[28] Panaretto K, Lee H, Mitchell M *et al*. Risk factors for preterm, low birth weight and small for gestational age birth in urban Aboriginal and Torres Strait Islander women in Townsville. *Aust N Z J Public Health* 2006;**30:** 163–70.

[29] Frederick IO, Williams MA, Sales AE, Martin DP, Killien M. Pre-pregnancy body mass index, gestational weight gain, and other maternal characteristics in relation to infant birth weight. *Matern Child Health J* 2008;**12:** 557–67.

[30] Kim YJ, Lee BE, Park HS, Kang JG, Kim JO, Ha EH. Risk factors for preterm birth in Korea: a multicenter prospective study. *Gynecol Obstet Invest* 2005;**60:**206–12.

[31] Mobasheri E, Golalipour MJ. The effect of pre-pregnancy body mass index on gestational weight gain and pregnancy outcomes in Gorgon, North Iran. *J Med Sci* 2007; **7:**905–08.

[32] Panahandeh Z, Purghasemi M. Prepregnancy body mass index and pregnancy weight gain in rural regions of Guilan province Iran. *Iran J Med Sci* 2007;**32:**36–39.

[33] Rasmussen KL, Borup K. Prepregnancy low body mass index is not a predictor of labor complications. *Gynecol Obstet Invest* 1992;**34:**79–81.

[34] Mercer BM, Goldenberg RL, Das A *et al*. The preterm prediction study: a clinical risk assessment system. *Am J Obstet Gynecol* 1996;**174:**1885–93.

[35] Rode L, Hegaard HK, Kjaergaard H, Moller LF, Tabor A, Ottesen B. Association between maternal weight gain and birth weight. *Obstet Gynecol* 2007;**109:**1309–15.

[36] Hauger MS, Gibbons L, Vik T, Belizan JM. Prepregnancy weight status and the risk of adverse pregnancy outcome. *Acta Obstet Gynecol Scand* 2008;**87:**953–59.

[37] Haas JS, Fuentes-Afflick E, Stewart AL *et al*. Prepregnancy health status and the risk of preterm delivery. *Arch Pediatr Adolesc Med* 2005;**159:**58–63.

[38] Sayers S, Powers J. Risk factors for aboriginal low birthweight, intrauterine growth retardation and preterm birth in the Darwin Health Region. *Aust N Z J Pub Health* 1997; **21:**524–30.

[39] Scholl TO, Hediger ML, Salmon RW, Belsky DH, Ances IG. Influence of prepregnant body mass and weight gain for gestation on spontaneous preterm

delivery and duration of gestation during adolescent pregnancy. *Am J Hum Biol* 1989;**1:**657–64.

40 Zhou W, Olsen J. Gestational weight gain as a predictor of birth and placenta weight according to pre-pregnancy body mass index. *Acta Obstet Gynecol Scand* 1997;**76:**300–07.

41 Johnson JWC, Longmate JA, Frentzen B. Excessive maternal weight and pregnancy outcome. *Am J Obstet Gynecol* 1992;**167:**353–72.

42 Ogunyemi D, Hullett S, Leeper J, Risk A. Prepregnancy body mass index, weight gain during pregnancy, and perinatal outcome in a rural black population. *J Matern Fetal Med* 1998;**7:**190–93.

43 De B, Lin S, Lohsoonthorn V, Williams MA. Risk of preterm delivery in relation to maternal low birth weight. *Acta Obstet Gynecol Scand* 2007;**86:**565–71.

44 Sahu MT, Agarwal A, Das V, Pandey A. Impact of maternal body mass index on obstetric outcome. *J Obstet Gynaecol Res* 2007;**33:**655–59.

45 Savitz DA, Dole N, Herring AH *et al*. Should spontaneous and medically indicated preterm births be separated for studying aetiology? *Paediatr Perinat Epidemiol* 2005;**19:** 97–105.

46 Barton JR, O'Nan JM, Bergauer NK, Jacques DL, Sibai BM. Does a lean prepregnancy body mass index influence outcome in pregnancies complicated by mild preeclampsia remote from term? *Hypertens Preg* 2001;**20:** 283–90.

47 Berkowitz GS, Blackmore-Prince C, Lapinski RH, Savitz DA. Risk factors for preterm birth subtypes. *Epidemiology* 1998;**9:**279–85.

48 Bhattacharya S, Campbell DM, Liston WA, Bhattacharya S. Effect of Body Mass Index on pregnancy outcomes in nulliparous women delivering singleton babies. *BMC Pub Health* 2007;**7:**168.

49 Bondevik GT, Lie RT, Ulstein M, Kvale G. Maternal hematological status and risk of low birth weight and preterm delivery in Nepal. *Acta Obstet Gynecol Scand* 2001; **80:**402–08.

50 Clausen T, Oyen N, Henriksen T. Pregnancy complications by overweight and residential area. A prospective study of an urban Norwegian cohort. *Acta Obstet Gynecol Scand* 2006;**85:**526–33.

51 Driul L, Cacciaguerra G, Citossi A, Martina MD, Peressini L, Marchesoni D. Prepregnancy body mass index and adverse pregnancy outcomes. *Arch Gynecol Obstet* 2008;**278:**23–26.

52 Dubois L, Girard M. Determinants of birthweight inequalities: population-based study. *Pediatr Int* 2006;**48:** 470–78.

53 Ehrenberg HM, Dierker L, Milluzzi C, Mercer BM. Low maternal weight, failure to thrive in pregnancy, and adverse pregnancy outcomes. *Am J Obstet Gynecol* 2003;**189:** 1726–30.

54 Gardosi J, Francis A. Early pregnancy predictors of preterm birth: the role of a prolonged menstruation-conception interval. *BJOG* 2000;**107:**228–37.

55 Gilboa SM, Correa A, Alverson CJ. Use of spline regression in an analysis of maternal prepregnancy body mass index and adverse birth outcomes: does it tell us more than we already know? *Ann Epidemiol* 2008;**18:** 196–205.

56 Hickey CA, Cliver SP, McNeal SF, Goldenberg RL. Low pregravid body mass index as a risk factor for preterm birth: variation by ethnic group. *Obstet Gynecol* 1997;**89:** 206–12.

57 Hulsey TC, Neal D, Bondo SC, Hulsey T, Newman R. Maternal prepregnant body mass index and weight gain related to low birth weight in South Carolina. *South Med J* 2005;**98:**411–15.

58 Lawoyin TO, Oyediran AB. A prospective study on some factors which influence the delivery of low birth weight babies in a developing country. *Afr J Med Med Sci* 1992;**21:** 33–39.

59 Lumme R, Rantakallio P, Hartikainen A, Jarvelin M. Pre-pregnancy weight and its relation to pregnancy outcome. *J Obstet Gynaecol* 1995;**15:**69–75.

60 Merlino A, Laffineuse L, Collin M, Mercer B. Impact of weight loss between pregnancies on recurrent preterm birth. *Am J Obstet Gynecol* 2006;**195:**818–21.

61 Monaghan SC, Little RE, Hulchiy O, Strassner H, Gladen BC. Risk factors for spontaneous preterm birth in two urban areas of Ukraine. *Paediatr Perinat Epidemiol* 2001;**15:**123–30.

62 Ogbonna C, Woelk GB, Ning Y, Mudzamiri S, Mahomed K, Williams MA. Maternal mid-arm circumference and other anthropometric measures of adiposity in relation to infant birth size among Zimbabwean women. *Acta Obstet Gynecol Scand* 2007;**86:**26–32.

63 Ronnenberg AG, Wang X, Xing H *et al*. Low preconception body mass index is associated with birth outcome in a prospective cohort of Chinese women. *J Nutr* 2003;**133:** 3449–55.

64 Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Very and moderate preterm births: are the risk factors different? *BJOG* 1999;**106:** 1162–70.

65 Adams MM, Sarno AP, Harlass FE, Rawlings JS, Read JA. Risk factors for preterm delivery in a healthy cohort. *Epidemiology* 1995;**6:**525–32.

66 Amin N, Abel R, Sampathkumar V. Maternal risk factors associated with low birth weight. *Indian J Pediatr* 1993;**60:** 269–74.

67 Begum F, Buckshe K, Pande JN. Risk factors associated with preterm labour. *Bangladesh Med Res Counc Bull* 2003; **29:**59–66.

68 Catov JM, Bodnar LM, Kip KE *et al*. Early pregnancy lipid concentrations and spontaneous preterm birth. *Am J Obstet Gynecol* 2007;**197:**610–17.

69 Conti J, Abraham S, Taylor A. Eating behavior and pregnancy outcome. *J Psychosom Res* 1998;**44:**465–77.

70 de Haas I, Harlow BL, Cramer DW, Frigoletto FD Jr. Spontaneous preterm birth: a case–control study. *Am J Obstet Gynecol* 1991;**165(5 Pt 1):**1290–96.

71 Delgado-Rodriguez M, Perez-Iglesias R, Gomez-Olmedo M, Bueno-Cavanillas A, Galvez-Vargas R. Risk factors for low birth weight: results from a case–control study in southern Spain. *Am J Phys Anthropol* 1998;**105:** 419–24.

72 Deshmukh JS, Motghare DD, Zodpey SP, Wadhva SK. Low birth weight and associated maternal factors in an urban area. *Indian Pediatr* 1998;**35:**33–36.

73 Gosselink CA, Ekwo EE, Woolson RF, Moawad A, Long CR. Dietary habits, prepregnancy weight, and

weight gain during pregnancy. Risk of pre term rupture of amniotic sac membranes. *Acta Obstet Gynecol Scand* 1992;**71:**425–38.

[74] Hashim TJ, Moawed SA. The relation of low birth weight to psychosocial stress and maternal anthropometric measurements. *Saudi Med J* 2000;**21:**649–54.

[75] Le HTT, Jareinpituk S, Kaewkungwal J, Pitiphat W. Increased risk of preterm birth among non-smoking, non-alcohol drinking women with maternal periodontitis. *Southeast Asian J Trop Med Pub Health* 2007;**38:** 586–93.

[76] Ojha N, Malla DS. Low birth weight at term: relationship with maternal anthropometry. *JNMA J Nepal Med Assoc* 2007;**46:**52–56.

[77] Pitiphat W, Joshipura KJ, Gillman MW, Williams PL, Douglass CW, Rich-Edwards JW. Maternal periodontitis and adverse pregnancy outcomes. *Commun Dent Oral Epidemiol* 2008;**36:**3–11.

[78] Spinillo A, Capuzzo E, Piazzi G, Ferrari A, Morales V, Di MM. Risk for spontaneous preterm delivery by combined body mass index and gestational weight gain patterns. *Acta Obstet Gynecol Scand* 1998;**77:**32–36.

[79] Yogev Y, Langer O. Spontaneous preterm delivery and gestational diabetes: the impact of glycemic control. *Arch Gynecol Obstet* 2007;**276:**361–65.

[80] Xue F, Willett WC, Rosner BA, Forman MR, Michels KB. Parental characteristics as predictors of birthweight. *Hum Reprod* 2008;**23:**168–77.

[81] al-Eissa YA, Ba'Aqeel HS. Risk factors for spontaneous preterm birth in a Saudi population. *Eur J Obstet Gynecol Reprod Biol* 1994;**57:**19–24.

[82] Karim E, Mascie-Taylor CG. The association between birthweight, sociodemographic variables and maternal anthropometry in an urban sample from Dhaka, Bangladesh. *Ann Hum Biol* 1997;**24:**387–401.

[83] Lawoyin TO. The relationship between maternal weight gain in pregnancy, hemoglobin level, stature, antenatal attendance and low birth weight. *Southeast Asian J Trop Med Public Health* 1997;**28:**873–76.

[84] Zeitlin JA, Ancel PY, Saurel-Cubizolles MJ, Papiernik E. Are risk factors the same for small for gestational age versus other preterm births? *Am J Obstet Gynecol* 2001; **185:**208–215.

[85] Mohsen MA, Wafay HA. Influence of maternal anthropometric measurements and serum biochemical nutritional indicators on fetal growth. *J Med Sci* 2007;**7:** 1330–34.

[86] Chumnijarakij T, Nuchprayoon T, Chitinand S *et al*. Maternal risk factors for low birth weight newborn in Thailand. *J Med Assoc Thai* 1992;**75:**445–52.

[87] Williams MA, Mittendorf R, Stubblefield PG, Lieberman E, Schoenbaum SC, Monson RR. Risk factors for preterm premature rupture of the membranes. *J Maternal–Fetal Neonat Med* 1993;**2:**27–33.

[88] Dhar B, Mowlah G, Kabir DM. Newborn anthropometry and its relationship with maternal factors. *Bangladesh Med Res Counc Bull* 2003;**29:**48–58.

[89] Hediger ML, Scholl TO, Schall JI, Miller LW, Fischer RL. Fetal growth and the etiology of preterm delivery. *Obstet Gynecol* 1995;**85:**175–82.

[90] Melamed N, Chen R, Soiberman U, Ben-Haroush A, Hod M, Yogev Y. Spontaneous and indicated preterm delivery in pregestational diabetes mellitus: etiology and risk factors. *Arch Gynecol Obstet* 2008;**278:**129–34.

[91] Ngare DK, Neumann C. Predictors of low birthweight at the community level. *East Afr Med J* 1998;**75:**296–99.

[92] Honest H, Bachmann LM, Ngai C, Gupta JK, Kleijnen J, Khan KS. The accuracy of maternal anthropometry measurements as predictor for spontaneous preterm birth–a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2005;**119:**11–20.

[93] A WHO Collaborative Study of Maternal Anthropometry and Pregnancy Outcomes. *Int J Gynecol Obstet* 1997;**57:** 1–15.

[94] Schieve LA, Perry GS, Cogswell ME *et al*. Validity of self-reported pregnancy delivery weight: an analysis of the 1988 National Maternal and Infant Health Survey. NMIHS Collaborative Working Group. *Am J Epidemiol* 1999;**150:**947–56.

[95] Lederman SA, Paxton A. Maternal reporting of prepregnancy weight and birth outcome: consistency and completeness compared with the clinical record. *Matern Child Health J* 1998;**2:**123–26.

[96] Johnston EM. Weight changes during pregnancy and the postpartum period. *Prog Food Nutr Sci* 1991;**15:** 117–57.

[97] Nohr EA, Vaeth M, Baker JL, Sorensen TI, Olsen J, Rasmussen KM. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *Am J Clin Nutr* 2008;**87:**1750–59.

[98] Institutes of Medicine. Nutrition during pregnancy. In: *Report of the Subcommittee on Nutritional Status and Weight Gain during Pregnancy*. Washington, DC: National Academy Press, 1990.

[99] Institute of Medicine (IOM). *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: The National Academies Press, 2009.

[100] Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA* 2009;**301:**636–50.

[101] Li R, Lu W, Jia J *et al*. Relationships between indices of obesity and its cardiovascular comorbidities in a Chinese population. [see comment]. *Circu J* 2008;**72:** 973–78.

Appendix 1

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