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RESEARCH

Overweight and obesity in mothers and risk of preterm birth and low birth weight infants: systematic review and meta-analyses

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ABSTRACT

Objective To determine the relation between overweight and obesity in mothers and preterm birth and low birth weight in singleton pregnancies in developed and developing countries.

Design Systematic review and meta-analyses.

Data sources Medline and Embase from their inceptions, and reference lists of identified articles.

Study selection Studies including a reference group of women with normal body mass index that assessed the effect of overweight and obesity on two primary outcomes: preterm birth (before 37 weeks) and low birth weight (<2500 g).

Data extraction Two assessors independently reviewed titles, abstracts, and full articles, extracted data using a piloted data collection form, and assessed quality.

Data synthesis 84 studies (64 cohort and 20 case-control) were included, totalling 1 095 834 women. Although the overall risk of preterm birth was similar in overweight and obese women and women of normal weight, the risk of induced preterm birth was increased in overweight and obese women (relative risk 1.30, 95% confidence interval 1.23 to 1.37). Although overall the risk of having an infant of low birth weight was decreased in overweight and obese women (0.84, 0.75 to 0.95), the decrease was greater in developing countries than in developed countries (0.58, 0.47 to 0.71 *v* 0.90, 0.79 to 1.01). After accounting for publication bias, the apparent protective effect of overweight and obesity on low birth weight disappeared with the addition of imputed "missing" studies (0.95, 0.85 to 1.07), whereas the risk of preterm birth appeared significantly higher in overweight and obese women (1.24, 1.13 to 1.37).

Conclusions Overweight and obese women have increased risks of preterm birth and induced preterm birth and, after accounting for publication bias, appeared to have increased risks of preterm birth overall. The beneficial effects of maternal overweight and obesity on low birth weight were greater in developing countries and disappeared after accounting for publication bias.

INTRODUCTION

The continuum of overweight and obesity is now the most common complication of pregnancy in many developed and some developing countries. In the United Kingdom, 33% of pregnant women are overweight or obese.[1] In the United States, 12%[2] to 38%[3] of pregnant women are overweight and 11%[4] to 40%[3] are obese. In India, 8% of pregnant women are obese and 26% are overweight[5] and in China, 16% are overweight or obese.[6]

Preterm birth is the leading cause of neonatal mortality and morbidity and childhood morbidity[7] followed by low birth weight.[8] Whether maternal overweight and obesity is associated with increased,[9] decreased,[10] or neutral risks[11] of preterm birth has been debated in the literature, with the uncertainty reflected in the American College of Obstetrics and Gynecology Committee opinion on obesity in pregnancy.[12] Even low birth weight, which is typically thought to be reduced in infants of overweight and obese women,[3] is sometimes associated with neutral risks.[5] To accurately risk stratify a pregnancy at the first antenatal visit, as is standard, it is important to know the effect of overweight and obesity in mothers on preterm birth and low birth weight. We therefore undertook a systematic, comprehensive, and unbiased accumulation and summary of the available evidence from all study designs with a reference group of normal weight women to determine the direction and magnitude of the association of maternal overweight and obesity with preterm birth and low birth weight in singleton pregnancies in developed and developing countries.

METHODS

We carried out a systematic review and meta-analyses in accordance with the Meta-analysis Of Observational Studies in Epidemiology consensus statement.[13]

With the help of a librarian we searched Medline (1950 to 2 January 2009) and Embase (1980 to 2 January 2009), using individual comprehensive search strategies. This study was part of a constellation of systematic reviews examining maternal anthropometry and preterm birth and low birth weight (see search strategy in web extra appendix 1). Additional eligible studies were sought by reviewing the reference lists of identified articles.

Study eligibility criteria

For the constellation of systematic reviews examining maternal anthropometry, we included randomised trials, cohort studies, and case-control studies if one or more of the following maternal anthropometry variables was assessed as an exposure variable: body mass index (*=assessed before pregnancy, during pregnancy or postpartum), weight*, gestational weight gain, attained weight, or height*; and one or more of the following outcomes was assessed: preterm birth (<37 weeks, 32-36 weeks, and <32 weeks) and low birth weight (<2500 g), very low birth weight (<1500 g), and extremely low birth weight (<1000 g). Studies were restricted to those in English. For this particular systematic review of maternal overweight and obesity, we included studies with any body mass index definition of overweight and obese or very obese, whether from self report, objective measurement, medical charts, or databases.

We excluded duplicate publications, studies published only as abstracts, those involving fewer than 10 patients, and those that examined outcomes in multiples unless stratification was done for singleton versus twin outcomes.

Outcome measures

Our primary outcomes were preterm birth (before 37 weeks) and low birth weight (<2500 g) in singletons. Where possible we subdivided preterm birth into spontaneous and induced. Secondary outcomes were late preterm birth (32-36 weeks) and moderate preterm birth (before 32 weeks), and very low birth weight (<1500 g) and extremely low birth weight (<1000 g).

We also reported the following outcomes for studies that met the above inclusion criteria and mentioned intrauterine growth restriction (defined as birth weight <10% for gestational age), birth weight (grams), and gestational age at birth (weeks).

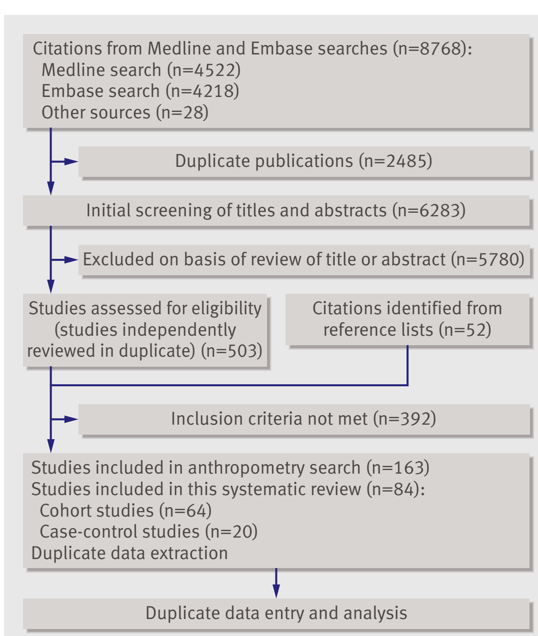

Fig 1 | **Study selection process**

Study and data collection processes

Two assessors (two of ZH, SDM, and SM) independently reviewed titles and abstracts of all identified citations. The full text article was retrieved if either reviewer considered the citation potentially relevant. Two reviewers (two of ZH, SDM and SM) independently evaluated each full text article. Disagreements were settled by discussion and consensus, with a third person as an adjudicator.

From full text articles and using a piloted data collection form, two reviewers independently extracted data on country of origin, years of study, study design, characteristics of participants, outcomes, and information on bias. We included information available from the publications. Inconsistencies were checked and resolved through the consensus process.

Data synthesis

We used Review Manager, version 5.0 (Cochrane Collaboration), for statistical analyses. For cohort studies we used relative risks to meta-analyse crude and separately, adjusted, dichotomous data, whereas for case-control studies we used odds ratios to pool crude and separately, matched or adjusted dichotomous data. Continuous data were analysed using a mean difference. Weighting of the studies in the meta-analyses was calculated on the basis of 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 pooled separately and then matched or adjusted data were pooled together. Where required and when the incidence of the outcome was rare, to be able to pool data, adjusted relative risks were calculated from adjusted odds ratios.[14] As is typical in meta-analyses, we did not adjust for multiple analyses. We focused on the combined results of overweight, obese, and very obese; however, where possible we also separately reported results for each individually in the summary tables. Clinical heterogeneity was evaluated. We calculated the I^2 value to measure heterogeneity. An I^2 value represents the percentage of total variation across studies due to heterogeneity rather than due to chance.[15] Values of 25%, 50%, and 75% have been regarded as representing low, moderate, and high heterogeneity.[15]

Sensitivity analyses were planned a priori using a few chosen groups to examine the effects of level of material wellbeing (developed *v* developing countries[16]), study quality (see web extra appendix 2), youth (adolescence *v* adulthood), and race. Three post hoc sensitivity analyses were carried out (see web extra appendix 3) to examine the effects of self reported compared with measured body mass index; body

Table 1 | Characteristics of cohort studies included in systematic review and meta-analyses of preterm birth and low birth weight in overweight and obese women compared with women of normal weight

Study (period)	Population	Setting	Body mass index (BMI): Self report or measured	BMI: When recorded	BMI: Definition of exposure (high BMI)	No of women: Exposed	No of women: Not exposed
Abenhaim* 2007[25] (1987-97)	All women who delivered live or stillborn infants ≥500 g	University of California, San Diego Medical Center, USA	Self report	In labour	30-39.9	NR	NR
Adams 1995[9] (1987-90)	Black and white enlisted service women who delivered live or stillborn singletons at or after 20 weeks' gestation	Four army medical centres, USA	NR	NR	≥26.0	67	1419
Ancel 1999[54] (1994-7)	Exposed: all consecutive single preterm births at 22-36 weeks. Unexposed: randomly selected 1 of every 10 consecutive term (>37 weeks) single births. Sample included live and stillborn infants	15 European countries	Measured	NR	>29.8 (*v* 18.3-29.8)	728	11 328
Baeten 2001[59] (1992-6)	Nulliparous women who delivered live singletons	Washington State, USA	Self report	NR	≥25	27 353	50 378
Barros 1996[51] (18 months)	Consecutive women who delivered live singleton at level 2 facility or for last four months of study at level 3 facility (teaching hospital)	Hospital de Famalicào and Hospital de S Joao Porto, Porto, Portugal	Self report	≤48 hours of birth	≥25	951	2158
Berkowitz 1998[26] (1986-94)	Women who delivered singletons; one pregnancy was randomly selected for women who had more than one eligible pregnancy	Mount Sinai Hospital, New York City, USA	NR	NR	>26.0	754	1668
Bhattacharya 2007[27] (1976-2005)	All primigravid women who delivered singletons after 24 weeks' gestation in Aberdeen city and district	Aberdeen maternity neonatal databank, UK	Measured	Before pregnancy	≥25	7323	14 076
Bianco 1998[60] (1988-95)	Morbidly obese women and non-obese women aged 20-34 with singletons	Mount Sinai Medical Centre, Toronto, Canada	Self report	NR	>35 (*v* 19-27)	613	11 313
Bondevik 2001[28] (1994-6)	Outpatient women at first antenatal visit	Patan Hospital, Kathmandu, Nepal	NR	NR	>24	313	661
Callaway 2006[29] (1998-2002)	Women with singletons booked for antenatal care	Mater Mother's Hospital, south Brisbane, Australia	Measured	<12 weeks' gestation	>25	4809	6443
Clausen 2006[30] (1995-7)	Women of Norwegian ancestry with an appointment for ultrasound screening	Aker Hospital, covered 14 of 23 districts from Oslo, Norway	NR	17-9 weeks' gestation	>25	690	2183
Cogswell 1995[50] (1990-1)	Women on low income at high nutritional risk enrolled in supplemental food programme with single, live, term infants; one infant selected from women who delivered more than one baby in 1990-1	Eight states in USA	Self report	NR	>26.0	19 732	33 809
Cnattingius* 1998[61] (1992-3)	Women born in Sweden, Denmark, Norway, Finland, or Iceland with information on prepregnancy BMI, who delivered singletons registered in Swedish medical birth register	Sweden	Self report	First antenatal visit	≥30	NR	NR
De 2007[48] (1996-2004)	Women who initiated prenatal care <20 weeks' gestation, were aged ≥18, could speak and read English, planned to carry pregnancy to term, and were to deliver at one of two hospitals	Swedish Medical Center, Seattle, or Tacoma General Hospital, Tacoma, Washington, USA	Self report	NR	≥25	634	1450
Dietz 2006[24] (1996-2001)	Women with singleton births from pregnancy risk assessment monitoring system	21 states in USA	Self report	NR	>26	33 582	59 088
Driul 2008[31] (2006)	Women with singletons and complete baseline maternal clinical information and pertinent outcome data	University of Udine, Italy	NR	NR	≥25	153	533
Dubois 2006[32] (1998-2002)	Random sample of children born in public health districts during 1998	Quebec, Canada	Self report	NR	≥25	568	1253
Frederick† 2008[46] (1996-2004)	English speaking women aged ≥18, who planned to deliver at one of two hospitals and were at ≤20 weeks' gestation at enrolment	Swedish Medical Center, Seattle, or Tacoma General Hospital, Tacoma, Washington, USA	Self report	Before pregnancy	>26	489	1629
Gardosi 2000[33] (1988-95)	Consecutive women with singleton live births	Hospital, Birmingham, UK	Measured	First antenatal visit	>29.4 (*v* 20.1-29.4)	2372	15 964
Gilboa 2008[34] (1981-9)	White or black women with liveborn infants at 25-40 weeks; exposed: randomly selected, without birth defects or pregestational diabetes	District of Columbia, Northern Virginia, Maryland, USA	Self report	NR	≥25	687	2218
Goldenberg 1998[10] (1992-4)	Women selected to reflect population by race and parity and identified at ≤24 weeks' gestation	National Institute of Child Health and Human Development Maternal Fetal Medicine Network, 10 centres in USA	NR	NR	>26	1037	1251
Haas 2005[55] (May 2001 to July 2002)	Women who delivered singletons, participated in Project WISH, and received prenatal care at a practice or clinic associated with the delivery hospitals and planned to deliver at one of these hospitals; were aged ≥18 at recruitment; spoke English, Spanish, or Cantonese; sought prenatal care <16 weeks' gestation; and could be contacted by telephone	Six delivery hospitals in San Francisco Bay area, California, USA	Self report	First antenatal visit <20 weeks	≥25	702	863
Hauger 2008[11] (2003-6)	Women with pregnancies ending in live birth or fetal death, at ≥ 22 weeks' gestation or birth weight >500 g	10 public hospitals in Buenos Aires city and province, Argentina	Self report	First antenatal visit	≥25	12 327	29 644
Hendler 2005[57] (1992-4)	Women with maternal height and prepregnancy weight available	10 medical centres in USA	NR	NR	>30 (*v* <30)	597	2313

Study (period)	Population	Setting	Body mass index (BMI): Self report or measured	Body mass index (BMI): When recorded	Body mass index (BMI): Definition of exposure (high BMI)	No of women: Exposed	No of women: Not exposed
Hickey 1997[35] (1982-6)	All women on low income who registered for prenatal care	Five clinical centres: California, Illinois, Ohio, Tennessee, Alabama, USA	Self report	Before pregnancy	›26.0	2775	6943
Hulsey 2005[36] (1998-9)	Women with live singleton with birth weight ≥500 g	South Carolina, USA	NR	NR	›26	27 236	45 916
Jensen 2003[21] (1992-6)	Women with oral glucose tolerance test who delivered first pregnancy in one of four hospitals	Four hospitals in Copenhagen, Denmark	NR	NR	≥25	1365	1094
Johnson 1992[58] (1987-9)	All women with singleton live births who delivered at ≥38 weeks and received prenatal care	Shands Hospital, Gainesville, Florida, USA	Self report	First antenatal visit	›26	815	2621
Kim 2005[47] (2001-4)	Women with singleton pregnancy at 20-42 weeks who had had obstetric ultrasound and were admitted to one of the included hospitals	Five institutions in Korea	Self report	NR	≥25	171	1112
Kumari 2001[22] (1996-8)	Women who attended antenatal clinic, weighing ≥90 kg during first 12 weeks of pregnancy	Al-Mafraq Hospital, Abu-Dhabi, United Arab Emirates	NR	NR	›40 (*v* 22-28)	188	300
Lawoyin 1992[37] (1988)	Randomly selected gravid women at first antenatal clinic visit with singletons	Random yet fair representation of whole city, Ibadan, Nigeria	Measured	NR	≥25	268	109
Leung 2008[6] (1995-2005)	Ethnically Chinese women with singleton pregnancy who presented at ≤20 weeks' gestation and gave birth at ≥24 completed weeks	University obstetric unit, Hong Kong, China	NR	NR	≥25	4633	22 041
Lumme 1995[38] (1985-6)	Women with singleton pregnancies	Northern Finland	NR	NR	≥25	1592	6433
Maddah 2005[44] (Jun 2002 to May 2003)	Women who attended one of six health centres randomly selected from total 12 centres in city	Six health centres, Rasht, Iran	Self report	NR	›26	82	414
Merlino 2006[39] (1996-2004)	All women delivering live or stillborn infant ›20 weeks	One medical centre, university, Cleveland, USA	Measured	NR	›25	957	1374
Mobasheri 2007[49] (2004-5)	Women who regularly attended two urban and rural centres for prenatal care	Gorgan, Iran	Self report	NR	›26	108	161
Monaghan 2001[40] (1992-5)	All pregnant women in two hospitals, with last menstrual period between 25 Dec 1992 and 23 Jul 1994	Dniprovski region of Kyiv and Dniprodzerzhinsk, Ukraine	Measured	NR	≥25	474	1387
Nohr 2007[23] (1996-2002)	Women with singletons who accepted invitation and signed consent form for Danish National Birth Cohort	Danish National Birth Cohort, Denmark	Self report	Early pregnancy	≥25	23 695	57 923
Ogbonna 2007[41] (1998-9)	Women living in urban centres near hospital and delivering at university affiliated hospital	Harare Maternity Hospital, Harare, Zimbabwe	Measured	Post partum, before discharge	›24.6	234	117
Ogunyemi 1998[62] (1990-5)	Consecutive black women on low income who registered for prenatal care in first trimester, who delivered singleton ›37 weeks	Western Alabama, USA	Self report	First antenatal visit	›26	281	223
Panahandeh 2007[52] (2002-3)	Women who delivered after 38 weeks who were cared for at one of seven health centres randomly selected from 15 centres	Seven local health centres (rural region), Guilan, Iran	NR	NR	›26	223	219
Panaretto* 2006[45] (2000-3)	All women with singletons presenting to Townsville Aboriginal and Islanders Health Service for antenatal care	Panaretto hospital, tertiary referral centre for north Queensland, Australia	Self report	First antenatal visit	›25	NR	NR
Rahaman 1990[56] (NR)	Exposed: 300 consecutive obstetric patients with BMI ›30. Unexposed: equivalent number with BMI 20-27	NR (assumed Trinidad, West Indies)	NR	NR	›30 (*v* 20-27)	290	299
Ray 2001[20] (1993-8)	First pregnancy in all consecutive women with singletons and with pregestational or gestational diabetes	Women's College Hospital, Toronto, Canada	NR	NR	≥25	275	218
Rode 2005[64] (1998-2001)	Women in Copenhagen first trimester study, who registered ‹ 15 weeks, who had a singleton cephalic delivery ›37 weeks	Three hospitals in Copenhagen, Denmark	Self report	NR	›25	1742	6350
Rode 2007[53] (Nov 1996 to Oct 1998)	Women with singleton, term pregnancies aged ≥18, fluent in Danish, without alcohol or drug misuse, and answered questionnaire at 12-18 and 37 weeks	University hospital in Copenhagen, Denmark	Self report	12-18 wks	›26	562	1531
Roman 2007[42] (2001-5)	Exposed: all obese women (prepregnancy BMI ›30) after 22 weeks. Unexposed: normal weight (prepregnancy BMI 18.5-25)	Sud-Reunion Hospital, Reunion Island, France	Self report	First antenatal visit	›30	2050	2066
Roman 2008[3] (1994-2004)	Women who received prenatal care and delivered vaginally or by caesarean section during labour	Medical University of South Carolina, Charleston, USA	Measured	At delivery	≥25	5393	1556
Ronnenberg 2003[43] (NR)	Full time employed textile workers, newly married, nulliparous, aged 20-34, with permission to have a child	AnQing, China	Measured	NR	19.8-26	272	146
Sahu 2007[5] (2005-6)	Women from all socioeconomic levels with singleton pregnancies	Queen Mary's Hospital, King George's Medical University, Lucknow, India	NR	NR	≥25	129	205
Salihu* 2008[4] (1989-97)	Women at 20-44 weeks with live births	Missouri, USA	Self report	First visit	›30 (*v* 18.9-24.5)	NR	NR
Savitz 2005[2] (Aug 1995 to Feb 2001)	Women who came to participating clinic before 30 weeks' gestation with singleton pregnancy, had access to telephone, were able to communicate in English, and planned to continue care and deliver at study hospital	University of North Carolina Hospitals, Wake County Human Services, and Wake Area Health Education Centre in central North Carolina, USA	Self report	24-29 weeks	›26	852	1102

Study (period)	Population	Setting	Body mass index (BMI): Self report or measured	Body mass index (BMI): When recorded	Body mass index (BMI): Definition of exposure (high BMI)	No of women: Exposed	No of women: Not exposed
Sayers* 1997[73] (1987-90)	Women with liveborn singletons, who self identified as aboriginal in delivery suite register	Royal Darwin Hospital, Darwin health region, Northern Territory, Australia	Measured	Post partum before discharge	›25.5	NR	NR
Scholl 1989[74] (NR)	2789 white, black, and Hispanic adolescents (‹18 years at entry of care) who delivered live singletons and were registered with Camden County Adolescent Family Life Project	Five hospitals and clinics in Camden County, West Jersey Health Systems, NJ, USA	Self report	First antenatal visit	›24.1	415	1164
Sebire 2001[63] (1989-97)	Women with singleton pregnancies with data in St Mary's maternity information system database	National Health Service Hospital, Northwest Thames Region, UK	Measured	First antenatal visit	›25	110 290	176 923
Siega-Riz† 1996[65] (1983-7)	Women at public health clinics undergoing first pregnancy	Public health clinics, West Los Angeles, USA	Self report	NR	›26	1227	2626
Smith* 2006[72] (1992-2001)	Probability based matching approach using maternal identifiers to link Scottish Morbidity Record, Scottish Stillbirth and Infant Death Enquiry, and prenatal screening database for first pregnancies in West of Scotland (yet have previous miscarriages as risk factor; singleton births)	Scottish Morbidity Record, Scottish Stillbirth and Infant Death Enquiry, and prenatal screening database in Institute of Medical Genetics	Height from Scottish Morbidity Registry, weight from biochemical database	NR	›30 (*v* 20-24)	NR	NR
Smith 2007[66] (1991-2001)	Women who had record in prenatal screening database, could be linked to Scottish Morbidity Record, had given birth to singleton weighing ›400 g between 22 and 43 weeks	Scotland, UK	Measured	Early pregnancy	›25	28 612	95 516
Sukalich 2006[67] (1998)	Women aged ‹19 who delivered at 1 of 16 hospitals at ›23 weeks	16 hospitals, New York State, USA	Self report	First antenatal visit	›25	1498	3324
Tsukamoto 2007[68] (2002-3)	Women with singletons 37-42 gestational weeks	Nagai Clinic, Saitama, Sagamihara Kyoudou, Kanagawa in Tokyo metropolitan area, Japan	Self report	Before pregnancy	›25	277	2301
Yaacob 2002[69] (2001)	Randomly selected sample of 276 postnatal women	Women's Hospital, Doha, Qatar	NR	NR	›30 (*v* 20-28)	75	75
Yekta 2006[70] (2002-3)	Pregnant women who enrolled in public care centres in urban areas during first eight weeks of pregnancy	Urmia, Iran	Self-report	NR	›26	100	140
Yogev 2005[71] (1999-2000)	Consecutive gravid women from maternal health clinics in metropolitan area of San Antonio	Inner city residents of San Antonio, Texas, USA	NR	NR	›27.3	1529	4861
Zhou 1997[75] (1984-7)	All pregnant women with singletons in two geographically well defined areas, who were part of community trial, at 36 weeks of pregnancy	Odense, Aalborg, Denmark	NR	NR	›26	648	4536
Total						337 814‡	704 968‡

NR=not reported.
*Studies with data that were not pooled in meta-analyses.
†Cohort studies although data were also presented in format that allowed pooling with case-control data; listed only in table 1 and not table 2.
‡At least this many participants, as some studies did not report numbers exposed and not exposed.

mass index assessed before pregnancy, during pregnancy, or post partum; and using exact cut-offs for body mass index with a reference body mass index of 20-25 versus those with cut-offs close to this.

Quality assessment

Two reviewers (two of ZH, SDM, and SM) independently assessed study quality using a predefined evaluation of six types of biases: selection, exposure, outcome, confounding, analytical, and attrition (see web extra appendix 2). This bias assessment tool has been described in other reviews undertaken by our group on determinants of preterm birth and low birth weight.[17]

To deal with 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[18 19]—that is, to adjust for any observed publication bias. A priori we decided to carry out the trim and fill analyses for outcomes with at least 10 studies as there were concerns of reliability for outcomes with fewer studies. We used the generic inverse variance method to calculate study specific weights. These analyses were done using the R statistical and programming software, version 2.9.0. (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Overall, 6283 non-duplicated titles and abstracts were identified (fig 1). After the screening process, 503 citations were selected to undergo review of the full text article, and a further 52 articles were identified from reference lists, yielding a total of 555 full text articles for review. The most common reasons for exclusion were failure to report outcomes of interest and study design.

Eighty four studies were included: 64 cohort studies[2-6 9-11 20-75] (58 with pooled data) and 20 case-control studies[76-95] (19 with pooled data), totalling at least (some studies did not report the number of patients)

Table 2 | Characteristics of case-control studies included in systematic review and meta-analyses of preterm birth and low birth weight in overweight and obese women compared with women of normal weight

Study (period)	Population	Setting	Body mass index: Self report or measured	Body mass index: When recorded	No of women: Cases	No of women: Controls
Al-Eissa* 1994 (one year, date NR)	Live births (birth weight appropriate for gestational age) identified over one year period. Cases: women who delivered preterm infants at 20-37 weeks. Controls: women who delivered infants at 37-42 weeks	King Khalid University Hospital, Riyadh, Saudi Arabia	NR	NR	118	118
Begum 2003[77] (1995)	Cases: women with spontaneous labour who delivered at ‹37 weeks. Controls: women with spontaneous labour who delivered at ›37 weeks	Tertiary hospital, northern India	NR	NR	94	88
Catov 2007[78] (1997-2001)	Cases: all women with preterm births (spontaneous onset or premature rupture of membranes). Controls: randomly chosen women delivered › 37 weeks, with first blood sample ‹15 weeks. Both groups: uncomplicated pregnancies	USA	NR	NR	90	199
Conti 1998[79] (1994-5)	Cases: consecutive women who delivered premature infants (‹37 weeks) with low birth weight (1000-2500 g). Controls: women who delivered infants ›2500 g	Major teaching hospital, Sydney, New South Wales, Australia	Self report	During pregnancy	54	86
de Haas† 1991[80] (1988-9)	Cases: women who delivered live singletons at 20-37 weeks, with delivery preceded by spontaneous labour or rupture of membrane without induction for maternal or fetal indications	Brigham and Women's Hospital, Boston, Massachusetts, USA	Measured	NR	114	232
Delgado-Rodriguez 1998[81] (1990-3)	Cases: women with live births ‹2500 g, living in referral area of hospital. Controls: women who delivered singletons ›2500 g	University of Granada Hospital, Granada, Spain	Self report (from chart)	NR	240	374
Dhar 2003[82] (1999)	Pregnant women who delivered liveborn babies; every third pregnant woman at maternal-child health training institute	Public maternity hospital, Dhaka, Bangladesh	Measured	NR	27	167
Gosselink† 1992[83] (1985-1990)	Women aged 15-45 who delivered singletons (with spontaneous onset of labour) and consented to be interviewed. Cases: women who delivered preterm. Controls: women who delivered ›39 weeks	University of Chicago and University of Iowa Hospitals, USA	Self report	NR	368	368
Hashim† 2000[84] (NR)	Randomly selected postpartum women within 24 hours after delivery (at ›37 weeks' gestation). Cases: women who delivered infants ‹2500 g. Controls: women who delivered infants ›2500 g	El-Shemasy Maternity and Children Hospital, Riyadh, Saudi Arabia	NR	NR	250	250
Hediger 1995[85] (Oct 1990 to Nov 1993)	Every third participant enrolled in larger study to prenatal care under same protocol. Women were recruited within one month of entry to have real time and Doppler ultrasound scan for research purposes at 32 weeks	Urban clinic in Camden, New Jersey, USA	Self report	First antenatal visit	46	244
Karim 1997[86] (NR)	Women living within four identified sections of Mirpur area with no immediate plans to move from current address, aged 17-35 on date of interview	One hospital: mother and child clinic in Mirpur area of Dhaka, India	Self report	Immediately after birth	51	196
Lawoyin 1997[87] (NR)	Consecutive women for whom complete information was available. Cases: women who gave birth to infants ‹2500 g. Controls: Women who gave birth to babies ›2500 g	Armed Forces Hospital, Tabuk, northwest Saudia Arabia	Measured	During pregnancy	50	478
Le† 2007[88] (Jul to Dec 2006)	Women who gave birth to singleton live infant, with normal mental health and ability to communicate and had ≥20 teeth. Controls: random sampling	Thai Nguyen Center General Hospital, Thai Nguyen, Thailand	Self report	After birth	130	260
Melamed 2008[89] (1996-2004)	All women followed from conception to delivery with type 1 or type 2 diabetes and no diabetes. Cases: women with preterm birth. Controls: women with term deliveries (note called cohort by authors but data extracted for this was case-control)	Rabin Medical Centre, Tel Aviv, Israel	NR	NR	119	329
Mohsen 2007[90] (2006)	Pregnant women at delivery and their full term (gestational age 37-42 weeks) newborns. Women without hypertension, diabetes, pregnancy toxaemia, antepartum haemorrhage, or any medical or obstetric problems, with normal vaginal delivery	Al-Mataria Teaching Hospital, Cairo, Egypt	Assumed measured ("Anthropometric measurements of the mother including weight, height and BMI were recorded")	Post partum	24	30
Ojha 2007[91] (2004-5)	Women who delivered at term. Cases: women who delivered low birth weight infants. Controls: women who delivered infants of normal birth weight	Paropakar Shree Panch Indra laxmi Devi Maternity Hospital, Thapathali, Nepal	Measured	Post partum	154	154
Pitiphat 2008[92] (1999-2002)	Participants of Project Viva, women with live infants and who were medically insured	One of eight Harvard Vanguard Medical Associates Centers, eastern Massachusetts, USA	Self report	Before pregnancy	105	1530
Yogev 2007[93] (1995-9)	Women with singletons and gestational diabetes first diagnosed in the current pregnancy	1 Hospital: San Antonio Texas, USA	Measured	Before pregnancy	163	1363
Xue 2008[94] (2001-2)	White 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 and Nurses' Health Study II USA	Self report	Post partum	1810	30 051
Zeitlin† 2001[95] (NR)	Women who delivered live or stillbirth singletons. Cases: women who delivered between 22 and 36 weeks. Controls: every 10th woman who delivered ≥37 weeks	17 European countries (Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Poland, Romania, Russia, Scotland, Slovenia, Spain, Sweden, and Turkey)	NR	NR	4707	7821
Total					8714	44 338

NR=not reported.
*Non-pooled study.
†Pooled studies with dichotomous data.

Study	Higher BMI: No of events	Higher BMI: Total	Lower BMI: No of events	Lower BMI: Total	Weight (%)	Risk ratio (random) (95% CI)
Adams 1995	16	67	159	1419	2.5	2.13 (1.36 to 3.35)
Ancel 1999	353	728	4434	11 328	2.8	1.24 (1.15 to 1.34)
Baeten 2001	1659	26 868	2642	49 321	2.8	1.15 (1.09 to 1.22)
Barros 1996	45	951	105	2158	2.6	0.97 (0.69 to 1.37)
Berkowitz 1998	466	754	1027	1668	2.8	1.00 (0.94 to 1.07)
Bhattacharya 2007	848	7323	1537	14 076	2.8	1.06 (0.98 to 1.15)
Bianco 1998	62	613	933	11 313	2.7	1.23 (0.96 to 1.57)
Bondevik 2001	13	313	40	661	2.2	0.69 (0.37 to 1.26)
Callaway 2006	352	4809	431	6443	2.8	1.09 (0.96 to 1.25)
Clausen 2006	29	690	87	2183	2.5	1.05 (0.70 to 1.59)
De 2007	65	634	119	1450	2.7	1.25 (0.94 to 1.67)
Dietz 2006	8804	33 582	13 786	59 088	2.8	1.12 (1.10 to 1.15)
Driul 2008	35	153	46	533	2.5	2.65 (1.77 to 3.96)
Gardosi 2000	173	2372	1056	15 946	2.8	1.10 (0.94 to 1.29)
Gilboa 2008	40	687	114	2218	2.6	1.13 (0.80 to 1.61)
Goldenberg 1998	69	1037	129	1251	2.7	0.65 (0.49 to 0.85)
Haas 2005	63	702	58	863	2.6	1.34 (0.95 to 1.88)
Hauger 2008	1130	12 327	10	99	2.3	0.91 (0.50 to 1.64)
Hendler 2005	37	597	259	2313	2.6	0.55 (0.40 to 0.77)
Hickey 1997	204	2775	521	6943	2.8	0.98 (0.84 to 1.14)
Jensen 2003	40	1365	27	1094	2.4	1.19 (0.73 to 1.92)
Kim 2005	18	171	66	1112	2.4	1.77 (1.08 to 2.91)
Leung 2008	344	4633	1392	22 041	2.8	1.18 (1.05 to 1.32)
Lumme 1995	83	1592	259	6433	2.7	1.29 (1.02 to 1.65)
Merlino 2006	86	957	149	1374	2.7	0.83 (0.64 to 1.07)
Monaghan 2001	20	474	53	1387	2.4	1.10 (0.67 to 1.83)
Nohr 2007	1146	23 595	2607	57 923	2.8	1.08 (1.01 to 1.15)
Rahaman 1990	8	290	20	299	1.9	0.41 (0.18 to 0.92)
Ray 2001	77	275	61	218	2.7	1.00 (0.75 to 1.33)
Ray 2001	77	275	61	218	2.7	1.00 (0.75 to 1.33)
Ronnenberg 2003	20	272	10	146	2.0	1.07 (0.52 to 2.23)
Sahu 2007	7	129	8	205	1.7	1.39 (0.52 to 3.74)
Savitz 2005	142	852	131	1102	2.7	1.40 (1.13 to 1.75)
Scholl 1989	62	378	194	1164	2.7	0.98 (0.76 to 1.28)
Sebire 2001	6225	110 290	9819	176 923	2.8	1.02 (0.99 to 1.05)
Siega-Riz 1996	51	1227	108	2626	2.6	1.01 (0.73 to 1.40)
Smith 2007	3602	28 612	4977	9551	2.8	0.24 (0.23 to 0.25)
Yekta 2006	6	100	8	140	1.6	1.05 (0.38 to 2.93)
Yogev 2005	156	1529	226	4861	2.7	2.19 (1.80 to 2.67)
Total (95% CI)		274 998		480 091	100.0	1.06 (0.87 to 1.30)
Total events	26 633		47 669			

Test for heterogeneity: τ^2=0.37, χ^2=5917.35, df=38, P<0.001, I^2=99%

Test for overall effect: z=0.57, P=0.57

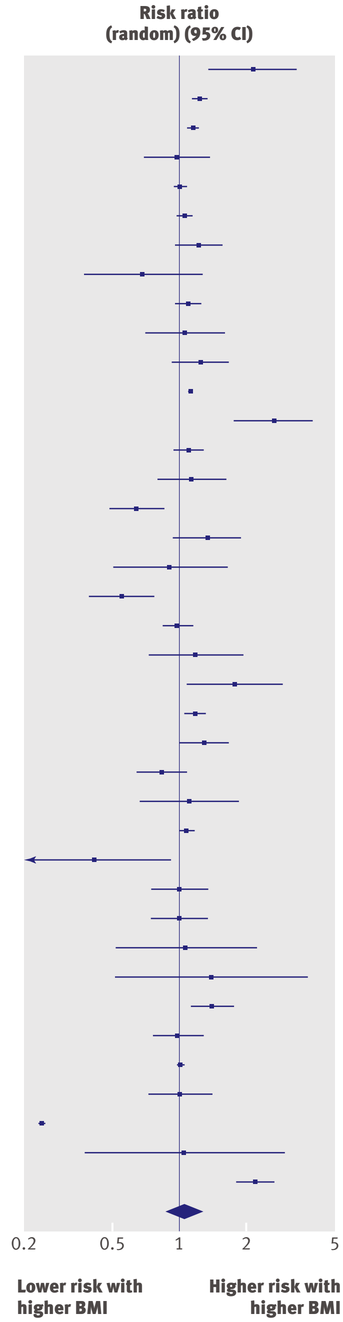

Fig 2 | **Forest plot of risk of preterm birth before 37 weeks in overweight and obese women compared with women of normal weight in cohort studies. BMI=body mass index**

1 095 834 women (fig 1, tables 1 and 2). The studies originated predominantly from developed countries, although developing countries were also represented. The majority of the studies assessed body mass index by self report. Most studies did not report the timing of body mass index assessment, although when reported it was most commonly at the first antenatal visit.

Preterm birth

In the pooled cohort studies the overall risk of preterm birth before 37 weeks did not differ significantly among overweight or obese women with singleton pregnancies (relative risk 1.06, 0.87 to 1.30, 38 studies, fig 2) compared with women of normal weight (table 3). However, among overweight and obese women the risk of induced preterm birth was increased (1.30, 1.23 to 1.37, five studies, fig 3). The heavier the woman, the higher the risk of induced preterm birth before 37 weeks, with overweight, obese, and very obese women having a relative risk of 1.15 (1.04 to 1.27), 1.56 (1.42 to 1.71), and 1.71 (1.50 to 1.94), respectively. The risk of spontaneous preterm birth

Study	Lower risk ratio in higher BMI: No of events	Lower risk ratio in higher BMI: Total	Normal BMI: No of events	Normal BMI: Total	Weight (%)	Risk ratio (random) (95% CI)
Adams 1995	4	67	38	1419	0.3	2.23 (0.82 to 6.06)
Berkowitz 1998	130	754	200	1668	6.5	1.44 (1.17 to 1.76)
Hickey 1997	55	2775	100	6943	2.5	1.38 (0.99 to 1.91)
Nohr 2007	398	23 595	753	57 923	18.8	1.30 (1.15 to 1.46)
Smith 2007	1983	73 806	2003	95 516	72.0	1.28 (1.20 to 1.36)
Total (95% CI)		100 997		163 469	100.0	1.30 (1.23 to 1.37)
Total events	2570		3094			

Test for heterogeneity: τ^2=0.00, χ^2=2.39, df=4, P=0.66, I^2=0%

Test for overall effect: z=9.83, P<0.001

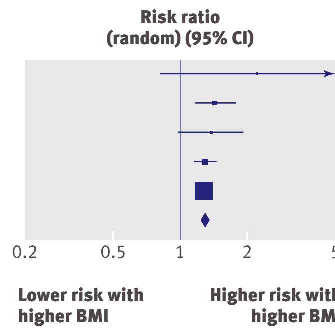

Fig 3 | Forest plot of risk of induced preterm birth before 37 weeks in overweight and obese women compared with women of normal weight in cohort studies. BMI=body mass index

did not differ (0.93, 0.85 to 1.01, 15 studies). Heterogeneity ranged from 0 to 99%, with most studies in the moderate to high range.

Overweight and obese women had an increased risk of preterm birth before 33 weeks (crude relative risk 1.26, 95% confidence interval 1.14 to 1.39). The heavier the woman, the higher the risk of early preterm birth, with overweight, obese, and very obese women having a relative risk of 1.16 (1.05 to 1.29), 1.45 (1.23 to 1.71), and 1.82 (1.48 to 2.24), respectively.

Compared with the number of studies that presented crude data, few presented matched or adjusted data (table 3). The pooled risks from adjusted or matched data were generally similar in magnitude and direction to that of the pooled crude data—for example, the risk of preterm birth before 37 weeks in overweight or obese women remained non-significant (1.02, 0.68 to 1.54), although the adjusted or matched risk for several outcomes with only one study differed (for example, the adjusted relative risk of spontaneous preterm

Table 3 | Summary table of preterm birth outcomes in cohort studies of overweight and obese women compared with women of normal weight

		Pooled crude data			Pooled adjusted or matched data		
Outcomes	Total No of studies	No of studies	Relative risk* (95% CI)	I2 (%)	No of studies	Relative risk* (95% CI)	I2 (%)
All births <37 weeks†:	40	38	1.06 (0.87 to 1.30)‡	99	4	1.02 (0.68 to 1.54)§	77
Overweight only	27	27	1.03 (0.98 to 1.07)	48	7	0.95 (0.85 to 1.06)	79
Obese only	3	3	1.10 (0.99 to 1.21)	84	1	1.17 (1.02 to 1.35)	NA
Very obese only	6	5	1.22 (0.86 to 1.72)	96	4	1.21 (0.84 to 1.74)	68
Spontaneous births <37 weeks:	15	15	0.93 (0.85 to 1.01)‡	70	1	2.29 (1.20 to 4.38)§	NA
Overweight	10	10	0.92 (0.87 to 0.97)	0	4	0.94 (0.80 to 1.10)	45
Obese	2	2	0.88 (0.74 to 1.04)	64	2	1.04 (0.92 to 1.17)	94
Very obese	2	2	0.87 (0.70 to 1.07)	0	2	0.95 (0.67 to 1.33)	57
Induced births <37 weeks:	5	5	1.30 (1.23 to 1.37)‡	0	2	1.30 (0.70 to 2.43)§	44
Overweight	3	3	1.15 (1.04 to 1.27)	29	2	1.03 (0.72 to 1.48)	37
Obese	1	1	1.56 (1.42 to 1.71)	NA	1	0.84 (0.71 to 0.98)	NA
Very obese	1	1	1.71 (1.50 to 1.94)	NA	1	1.82 (1.47 to 2.26)	NA
Births 32-36 weeks:	4	4	1.15 (0.95 to 1.38)‡	86	1	2.16 (1.13 to 4.12)§	NA
Overweight	2	2	0.98 (0.94 to 1.03)	0	1	1.21 (0.90 to 1.62)	NA
Obese	2	2	0.99 (0.95 to 1.03)	0	0	NA	
Very obese	2	2	1.03 (0.97 to 1.09)	0	1	2.05 (1.14 to 3.70)	NA
Births <33 weeks:	12	11	1.26 (1.14 to 1.39)‡	76	2	1.23 (0.87 to 1.72)§	0
Overweight	7	7	1.16 (1.05 to 1.29)	65	4	1.08 (0.79 to 1.50)	90
Obese	3	3	1.45 (1.23 to 1.71)	57	2	1.49 (0.89 to 2.50)	74
Very obese	3	3	1.82 (1.48 to 2.24)	24	2	2.02 (1.24 to 3.29)	0

NA=not applicable.
*Calculated using random effects, inverse variance.
†Spontaneous, induced, and unspecified.
‡Represents pooled relative risk for each of individual rows below and also includes risk in studies that did not stratify by overweight, obese, and very obese, but rather presented combined risk.
§Represents pooled relative risk for studies that originally examined all women with a high body mass index as one group rather than subdividing into overweight, obese, and very obese, as we believe it is methodologically incorrect to pool adjusted risks for overweight women with adjusted risks for obese women within one study. For this reason, the total number of studies for each outcome in adjusted or matched data column is sometimes lower than the number of studies in following rows.

Table 4 | **Perinatal outcomes in case-control studies according to difference in maternal body mass index**

Outcome	Total No of studies	Pooled crude data: No of studies	Pooled crude data: Mean difference of body mass index (95% CI)*	Pooled crude data: I^2 (%)	Pooled matched data: No of studies	Pooled matched data: Mean difference of body mass index (95% CI)*	Pooled matched data: I^2 (%)
Preterm births							
Birth ‹37 weeks:	7	6	−0.33 (−1.19 to 0.53)	86	1	−0.70 (−2.23 to 0.83)	NA
Spontaneous birth	4	0	−0.90 (−1.77 to −0.02)	82	0	NA	NA
Preterm birth ‹33 weeks	2	2	0.72 (−2.16 to 0.73)	0	0	NA	NA
Low birth weight							
Low birth weight (‹2500 g)	8	7	−1.15 (−1.87 to −0.44)	84	1	−1.20 (−1.85 to −0.55)	NA
Intrauterine growth restriction§	2	1	−1.70 (−2.64 to −0.76)	NA	1	−0.60 (−2.42 to 1.22)	NA

NA=not applicable.
*Calculated using random effects, inverse variance.
†No values for induced preterm birth before 37 weeks or birth 32-33 to 36 weeks.
‡No values for birth weights of 1500-2500 g, ‹1500 g, or ‹1000 g.
§Less than 10% for gestational age.

birth before 37 weeks was 2.29, 95% confidence interval 1.20 to 4.38).

The results of six cohort studies[4,25,45,61,72,73] not included in the meta-analysis (the format of the data did not permit pooling) generally supported the pooled data. One study showed an increased risk of preterm birth before 37 weeks[45] in overweight and obese women and another showed a slight decreased risk.[4] Similar to the pooled data, there were decreases in spontaneous preterm birth before 37 weeks[4,72] and increases in the risk of induced preterm birth before 37 weeks.[4,54] Preterm birth (32-36 weeks) was significantly increased in overweight and obese women in one study[25] but not in another.[61] Unlike the pooled data there was no significant increase in preterm birth before 32 weeks.[4,25,61]

Data from seven case-control studies that examined maternal body mass index as a continuous variable also generally supported the findings of the cohort data. The mean body mass index of women with preterm birth before 37 weeks overall did not differ significantly from those with term births (−0.33 body mass index unit, −1.19 to 0.53), although women with spontaneous preterm birth had a slightly lower body mass index (−0.90, −1.77 to −0.02; table 4).

A few case-control studies reported body mass index as a dichotomous variable (high versus reference; table 5) There was a trend towards preterm birth before 37 weeks in overweight or obese women overall (crude odds ratio 1.16, 95% confidence interval 0.99 to 1.37), although not in the matched data (odds ratio 1.08, 0.39 to 2.95). The risk of spontaneous preterm birth in overweight or obese women was increased in those in the matched data (1.79, 1.73 to 2.84) but not the crude data (1.00, 0.18 to 5.53). One case-control study that could not be pooled found a trend towards decreased spontaneous preterm birth (crude odds ratio 0.58, 95% confidence interval 0.33 to 1.03).

Low birth weight

In the pooled cohort studies, overweight and obese women had a decreased risk of having an infant of low birth weight (relative risk 0.84, 95% confidence interval 0.75 to 0.95, 28 studies, fig 4) but an increased risk of having an infant of very low birth weight (<1500 g, 1.61, 1.42 to 1.82, two studies) or extremely low birth weight (<1000 g, 1.31, 1.08 to 1.59, one study; table 6). The heavier the woman, the higher the risk of having an extremely low birth weight infant, with relative risks in overweight, obese, and very obese women of 1.18 (0.94 to 1.47), 1.43 (1.05 to 1.95), and 1.98 (1.36 to 2.89), respectively.

Two cohort studies with non-pooled data showed similar risks of low birth weight in overweight and

Table 5 | **Risk of poor perinatal outcomes in case-control studies of overweight and obese women compared with women of normal weight**

Outcome*	Pooled crude data: No of studies	Pooled crude data: Odds ratio (95% CI)	Pooled crude data: I^2 (%)	Pooled matched data: No of studies	Pooled matched data: Odds ratio (95% CI)	Pooled matched data: I^2 (%)
Preterm birth ‹37 weeks	2	1.16 (0.99 to 1.37)	0	2	1.08 (0.39 to 2.95)	89
Spontaneous preterm birth ‹37 weeks	1	1.00 (0.18 to 5.53)	NA	1	1.79 (1.13 to 2.84)	NA
Low birth weight (‹2500 g)	1	0.51 (0.36 to 0.74)	NA	0	NA	NA

NA=not applicable.
*No values for induced preterm births before 37 weeks, births 32-36 weeks, and births before 32 weeks; birth weights of 1500-2500 g, ‹1500 g, and ‹1000 g; intrauterine growth restriction; mean birth weight; and gestational age at delivery.
†Calculated using random effects, Mantel Haenszel.

Study	Lower risk ratio in higher BMI: No of events	Lower risk ratio in higher BMI: Total	Normal BMI: No of events	Normal BMI: Total	Risk ratio (random) (95% CI)	Weight (%)	Risk ratio (random) (95% CI)
Baeten 2001	1164	27 353	2067	50 378		7.6	1.04 (0.97 to 1.11)
Bhattacharya 2007	488	7323	980	14 076		7.3	0.96 (0.86 to 1.06)
Bianco 1998	43	613	694	11 313		5.2	1.14 (0.85 to 1.54)
Bondevik 2001	30	313	114	661		4.3	0.56 (0.38 to 0.81)
Clausen 2006	18	690	65	2182		3.2	0.88 (0.52 to 1.47)
Cogswell 1995	445	19 732	913	33 809		7.3	0.84 (0.75 to 0.93)
Dubois 2006	13	568	49	1253		2.6	0.59 (0.32 to 1.07)
Frederick 2008	25	489	63	1629		3.6	1.32 (0.84 to 2.08)
Gilboa 2008	18	687	61	2218		3.1	0.95 (0.57 to 1.60)
Hulsey 2005	1929	27 236	2984	45 916		7.7	1.09 (1.03 to 1.15)
Johnson 1992	6	815	32	1621		1.5	0.37 (0.16 to 0.89)
Lawoyin 1992	11	268	11	109		1.7	0.41 (0.18 to 0.91)
Lumme 1995	61	1592	170	6433		5.3	1.45 (1.09 to 1.93)
Maddah 2005	3	82	23	414		0.9	0.66 (0.20 to 2.14)
Mobasheri 2007	2	108	5	161		0.5	0.60 (0.12 to 3.02)
Ogbonna 2007	23	234	16	117		2.6	0.72 (0.40 to 1.31)
Ogunyemi 1998	12	281	7	223		1.4	1.36 (0.54 to 3.40)
Panahandeh 2007	16	223	25	219		2.6	0.63 (0.35 to 1.14)
Rahaman 1990	9	290	29	299		2.0	0.32 (0.15 to 0.66)
Rode 2005	21	1742	51	6350		3.2	1.50 (0.91 to 2.49)
Rode 2007	5	562	17	1531		1.2	0.80 (0.30 to 2.16)
Roman 2008	186	5393	128	1556		6.2	0.42 (0.34 to 0.52)
Sahu 2007	14	129	22	205		2.4	1.01 (0.54 to 1.90)
Scholl 1989	27	378	97	1164		4.0	0.86 (0.57 to 1.29)
Sukalich 2006	103	1498	309	3324		6.2	0.74 (0.60 to 0.92)
Tsukamoto 2007	13	277	105	2301		2.8	1.03 (0.59 to 1.81)
Yekta 2006	6	100	15	140		1.4	0.56 (0.23 to 1.39)
Zhou 1997	9	648	77	4536		2.2	0.82 (0.41 to 1.62)
Total (95% CI)		99 624		194 138		100.0	0.84 (0.75 to 0.95)
Total events	4700		9129				

Test for heterogeneity: τ^2=0.05, χ^2=138.95, df=27, P<0.001, I^2=81%

Test for overall effect: z=2.81, P=0.005

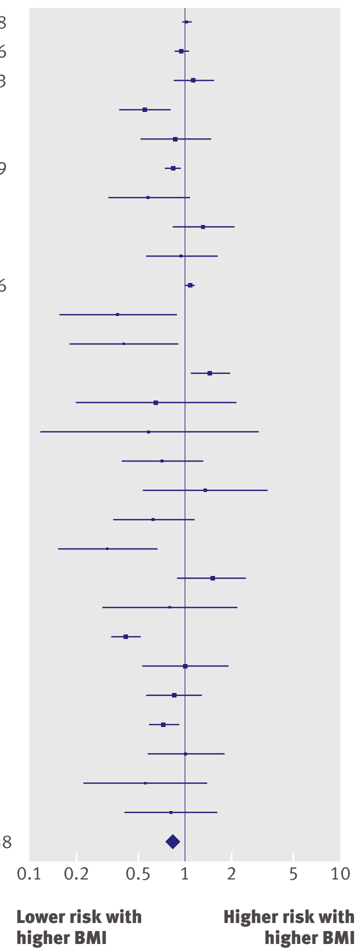

Fig 4 | Forest plot of risk of having an infant of low birth weight (<2500 g) in overweight and obese women compared with women of normal weight in cohort studies. BMI=body mass index

obese women compared with women of normal weight (adjusted odds ratios 1.4, 95% confidence interval 0.9 to 2.1[45] and 0.3, 0.1 to 1.0).[73]

In the seven pooled case-control studies women with low birth weight singletons had a lower maternal body mass index than women with singletons of appropriate weight in both the crude data (−1.15 body mass index units, 95% confidence interval −1.87 to −0.44) and the single study of matched data (−1.20, −1.85 to −0.55; table 4). The single case-control study that dichotomised body mass index into high versus reference also found a decreased risk of infants with low birth weight among mothers with a high body mass index (odds ratio 0.51, 95% confidence interval 0.36 to 0.74; table 5).

Other outcomes

In the pooled cohort studies, overweight and obese women had a lower risk of infants with intrauterine growth restriction than women of normal weight (crude relative risk 0.79, 0.72 to 0.88, table 6), and infants with higher mean birth weights by 70.8 g (54.4 g to 87.2 g) despite shorter mean gestations (by −0.06 weeks, 95% confidence interval −0.12 weeks to −0.01 weeks).

One case-control study reported that women with singletons showing intrauterine growth restriction had a lower mean body mass index than women with infants of normal growth (−1.70 body mass index units, 95% confidence interval −2.64 to −0.76; table 4).

A priori defined sensitivity analyses for preterm birth

Many of the categories in the sensitivity analyses had few studies, limiting our power to draw conclusions. In developing countries, the risk of preterm birth in overweight and obese women were similar to those of women in developed countries (relative risk 0.83, 95% confidence interval 0.61 to 1.12 and 1.09, 0.87 to 1.36; table 7).

No studies were of low quality. There was no significant increase in preterm birth among adolescents compared with adults (0.98, 0.76 to 1.28, one study, and 1.09, 0.95 to 1.25, four studies). Only one study reported on ethnicity; the risk of preterm birth was

Table 6 | Risk of low birth weight and other perinatal outcomes in cohort studies of overweight and obese women compared with women of normal weight

		Pooled crude data			Pooled matched data		
Outcome	Total No of studies	No of studies	Relative risk* (95% CI)	I^2 (%)	No of studies	Relative risk* (95% CI)	I^2 (%)
All low birth weight (<2500 g)†:	31	28	0.84 (0.75 to 0.95)‡	81	4	0.70 (0.53 to 0.93)	20
Overweight	21	21	0.92 (0.80 to 1.05)	73	4	1.00 (0.85 to 1.19)	0
Obese	4	4	0.63 (0.34 to 1.19)	92	1	0.71 (0.38 to 1.33)	NA
Very obese	6	5	0.81 (0.42 to 1.53)	88	1	0.30 (0.09 to 1.01)	NA
Moderately low birth weight (1500-2500 g)§:	1	1	0.99 (0.93 to 1.05)‡	NA	0	NA	NA
Overweight	1	1	1.04 (0.95 to 1.13)	NA	1	0.95 (0.64 to 1.41)	NA
Very low birth weight (<1500 g)¶:	2	2	1.61 (1.42 to 1.82)‡	0	0	NA	
Overweight	1	1	1.42 (1.18 to 1.70)	NA	1	1.54 (1.22 to 1.94)	NA
Very obese	1	1	1.54 (0.75 to 3.15)	NA	0	NA	NA
Extremely low birth weight (<1000 g):	1	1	1.31 (1.08 to 1.59)‡	NA	0	NA	NA
Overweight	1	1	1.18 (0.94 to 1.47)	NA	1	1.27 (0.93 to 1.74)	NA
Obese	1	1	1.43 (1.05 to 1.95)	NA	1	1.55 (0.99 to 2.44)	NA
Very obese	1	1	1.98 (1.36 to 2.89)	NA	1	2.80 (1.72 to 4.57)	NA
Intrauterine growth restriction**:	11	9	0.79 (0.72 to 0.88)‡	58	3	1.15 (0.79 to 1.66)	0
Overweight	7	7	0.79 (0.73 to 0.86)	34	2	0.69 (0.63 to 0.76)	0
Obese	1	1	1.01 (0.77 to 1.30)	NA	0	NA	
Very obese	3	2	0.81 (0.61 to 1.08)	0	1	1.06 (0.18 to 6.31)	NA
Mean difference in birth weight (g):	10	9	70.8 (54.5 to 87.2)‡	89	1	172.0 (137.1 to 206.9)	NA
Overweight	7	7	68.2 (50.0 to 86.4)	92	0	NA	NA
Obese	1	1	25.0 (−41.2 to 91.2)	NA	0	NA	NA
Very obese	2	2	49.9 (−30.5 to 130.4)	62	0	NA	NA
Mean difference in gestational age at delivery (weeks):	6	5	−0.06 (−0.12 to −0.01)‡	0	1	0.00 (−0.14 to 0.14)	NA
Overweight	3	3	−0.08 (−0.16 to 0.00)	0	0	NA	NA
Obese	1	1	0.10 (−0.13 to 0.33)	NA	0	NA	NA
Very obese	2	2	−0.05 (−0.18 to 0.08)	0	0	NA	NA

NA=not applicable.
*Calculated using random effects, inverse variance. Total number of studies for each outcome are sometimes lower than number of studies in following rows (for explanation see footnote to table 3).
rows below and also includes risk in studies that did not stratify by overweight, obese, and very obese, but rather presented combined risk.
†Of all babies, including those of low birth weight at term and preterm.
‡Represents pooled relative risk for each of individual.
§No values for obese and very obese women.
¶No values for obese women.
**Less than 10% for gestational age.

not significantly increased in overweight and obese black women (0.84, 0.69 to 1.03) or white women (1.03, 0.77 to 1.38).

A priori defined sensitivity analyses for low birth weight

The decreased risk of low birth weight in overweight and obese women compared with women of normal weight in developing countries was greater than in developed countries (0.58, 0.47 to 0.71, 11 studies *v* 0.90, 0.79 to 1.01, 20 studies; table 8). In developing countries, the heavier the woman the smaller the risk of having an infant of low birth weight: relative risks for overweight, obese, and very obese women were, respectively, 0.88 (0.64 to 1.23), 0.39 (0.11 to 1.34), and 0.29 (0.10 to 0.89).

Only one study was of low quality, limiting conclusions on the effect of study quality. Overweight and obese adolescents but not adults were at a decreased risk of having an infant of low birth weight (0.76, 0.63 to 0.92 *v* 1.0.8, 0.82 to 1.42).

No studies specified whether their population was white and therefore the effect of ethnicity on low birth weight could not be examined.

Quality assessment

Quality assessment (tables 9 and 10) was based on the evaluation of six types of bias. Selection bias was unlikely as women with high and normal body mass indices were usually drawn from the same populations, whereas exposure bias was possible given that weight was self reported in most studies.

Little bias was present in our outcomes as they had standard definitions and were objectively measured—for example, low birth weight was always defined as birth weight <2500 g.

Confounding variables that might explain part or all of the relation between overweight and obesity and preterm birth and low birth weight were incompletely dealt with in several ways: by exclusion, by matching, by comparison of some variables and determining that

Table 7 | Sensitivity analyses for preterm birth in cohort studies of overweight and obese women compared with women of normal weight

	All studies			Overweight			Obese			Very obese		
Outcomes	No of studies* (No of women)	Relative risk† (95% CI)	I^2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I^2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I^2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I^2 (%)
Developed countries‡	31 (728 566)	1.09 (0.87 to 1.36)	99	22 (699 905)	1.03 (0.98 to 1.07)	57	3 (200 753)	1.10 (0.99 to 1.21)	84	5 (201 485)	1.22 (0.86 to 1.72)	96
Developing countries‡	8 (18 578)	0.83 (0.61 to 1.12)	32	5 (12 591)	1.05 (0.80 to 1.36)	0	0	NA	NA	1 (488)	0.10 (0.01 to 0.75)	NA
Low quality studies	0	NA		0	NA		0	NA		0	NA	
Other quality studies	40 (845 165)	1.13 (1.01 to 1.26)	97	27 (712 496)	1.03 (0.98 to 1.07)	48	3 (200 753)	1.10 (0.99 to 1.21)	84	6 (201 973)	1.14 (0.80 to 1.62)	95
Adolescence	1 (1542)	0.98 (0.76 to 1.28)	NA	0	NA	NA	0	NA	NA	0	NA	NA
Adults	4 (24 146)	1.09 (0.95 to 1.25)	15	2 (2269)	0.92 (0.65 to 1.30)	0	0	NA	NA	1 (11 926)	1.23 (0.96 to 1.57)	NA
Black women	1 (4300)	0.84 (0.69 to 1.03)	NA	0	NA	NA	0	NA	NA	0	NA	NA
White women	1 (3495)	1.03 (0.77 to 1.38)	NA	0	NA	NA	0	NA	NA	0	NA	NA
Body mass index												
Self reported	16 (306 500)	1.11 (1.04 to 1.18)	56	9 (151 826)	1.07 (1.03 to 1.10)	0	1 (72 998)	1.13 (1.10 to 1.17)	NA	2 (77 758)	1.24 (1.19 to 1.29)	0
Measured	8 (476 645)	1.22 (0.87 to 1.72)	99	6 (432 550)	0.97 (0.94 to 0.99)	0	2 (127 755)	1.08 (0.90 to 1.30)	85	3 (123 727)	1.23 (0.58 to 2.65)	96
Prepregnancy	28 (347 010)	1.11 (1.04 to 1.19)	81	20 (259 522)	1.06 (1.01 to 1.11)	19	1 (72 998)	1.13 (1.10 to 1.17)	NA	3 (84 449)	1.24 (1.19 to 1.29)	0
During pregnancy	10 (494 457)	1.13 (0.81 to 1.56)	99	6 (450 047)	0.97 (0.94 to 1.00)	8	2 (127 755)	1.08 (0.90 to 1.30)	85	3 (117 524)	0.77 (0.29 to 2.03)	95
Post partum	0	NA	NA	0	NA	NA	0	NA	NA	0	NA	NA
Cut-off values:												
20-25, 25-30	9 (441 974)	0.94 (0.53 to 1.65)	100	9 (504 179)	0.99 (0.96 to 1.03)	32	2 (127 755)	1.08 (0.90 to 1.30)	85	3 (123 727)	1.23 (0.58 to 2.65)	96
Close to 20-25, 25-30	25 (267 008)	0.97 (0.85 to 1.09)	91	18 (208 317)	1.06 (0.99 to 1.13)	27	1 (72 998)	1.13 (1.10 to 1.17)	NA	1 (65 832)	1.24 (1.19 to 1.29)	NA
Not close to 20-25, 25-30	6 (52 088)	1.12 (0.83 to 1.51)	92	0	NA	NA	0	NA	NA	2 (12 414)	0.43 (0.03 to 5.19)	84

No studies were of low quality. NA=not applicable.
*Crude and matched data were pooled for sensitivity analyses.
†Calculated using random effects, inverse variance.
‡Assigned according to Central Intelligence Agency[16] criteria. Zeitlin[95] included 17 European countries that comprised both developed and developing countries and hence was not included in sensitivity analyses for developing and developed countries.

they were not significantly different between the exposed and unexposed women, and by using multiple regression to control for some variables that were significantly different between the two groups. Most studies assessed some confounding variables, but none addressed all. Many studies did not calculate a sample size or power calculation. Attrition bias was rare given that follow-up occurred during the hospital admission for birth.

Trim and fill analyses

The trim and fill analysis of preterm birth before 37 weeks suggested that nine studies were "missing" from the initially meta-analysed relative risk of 1.06 (95% confidence interval 0.87 to 1.30); when the nine studies were imputed yielding a risk based on a total of 49 studies, the risk of preterm birth before 37 weeks was significantly higher in overweight and obese women than normal weight women (1.24, 1.13 to 1.37, see web extra appendix 4). The trim and fill analysis resulted in no additional imputed studies for preterm birth before 32 weeks (with the original studies showing an increased risk in overweight or obese mothers). The risk of spontaneous preterm birth in overweight or obese women was similar with four additional imputed studies (0.89, 0.81 to 0.97). After accounting for publication bias, the apparent protective effect of overweight or obesity on low birth weight disappeared with the addition of nine imputed studies, yielding an overall risk based on 40 studies (0.95, 0.85 to 1.07, see web extra appendix 4).

DISCUSSION

In this systematic review and meta-analyses, we determined that overweight and obese women have an increased risk of a preterm birth before 32 weeks, induced preterm birth before 37 weeks, and, accounting for publication bias, preterm birth before 37 weeks overall. The beneficial effects of overweight or obesity on low birth weight were greater in developing

Table 8 | Sensitivity analyses for low birth weight in cohort studies of overweight and obese women compared with women of normal weight

	All studies			Overweight			Obese			Very obese		
Outcomes	No of studies* (No of women)	Relative risk† 95% CI)	I2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I2 (%)	No of studies* (No of women)	Relative risk† (95% CI)	I2 (%)
Developed countries‡	20 (293 806)	0.90 (0.79 to 1.01)	85	15 (221 318)	0.93 (0.80 to 1.07)	80	3 (22 766)	0.69 (0.34 to 1.37)	94	4 (32 364)	0.85 (0.44 to 1.65)	91
Developing countries‡	11 (4710)	0.58 (0.47 to 0.71)	0	6 (1549)	0.88 (0.64 to 1.23)	0	1 (186)	0.39 (0.11 to 1.34)	NA	2 (615)	0.29 (0.10 to 0.89)	0
Low quality studies	1 (150)	0.60 (0.23 to 1.57)	NA	0	NA	NA	0	NA	NA	0	NA	NA
Remainder of studies	30 (298 366)	0.82 (0.73 to 0.93)	82	21(222 867)	0.92 (0.80 to 1.05)	73	4 (22 952)	0.63 (0.34 to 1.19)	92	6 (32 979)	0.72 (0.39 to 1.31)	86
Adolescents	2 (6364)	0.76 (0.63 to 0.92)	0	1 (4305)	0.75 (0.58 to 0.96)	NA	1 (3671)	0.78 (0.52 to 1.15)	NA	1 (3494)	0.63 (0.34 to 1.17)	NA
Adults	3 (14 515)	1.08 (0.82 to 1.42)	0	1 (1708)	2.04 (0.69 to 5.98)	NA	0	NA	NA	0	NA	NA
Black women§	1 (504)	1.36 (0.54 to 3.40)	NA	1 (301)	2.86 (1.04 to 7.89)	NA	0	NA	NA	0	NA	NA
Infant born at term	4 (10 580)	0.93 (0.57 to 1.53)	59	3 (8260)	1.28 (0.72 to 2.27)	41	0	NA	NA	0	NA	NA
Infant born at term and preterm	28 (289 478)	0.81 (0.71 to 0.91)	28	18 (214 607)	0.90 (0.78 to 1.03)	76	4 (22 952)	0.63 (0.34 to 1.19)	92	6 (32 979)	0.72 (0.39 to 1.31)	86
Body mass index												
Self reported	17 (177 230)	0.88 (0.77 to 1.01)	65	12 (131 837)	0.93 (0.83 to 1.04)	17	1 (3671)	0.78 (0.52 to 1.15)	NA	2 (15 420)	0.90 (0.51 to 1.60)	66
Measured	4 (29 076)	0.60 (0.34 to 1.07)	94	4 (24 094)	0.66 (0.41 to 1.06)	87	3 (22 766)	0.69 (0.34 to 1.37)	94	3 (17 071)	0.70 (0.19 to 2.61)	93
Prepregnancy	24 (271 847)	0.84 (0.74 to 0.97)	83	17 (200 246)	0.92 (0.78 to 1.08)	77	3 (7018)	0.50 (0.28 to 0.92)	76	5 (18 746)	0.57 (0.30 to 1.08)	82
During pregnancy	4 (25 579)	0.83 (0.62 to 1.10)	60	3 (22 382)	0.89 (0.79 to 1.00)	0	1 (15 934)	1.10 (0.93 to 1.30)	NA	1 (14 233)	1.74 (1.14 to 2.66)	NA
Post partum	1 (351)	0.72 (0.40 to 1.31)	NA	1 (239)	0.96 (0.50 to 1.83)	NA	0	NA	NA	0	NA	NA
Cut-off values:												
20-25, 25-30	5 (110 404)	1.02 (0.88 to 1.19)	69	3 (78 291)	1.08 (0.73 to 1.61)	81	2 (16 120)	0.79 (0.30 to 2.04)	63	2 (14 360)	1.06 (0.19 to 5.88)	48
Close to 20-25, 25-30	22 (167 456)	0.74 (0.62 to 0.88)	84	17 (136 928)	0.87 (0.73 to 1.03)	75	2 (6832)	0.53 (0.26 to 1.09)	88	2 (6205)	0.47 (0.32 to 0.70)	31
Not close to 20-25, 25-30	4 (20 656)	0.95 (0.58 to 1.56)	60	1 (7648)	1.06 (0.55 to 2.02)	NA	0	NA	NA	2 (12 414)	0.67 (0.18 to 2.45)	78

NA=not applicable.
*Crude and matched data were pooled for sensitivity analyses.
†Calculated using random effects, inverse variance.
‡Assigned according to Central Intelligence Agency[16]criteria and Zeitlin[95] included 16 European countries that comprised both developed and developing countries and hence was not included in sensitivity analyses for developing and developed countries.
§No values for white women.

countries than developed countries and disappeared after accounting for publication bias.

This systematic review tackles the uncertainty reflected in guidelines from both the American College of Obstetrics and Gynecology and the Institutes of Medicine[96 97] on the relation between overweight and obesity in mothers and preterm birth. The 1990 Institutes of Medicine guidelines focused predominantly on problems with birth weight because of the ease of measurement and acknowledged a dearth of information on obese women in particular and on preterm birth in general,[96] the leading cause of neonatal morbidity and mortality.[7] The revised 2009 guidelines stated that compared with low birth weight, the literature on preterm birth is "more ambiguous because of a less extensive body of epidemiologic evidence"[97]; however, we included 40 studies on preterm birth. Overweight and obesity were associated with increased risks of both induced preterm birth before 37 weeks and overall preterm birth before 32 weeks, and potentially preterm birth before 37 weeks overall. The significant increase in induced preterm birth in overweight and obese women may account for the trend towards a decrease in spontaneous preterm birth.

Comparison with other studies

To our knowledge this is the first comprehensive systematic review on the effect of maternal overweight or obesity on preterm birth and low birth weight. Two previous studies have tackled a limited portion of the literature. A systematic review on spontaneous preterm birth found no association with maternal

Table 9 | Quality assessment based on evaluation of bias in cohort studies of preterm birth and low birth weight in overweight and obese women compared with women of normal weight

Study	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias*	Analytical bias	Attrition bias	Overall likelihood of bias
Abenhaim† 2007[25]	Low	Low	Low	Minimal. Adjusted for age, parity, smoking, diabetes	Low	Minimal	Low
Adams 1995[9]	Minimal	Minimal	NR	Low. Assessed but not different: parity, smoking, race, sex of infant, marital status. Adjusted for medical centre	NR	Minimal	Low
Ancel 1999[54]	Minimal	Minimal	Minimal	Low. Adjusted for country of residence. Assessed, but not different: NR. Confounders assessed, different, and not controlled for: age, education, social class, smoker, previous preterm birth, marital status, previous abortion	Low	Minimal	Low
Baeten 2001[59]	Minimal	Low	Minimal	Minimal. Adjusted for age, education, smoking, pre-eclampsia, insurance, marital status	NR	Minimal	Low
Barros 1996[51]	Low	Minimal	Minimal	NA (primary exposure not anthropometry)	Low	Moderate	Low
Berkowitz 1998[26]	Low	Low	Low	Minimal. Adjusted for age, smoking, insurance, drug use, birth place, clinic service, prenatal care began >12 weeks. Assessed, but not different: in vitro fertilisation. Confounders assessed, different, and not controlled for: diabetes, hypertension	NR	Low	Low
Bhattacharya 2007[27]	Low	Low	Minimal	Minimal. Adjusted for sociodemographic characteristics, year of delivery, gestational hypertension and pre-eclampsia, induced labour. Assessed, but not different: age, husband's social class, diabetes. Confounders assessed, different, and not controlled for: booking week, height, married or cohabiting, smoking	Low	Minimal	Low
Bianco 1998[60]	Low	Low	Low	Low. Assessed, but not different: age. Confounders assessed, different, and not controlled for parity, education, hypertension, diabetes, substance misuse, race, marital status, clinical service	Low	Minimal	Low
Bondevik 2001[28]	Low	Minimal	Minimal	NA (primary exposure not anthropometry)	NR	Minimal	Low
Callaway 2006[29]	Low	Minimal	Minimal	Minimal. Adjusted for age, parity, education, smoking, race	Low	Minimal	Low
Clausen 2006[30]	Low	NR	Minimal	Minimal. Adjusted for low birth weight, age, parity, education, smoking, Oslo east, living alone. For preterm birth: parity, smoking, living alone	Low	NR	Low
Cogswell 1995[50]	Low	Minimal	Minimal	Minimal. Adjusted for age, sex of the infant, gestational age, maternal height, drinking status, race	Moderate	Minimal	Moderate
Cnattingius† 1998[61]	Minimal	Low	Minimal	Minimal. Adjusted for age, parity, education, smoking, total weight gain, height, mother living with father	Low	Minimal	Low
De 2007[48]	Low	Minimal	Minimal	NA (primary exposure not anthropometry)	Low	Minimal	Low
Dietz 2006[24]	Minimal	Low	Minimal	Minimal. Adjusted for parity, race, marital status, Medicaid recipient	Low	Minimal	Low
Driul 2008[31]	Low	Low	Low	Moderate (potential confounders not assessed by original study)†	NR	Minimal	Moderate
Dubois 2006[32]	Minimal	Minimal	Minimal	Low. Matched for age, gestational age	Low	Low	Low
Frederick 2008[46]‡	Low	Minimal	Minimal	Minimal. Matched for age, education, smoking, pre-eclampsia, gestational diabetes, race, marital status, preterm birth, sex of infant	Low	Minimal	Low
Gardosi 2000[33]	Low	Minimal	NR	Minimal. Adjusted for age, smoking, weight at first visit, race, history of abortion, alcohol use	Low	Minimal	Low
Gilboa 2008[34]	Low	Minimal	Minimal	Minimal. Adjusted for age, parity, education, smoking, pre-eclampsia, alcohol use, race of infant, sex of infant	Low	Minimal	Low
Goldenberg 1998[10]	Minimal	Minimal	NR	Minimal. Assessed, but not different: age, previous abortion, education, smoker, pelvic pressure, drug or alcohol use, urinary tract infection, most medical complication, diarrhoea	Low	Low	Low
Haas 2005[55]	Minimal	Minimal	Minimal	Minimal. Adjusted for age, country of birth, race/ethnicity, level of education, parity, site of care, body mass index, before pregnancy: physical function, depressive symptoms, chronic health conditions, level of exercise, and smoking status, during pregnancy: smoking status, physical function, depressive symptoms, use of illicit drugs, eclampsia or pre-eclampsia, gestational diabetes, other pregnancy complications, and inadequate prenatal care	Low	Minimal	Low
Hauger 2008[11]	Minimal	Minimal	NR	Minimal. Adjusted for age, parity, smoking, pre-eclampsia, diabetes, gestational diabetes, hypertension, caesarean section, number of prenatal visits	Minimal	Moderate	Low
Hendler 2005[57]	Minimal	Minimal	NR	Minimal. Adjusted for age, smoking, ethnicity, prepregnancy body mass index, previous preterm birth	Minimal	Minimal	Low
Hickey 1997[35]	High	Minimal	NR	Minimal. Adjusted for age, parity, education, smoking, previous preterm birth last birth, height	Moderate	Minimal	Moderate
Hulsey 2005[36]	Low	Minimal	Minimal	Minimal. Adjusted for hypertension, ethnicity, diabetes, use of prenatal care, Women's, Infants, and Children (special supplemental food programme for women, infants, and children) participation, intention of pregnancy	Low	Minimal	Low
Jensen 2003[21]	Minimal	Low	Minimal	Minimal. Adjusted for age, parity, smoking, gestational diabetes, race, clinical centre, weight gain, gestational age	NR	Minimal	Low
Johnson 1992[58]	Minimal	Minimal	Minimal	Minimal. Matched for ethnicity, marriage, tobacco, alcohol, drugs, parity, sex of fetus	Low	Minimal	Low

Study	Selection bias	Exposure bias	Outcome assess-ment bias	Confounding factor bias*	Analytical bias	Attrition bias	Overall likelihood of bias
Kim 2005[47]	Minimal	Minimal	Minimal	Minimal. Adjusted for nulliparous women: income, passive smoking, body mass index, vaginal bleeding, coffee drinking, drug misuse. For multiparous women: vaginal bleeding, alcohol misuse, previous spontaneous abortion, previous preterm delivery, previous pre-eclampsia, drug misuse, housework	Low	Minimal	Low
Kumari 2001[22]	Low	Low	Minimal	Minimal. Matched for age, parity. Confounders assessed, different, and not controlled for: pregnancy induced hypertension, diabetes, gestational diabetes	Low	Minimal	Low
Lawoyin 1992	Low	Minimal	Minimal	Moderate (potential confounders not assessed by original study)*	NR	Low	Moderate
Leung 2008[6]	Low	Low	Low	Minimal. Adjusted for age, parity, diabetes, year delivered, previous caesarean section, gestational age at booking	Low	Minimal	Low
Lumme 1995[38]	Minimal	Minimal	NR	Minimal. Adjusted for age, parity, education, smoking, race	Low	Low	Low
Maddah 2005[44]	Moderate	Minimal	NR	Moderate (potential confounders not assessed by original study)*	Moderate	Minimal	Moderate
Merlino 2006[39]	Low	Low	Low	Minimal. Assessed, but not different: preterm birth, gestational age. Confounders assessed, different, and not controlled for age	High	Minimal	Moderate
Mobasheri 2007[49]	Low	Minimal	NR	Low. Assessed, but not different: working status. Confounders assessed, different, and not controlled for education	Low	Minimal	Low
Monaghan 2001[40]	Minimal	Minimal	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[23]	Minimal	Minimal	Low	Minimal. Adjusted for age, parity, social-occupational status, mother's height, alcohol use, smoking	Low	Minimal	Low
Ogbonna 2007[41]	Low	Minimal	Minimal	Minimal. Adjusted for age, parity, education, marital status, gravidity, human immunodeficiency virus, malaria infection, multivitamin use	NR	Minimal	Low
Ogunyemi 1998[62]	Low	Minimal	NR	Minimal. Adjusted for body mass index, neonatal intensive care, previous low birth weight suspect. Adjusted for previous cesarean, previous fetal death, asthma, caesarean delivery, vomiting, pre-eclampsia, hypertension	Low	Minimal	Low
Panahandeh 2007[52]	Low	Minimal	Minimal	Minimal. Adjusted for age, parity, education, working status, pregnancy body mass index, height	Low	Minimal	Low
Panaretto† 2006[45]	Low	Minimal	Low	Low. Assessed, but not different: for preterm birth: hypertension, interval between pregnancies. For low birth weight: drug use. For small for gestational age: drug use, age	Low	Minimal	Low
Rahaman 1990[56]	Low	NR	NR	Minimal. Assessed, but not different: pre-eclampsia, hypertension, medical complication, diabetes. Confounders assessed, different, and not controlled for: age, gestational age	Low	Minimal	Moderate
Ray 2001[20]	Low	Minimal	Low	Minimal. Adjusted for diabetes class, age, parity, hypertension, previous preterm birth, history of caesarean section or uterine surgery, history of neonatal death or stillbirth, net weight gain during pregnancy	Low	Minimal	Low
Rode 2005[64]	Minimal	NR	Low	Moderate. Adjusted for pre-eclampsia	NR	Minimal	Moderate
Rode 2007[53]	Low	Minimal	Minimal	Minimal. Assessed, but not different: marital status, alcohol intake, caffeine intake, gestational age. Confounders assessed, different, and not controlled for: age, parity, education, smoking, pre-eclampsia, weight gain	Low	Minimal	Low
Roman 2007[42]	Low	Minimal	Low	Minimal. Matched for age, parity. Assessed, but not different: fetal malformation, pregnancy termination. Confounders assessed, different, and not controlled for: pre-eclampsia, pregnancy induced hypertension, diabetes, gestational diabetes, hypertension, race	Low	Minimal	Low
Roman 2008[3]	Low	Minimal	NR	Minimal. Adjusted for age, parity, race, insurance, prenatal care	NR	Low	Low
Ronnenberg 2003[43]	Low	Minimal	Minimal	Minimal. Adjusted for age, education, sex of infant, height, work stress, maternal exposure to dust or noise or passive smoking	Low	NR	Low
Sahu 2007[5]	Low	Minimal	NR	Low. Assessed, but not different: sex of fetus. Confounders assessed, different, and not controlled for: gestational diabetes, pregnancy induced hypertension, anaemia	Low	Minimal	Low
Salihu† 2008[4]	Minimal	Minimal	Minimal	Minimal. Matched for age, parity, education, smoking, year delivery, race, marital status, adequacy of prenatal care, gender of infant, maternal height, weight gain. Confounders assessed, different, and not controlled for: hypertension, anaemia, pre-eclampsia, diabetes, placental abruption, placenta previa	Low	Minimal	Low
Savitz 2005[2]	Minimal	Minimal	NR	Minimal. Adjusted for age, parity, education, smoking, race, previous preterm birth, marital status, poverty index	Low	Minimal	low
Sayers† 1997[73]	Low	Minimal	Minimal	Minimal. Adjusted for smoking, male infant, aboriginal ancestor	Moderate	Minimal	Low
Scholl 1989[74]	Low	Minimal	Minimal	Minimal. Adjusted for low birth weight, intrauterine growth restriction, age, weight gain adequacy, smoking, ethnicity; for preterm birth: age, weight gain adequacy, previous preterm birth, adequacy of prenatal care. Assessed, but not different: clinical pay status, parity	Low	Minimal	Low
Sebire 2001[63]	Minimal	Low	Low	Minimal. Matched for age, parity, smoking, pre-eclampsia, pre-existing diabetes, gestational diabetes, race, hypertension	Moderate	Minimal	Low
Siega-Riz 1996[65]‡	Low	Minimal	NR	Moderate. Confounders assessed, different, and not controlled for: education, hypertension, smoking, marital status, race	Low	Minimal	Moderate

Study	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias*	Analytical bias	Attrition bias	Overall likelihood of bias
Smith† 2006[72]	Minimal	Low	Low	Low (because assumed). Assessed, but not different: age. Confounders assessed, different, and not controlled for (assumed from table 2) α fetoprotein, human chorionic gonadotrophin, smoking, previous miscarriage, marital status, previous therapeutic abortions	Low	Minimal	Low
Smith 2007[66]	Minimal	Low	Minimal	Minimal. Adjusted for age, parity, smoking, marital status, maternal height, deprivation category, previous spontaneous early pregnancy losses, and therapeutic abortions	Minimal	Minimal	Low
Sukalich 2006[67]	Minimal	Low	Low	Minimal. Assessed, but not different: age, smoking, diabetes, previous caesarean section. Confounders assessed, different, and not controlled for: parity, hypertension, medical, maternal weight gain, race	Low	Minimal	Low
Tsukamoto 2007[68]	Minimal	Minimal	Minimal	Minimal. Adjusted for age, parity, maternal weight gain. Assessed, but not different: pregnancy induced hypertension. Confounders assessed, different, and not controlled for: gestational diabetes	Low	Minimal	Low
Yaacob 2002[69]	Low	Minimal	Minimal	Low. Matched for age, parity. Assessed, but not different: hypertension, gestational diabetes	High	NR	High
Yekta 2006[70]	Low	Minimal	NR	Minimal. Adjusted for age, parity, education	Low	Minimal	Low
Yogev 2005[71]	Low	Minimal	NR	Moderate (potential confounders not assessed by original study)*	Low	Minimal	Moderate
Zhou 1997[75]	Low	Minimal	Minimal	Moderate (confounders not assessed)*	Moderate	Low	Moderate

NR=not reported; NA=not applicable.
*Assessment of confounding factor bias was done by evaluation of each studies' assessment of potential confounders by four methods: adjustment with regression, matching, assessment of potential confounders on univariate analyses that were found to be not significantly different between groups, and assessment of potential confounders on univariate analyses that were different between groups and not controlled for.
‡Although these were cohort studies, data within manuscript were also presented in format that allowed pooling with data from case-control studies; however, data are listed only in tables with cohort studies.

anthropometry (likelihood ratio 0.96, 95% confidence interval 0.66 to 1.40).[98] However, the quality assessment of studies was limited and several large studies have been published since the literature search ended in 2002. A World Health Organization study meta-analysed 25 datasets identified by researchers attending a 1990 conference but lacked the literature search that is the standard basis of a systematic review.[99] Compared with women with higher body mass indices (>75% quartile), women in the lower fourth (<25%) had an increased risk of low birth weight (odds ratio 1.8, 95% confidence interval 1.7 to 2.0) and preterm birth (1.3, 1.1 to 1.4).

Strengths and limitations of the review

The strengths of our meta-analysis include the thoroughness with which the outcomes of preterm birth and low birth weight were assessed (preterm birth was examined before 37 weeks, 32-36 weeks, and before 32 weeks, overall as well as spontaneous and induced, and besides low birth weight we examined very low birth weight and extremely low birth weight). We explored the effect of gradations in maternal body mass index (overweight, obese, and very obese), carried out an extensive quality assessment, and investigated heterogeneity with sensitivity analyses. We compared the results of crude, and matched or adjusted, data to try to determine if the observed perinatal risks were due to body mass index independently or were explained by confounding factors. Finally, we robustly assessed bias using the trim and fill method.

Limitations of this systematic review include potential residual confounding by factors that might account for the observed association between obesity and perinatal outcomes, which were not adjusted for in some or all of the original studies, such as smoking or low socioeconomic status. Gestational weight gain, which was not taken into account by most of the studies, can influence outcomes such as preterm birth and low birth weight. However, prepregnancy body mass index is the strongest predictor of outcomes, not gestational weight gain.[100] Moreover, it is useful to be able to predict a woman's risk of preterm birth or having an infant of low birth weight on the basis of information available at the start of the pregnancy such as prepregnancy body mass index.

We pooled data based on the original studies' definitions of overweight, obese, and very obese, as have other meta-analyses.[101] This overcomes the problem of varying cut-offs between studies and allows the cut-offs to be appropriate to the specific population. Thus, in the normal, overweight, obese, and very obese categories, body mass index ranged from 18.3 to 29.8, 24.6 to 30.0, 29.0 to 40.0, and ≥34.9 to ≥40.0, respectively. Using population specific cut-offs for body mass index is an established practice in other areas of medicine, including using lower body mass index cut-offs for obesity in Asian than white populations since lower cut-offs have been associated with increased risks of cardiovascular disease.[102]

Future research is needed to try to determine why overweight and obese women are at risk of preterm birth, and to determine effective methods of weight loss in women of childbearing age before pregnancy.

Conclusions and implications

In conclusion, overweight and obese women have higher risks of preterm birth before 32 weeks and induced preterm birth before 37 weeks, and accounting for publication bias, possible preterm birth before

Table 10 | Quality assessment based on evaluation of bias in case-control studies of preterm birth and low birth weight in overweight and obese women compared with women of normal weight

Study	Selection bias	Exposure bias	Outcome assessment bias	Confounding factor bias*	Analytical bias	Attrition bias	Overall likelihood of bias
Al-Eissa† 1994	Low	Minimal	NR	Minimal. Adjusted for age <20 years, previous preterm birth, previous low birth weight, mud house as dwelling, first or second degree relatives, non-relatives, previous spontaneous abortion, inadequate prenatal care, antepartum haemorrhage, interval between pregnancies <12 months, vaginal bleeding in first or second trimester	Low	Minimal	Low
Begum 2003[77]	Minimal	Minimal	NR	Minimal. Assessed, but not different: age, parity, previous preterm birth, gravida, previous abortion. Confounders assessed, different, and not controlled: income, education	Low	Minimal	Low
Catov 2007[78]	Minimal	Minimal	Minimal	Moderate (confounders not assessed)*	Low	Minimal	Low
Conti 1998[79]	Low	Minimal	Minimal	Minimal. Matched for age, parity, insurance	Low	Minimal	Low
de Haas* 1991[80]	Low	Minimal	Minimal	Minimal. Matched for age, delivery date, education, marital status, race	High	Low	Moderate
Delgado-Rodriguez 1998[81]	Low	Minimal	Minimal	Minimal. Assessed, but not different: age, parity, smoking. Confounders assessed, different, and not controlled: education, social class, pregnancy induced hypertension	Low	Minimal	Low
Dhar 2003[82]	Low	Minimal	Minimal	Minimal. Adjusted for age, parity, antenatal care, birth to conception interview, sex of new born, gestational age, hypertension, body mass index after delivery, weight, haemoglobin level, mean arm circumference, income, education, father's education, father's occupation	Low	Minimal	Low
Gosselink* 1992[83]	Low	Minimal	NR	Minimal. Matched for age, parity, race	NR	Minimal	Low
Hashim* 2000[84]	Low	Minimal	Minimal	Minimal. Assessed, but not different: parity, education, social class, antenatal visits, newborn sex, presence of household helper, occupation, consanguinity. Confounders assessed, different, and not controlled: age	Low	Minimal	Low
Hediger 1995[85]	Low	Minimal	Minimal	Minimal. Assessed, but not different: smoking, maternal height, prepregnancy body mass index, gestational age at delivery, medical recipient, primiparous women	Low	Minimal	Low
Karim 1997[86]	Moderate	Minimal	Minimal	Minimal. Adjusted for age, education, income. Assessed, but not different: parity, age of last surviving child, husband's occupation, place of delivery. Confounders assessed, different, and not controlled: sex of child	Low	Minimal	Moderate
Lawoyin 1997[87]	Minimal	Minimal	Minimal	Low. Assessed, but not different: haemoglobin level	Low	Low	Low
Le* 2007[88]	Low	Minimal	Low	NA (primary exposure not anthropometry)	Low	Minimal	Low
Melamed 2008[89]	Low	Minimal	Minimal	NA (primary exposure not anthropometry)	Low	Minimal	Low
Mohsen 2007[90]	Low	Minimal	Minimal	Moderate (confounders not assessed)*	Low	Minimal	Moderate
Ojha 2007[91]	Low	Minimal	Minimal	Low. Matched for age, parity	NR	Minimal	Low
Pitiphat 2008[92]	Minimal	Minimal	Minimal	NA (primary exposure not anthropometry)	NR	Minimal	Low
Yogev 2007[93]	Low	Minimal	NR	NA (primary exposure not anthropometry)	Low	Minimal	Low
Xue 2008[94]	Low	Low	Minimal	Moderate (confounders not assessed)*	NR	Minimal	Moderate
Zeitlin* 2001[95]	Minimal	Minimal	Minimal	Minimal. Adjusted for obstetric history, marital status, body mass index <18.3 or >29.8, smoking in third trimester, age at completion of schooling	Low	Minimal	Low

*Confounding factor bias was done by evaluation of each studies' assessment of potential confounders by four methods (see footnote to table 9).
†Non-pooled study.

37 weeks overall. Unlike many causes of preterm birth, maternal overweight and obesity represent a potentially preventable cause of the leading source of neonatal mortality and morbidity and morbidity through childhood.[7] Surveillance for preterm birth should be considered in overweight and obese women. Moreover, although some of the inductions may have been medically indicated, some were likely not, and represent another area for clinicians to focus on for the prevention of preterm birth. The beneficial effects of maternal overweight or obesity on low birth weight were higher in developing countries than developed countries and disappeared when publication bias was taken into account. Clinicians need to be aware that overweight or obesity in women is not protective against having infants of low birth weight and should consider surveillance when indicated. Ideally, overweight or obese women should have prepregnancy counselling so that they are informed of their perinatal risks and can try to optimise their weight before pregnancy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The effect of overweight or obesity in women on risk of preterm birth is debated in the literature

Uncertainty is reflected in national guidelines, although it is widely believed that the risk of having an infant of low birth weight is decreased in overweight or obese women

WHAT THIS STUDY ADDS

Overweight or obese women have increased risks of preterm birth before 32 weeks and induced preterm birth before 37 weeks, and, accounting for publication bias, preterm birth before 37 weeks overall

The beneficial effects of overweight or obesity on low birth weight were greater in developing than developed countries and disappeared after accounting for publication bias

Overweight and obese women should be counselled before pregnancy on their perinatal risks, and appropriate surveillance should be considered during pregnancy

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