

Associations of Prepregnancy Body Mass Index and Gestational Weight Gain with Intelligence in Offspring: A Systematic Review and Meta-analysis

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Abstract

Background: As a growing health problem, maternal obesity may have an adverse effect on offspring neurodevelopment. The effects of maternal overweight and obesity and excessive gestational weight gain on offspring intelligence remains unclear. This meta-analysis aimed to assess the influence of prepregnancy body mass index (BMI) and gestational weight gain on children's intelligence.

Methods: We systematically searched PubMed, Embase, Cochrane Library and Ovid Medline from their inception through July 2020. Studies assessing the association between prepregnancy BMI or gestational weight gain and children's intelligence (from 3 years to 10 years) were screened manually before final inclusion. We included prospective and retrospective cohorts that analysed the association between prepregnancy BMI or gestational weight gain and intelligence of offspring. We used the Mantel-Haenszel fixed-effects method to compute the weight mean difference (WMD) and 95% confidence interval (CI) of each study.

Results: Twelve articles were included in the systematic review, and six of them were included in the meta-analysis. There was a significant full-scale IQ reduction in children of overweight and obese women, with WMDs of -3.25 (95% CI: -3.05, -2.42) and -4.85 (95% CI: -5.93, -3.76), respectively. Compared with that in the control group, the WMDs for performance IQ were -2.40 (95% CI: -3.45, -1.34) and -5.28 (95% CI: -7.22, -3.34) in the overweight and obesity groups, respectively, and the WMDs for verbal IQ were -3.47 (95% CI: -4.38, -2.56) and -5.71 (95% CI: -7.13, -4.29), respectively. However, there was no significant reduction in children's full-scale intelligence scores due to excessive weight gain; the WMD was -0.14 (95% CI: -0.92, 0.65).

Conclusions: Prepregnancy overweight and obesity might have disadvantageous consequences on children's intelligence; however, we observed no significant difference between excessive and normal gestational weight gain. Therefore, weight control before pregnancy is more important than that during pregnancy in terms of children's intelligence.

Trial registration: This systematic review and meta-analysis have been registered in PROSPERO (Number: CRD42020199215).

Background

Overweight and obesity (OWO) is an increasing public health concern globally and has been considered a critical factor for diverse disorders, such as cardiovascular diseases, diabetes, cancers, and even COVID-19 cases[1]. According to the World Health Organization (WHO), approximately 40% of the world's population is overweight, and approximately 13% is obese[2]. In China, the prevalence of overweight increased to 39.6% in 2009 from 25.1% in 1997, and the prevalence of obesity in adolescents alone more than doubled from 1991 to 2015 [3], casting a shadow on the development of the younger generation. Maternal OWO is another major concern, as it usually predisposes the offspring to an array of developmental disorders, in addition to predisposing the mother to health problems.

Maternal obesity has been shown to be involved in a diverse set of severe complications of pregnancy, such as gestational diabetes, preeclampsia, postpartum haemorrhage, and thromboembolism. In addition, maternal obesity predicts an array of adverse outcomes among infants, such as preterm birth, congenital abnormalities, and macrosomia.[4] Some studies suggest that maternal obesity may have long-lasting effects on children's development during their childhood and later adult life. For example, the offspring of an obese mother are more susceptible to cardiovascular diseases, metabolic disorders, and allergic diseases.[5–7] However, weight management during pregnancy is a common problem for gravidas. In 2017, nearly half of women, especially overweight and obese women, exceeded their weight gain goal.[8] Similar to maternal obesity, excessive gestational weight gain (GWG) leads to an increasing incidence of adverse outcomes.

Recent studies have shown that maternal OWO has adverse effects on offspring intelligence and makes offspring susceptible to psychological disorders. Foetal brain development begins during the first trimester of pregnancy, and intrauterine exposure to adipose tissue, hyperglycaemia and other adverse environmental factors may have a critical influence on the child's nervous system. There is growing evidence that both maternal OWO and excessive GWG are negatively associated with offspring neurodevelopment, increasing the risks of attention deficit hyperactivity disorder (ADHD) [9], autism[10], and intellectual disability[11], which has been putatively hypothesized to be an outcome of decreased production of neurotrophic factors through epigenetic regulation, which impairs hippocampal progenitor cell division and neurogenesis.[12] Additionally, obesity during pregnancy also contributes to systemic and intrauterine inflammation, leading to foetal brain injuries and impaired nervous system development[13].

Several systematic reviews have examined the association between maternal prepregnancy BMI and offspring neurodevelopment, and these studies found that prepregnancy OWO had an adverse impact on children's neurodevelopment[14] and predisposed children to emotional/behavioural problems[15], eating disorders, ADHD and psychotic diseases[16]. However, all of them failed to systematically study the effect of maternal OWO on children's intelligence. Thus, in this systematic review based on a meta-analysis, we would like to assess the effect of prepregnancy body mass index (BMI) and gestational weight on the intelligence of offspring, potentially providing valuable information for policy makers in the field of eugenics.

Methods

This systematic review and meta-analysis is registered in PROSPERO (Number: CRD42020199215) and is reported according to MOOSE (Meta-analysis Of Observational Studies in Epidemiology) Guidelines[17].

Search strategy and selection criteria

We performed a systemic search covering the PubMed, Embase, Cochrane Library and Ovid Medline databases without language restrictions from their inception through July 2020. We used combined key terms that are summarized as follows: 'prepregnancy', 'maternal', 'gestational weight gain', 'obesity', 'BMI', 'intelligence', 'mental', and 'cognition'. (Additional file 1) A manual search was performed by using the reference lists of key articles. Two authors (SMZ and YCH) independently reviewed the study titles and abstracts, and candidate full texts were retrieved and perused by the same authors to determine whether they met the inclusion criteria.

Selection criteria

In this study, we considered prepregnancy overweight, obesity, and excessive gestational weight gain to be maternal obesity. Prospective and retrospective cohorts that analysed the association between prepregnancy BMI/GWG and intelligence of offspring were considered for inclusion in this systematic review and meta-analysis. The inclusion criteria were as follows: 1) participants: mother-child pairs, with the child's age up to 12 years; 2) exposure: prepregnancy overweight, obesity and excessive gestational weight gain; 3) control: normal prepregnancy weight for pre-pregnancy overweight and obesity, and gestational weight gain as recommended for excessive gestational weight gain; 4) primary outcome: children's full-scale intelligence quotient assessed by standardized tests; and 5) secondary outcome: children's performance and verbal intelligence quotient assessed by standardized tests. Studies were excluded if 1) children were born preterm or had low or very low birth weight; 2) children had any pathological status that might affect the results of intelligence assessment; and 3) the sample size of the cohort study was less than 100. When two articles extracted data from the same cohort, we selected the one that was published earlier, and when the intelligence of children in the same cohort was evaluated at different ages, their data were analysed as two independent samples.

Data extraction and quality assessment

Two authors (SMZ and YCH) independently extracted the following data from all eligible studies: maternal age at birth, age of the child at evaluation, total number of mother-child pairs, and tool for the intelligence assessment and dimensions covered. Disagreements were resolved by discussion with an additional author (CZ). The diagnosis of overweight and obesity was made according to the WHO[18] and Working Group on Obesity in China[19], and we classified GWG as below, within and above the age-standardized z scores[20] or 2009 Institute of Medicine recommendations[21]. Two authors evaluated the quality of eligible studies independently using the Newcastle-Ottawa Scale (NOS)[22]. We evaluated the selection, ascertainment of exposure, adjustment of covariates, assessment and follow-up for outcomes for each study. A study was classified as high quality if it received more than 7 stars[23].

Data synthesis and statistical analysis

Two authors (SMZ and YCH.) extracted IQ test scores from eligible studies. The data were checked and entered in STATA 14 by another researcher (CZ). We used the Mantel-Haenszel fixed-effects method to compute the weight mean difference (WMD) and 95% confidence interval (CI) of each study, as effect measures[24]. The I^2 statistical parameter was used to assess heterogeneity, and it was considered moderate to high heterogeneity if the I^2 value was $>50\%$ [25]. In this meta-analysis, I^2 values were less than 50%, so it was appropriate to use a fixed-effect model. If the two-sided p value was <0.05 , it was considered statistically significant.

To assess the influence of a single study on the summary WMD and to examine whether it contributed to a large portion of the heterogeneity, sensitivity analysis was carried out by removing studies one by one. Publication bias was assessed using Egger's linear regression test, Begg's rank correlation and visual inspection of funnel plots[26, 27]. These analyses were carried out with Stata 14.

Results

In total, 5199 articles were retrieved after the initial search; among them, 1830 were removed as duplicates, and 53 were left after screening the title and abstract. Finally, 12[28–39] studies were eligible for systematic review. (Fig. 1) Of these 12 articles, 6[28–30, 33, 36, 39] offered sufficient data for statistical analysis. Among these six studies, five analysed the association between maternal prepregnancy obesity and overweight and children's intelligence[28–30, 33, 36], and three analysed the impact of excessive weight gain and children's intelligence[30, 36, 39]. In one cohort, the intelligence of children was evaluated at different ages, and their data were analysed as two independent samples[36]. Most of the articles were ranked as high quality according to the NOS scale. Publication bias was assessed using Egger's linear regression test, Begg's rank correlation and visual inspection of funnel plots, and we did not find any significant bias.

Study characteristics

Table 1 summarizes the main characteristics of the included studies for systematic review. All 12 articles were prospective cohort studies between 2003 and 2019. Five were from the USA, two from China and the UK each, and one from Canada, Denmark, and Norway and Sweden each. Of the 6

cohorts for meta-analysis, the sample size ranged from 355 to 30212. The maternal age at birth ranged from 21 to 35 years, and children's intelligence was evaluated between 3 years and 10 years. Five studies [28, 29, 32, 34, 35, 37, 39] used the Wechsler scale to measure IQ, two reported IQ[33, 36] based on Differential Intelligence Scales, and two reported IQ[30, 38] based on the Stanford-Binet test. They measured different dimensions of intelligence, including full-scale, verbal, nonverbal, and performance intelligence (FIQ, VIQ, nVIQ and PIQ) scores. We included only studies providing data for overweight and obesity separately or studies that showed total GWG.

Table 1
Characteristics of the included studies

Reference and type of study	Maternal Age(ys)	Maternal BMI reference values	GWG reference values	Age of child at evaluation	Other confounders	Sample size	Intelligence assessment and dimensions
Coo et al. 2019 Cohort prospective, ALSPAC (UK)	Ctrl:29.4 Overweight: 29.1 Obese:29.7	WHO	ND	8	child's sex, maternal age, parity, marital status, pre-existing hypertension, smoking or alcohol consumption during pregnancy, socioeconomic status, pre-eclampsia, caesarean delivery, preterm birth, birth weight and breastfeeding duration	4324	Wechsler Intelligence Scale for Children (WISC)-III: Verbal Scale Performance Scale Full-Scale IQ
Zhu et al. 2019 Cohort prospective(Women's hospital, School of Medicine, Zhejiang University in Hangzhou, China)	ND	Working Group on Obesity in China	ND	Ctrl:4.82 Underweight:4.88 Overweight: 4.82 Obese:4.74	paternal age, parental education, children's sex, fetal distress, birth weight, gestational age, preterm birth, mode of delivery, feeding patterns, pregnancy and ART complications	1904	Chinese Version of the Wechsler Intelligence Scale for Children-Revised(C-WISC): Verbal Scale Performance Scale Full-Scale IQ
Pugh et al. 2015 Cohort prospective, MHPCD (USA)	ND	WHO	gestational age-standardized z scores	10	maternal age, race, parity, employment, education, income, and marital status	530	Stanford Binet Intelligence Scale 4th Edition (SBIS): IQ Wisconsin Card Sorting Test (WCST) and Trail Making Test Part B (TMT-B) : Executive function

ALSPAC,Avon Longitudinal Study of Parents and Children; ND, Not defined; Ctrl,Control;BMI, Body Mass Index; WHO (World Health Organization): normal (18.5 to 24.9); overweight (25.0 to 29.9);and obese (30 to 39.9);MHPCD, The Maternal Health Practices and Child Development; DNBC, Danish National Birth Cohort; CPP, The Collaborative Perinatal Project.

Reference and type of study	Maternal Age(ys)	Maternal BMI reference values	GWG reference values	Age of child at evaluation	Other confounders	Sample size	Intelligence assessment and dimensions
Monthé-Drèze et al. 2019 Cohort prospective, Project Viva(USA)	32.2	WHO	ND	3.2 7.7	maternal age, education, household income, race/ethnicity, parity, smoking status before learning of pregnancy, paternal education	1246(3.2y) 1070(7.7y)	Peabody Picture Vocabulary Test-3rd edition (PPVT-III) (3.2y): receptive language Kaufman Brief Intelligence Test-2nd edition (KBIT-II) (7.7y): verbal and non-verbal intelligence
Eriksen et al. 2013 Cohort prospective, DNBC (Danmark)	30.8	WHO	ND	5.0-5.3	parity, maternal prenatal smoking, average alcohol intake per week during pregnancy, birth weight and gestational age	1782	Wechsler Primary and Preschool Scales of Intelligence – Revised (WPPSI-R): Verbal IQ Performance IQ Full-Scale IQ
Neggers et al. 2003 Cohort prospective (University of Alabama in Tuscaloosa and Birmingham, AL, USA)	21.6	Underweight : <19.8 Normal : 19.8–26.0 Overweight : 26.1–29 Obese : >29	ND	5.3	Mother's PPVT scores, zinc supplementation status, smoking and alcohol use and child's birth weight, childcare status, and home environment	355	Differential Ability Scales (DAS): Verbal ability Nonverbal ability IQ
Krzeczkowski et al. 2018 Cohort prospective, MIREC(Canada)	32.8	WHO	ND	3.39	gestational diet quality, home environment, maternal depression, prenatal smoking and maternal education	808	Wechsler Preschool and Primary Scale of Intelligence-III (WPPSI-III): Verbal IQ Performance IQ Full-Scale IQ

ALSPAC,Avon Longitudinal Study of Parents and Children; ND, Not defined; Ctrl,Control;BMI, Body Mass Index; WHO (World Health Organization): normal (18.5 to 24.9); overweight (25.0 to 29.9);and obese (30 to 39.9);MHPCD, The Maternal Health Practices and Child Development; DNBC, Danish National Birth Cohort; CPP, The Collaborative Perinatal Project.

Reference and type of study	Maternal Age(ys)	Maternal BMI reference values	GWG reference values	Age of child at evaluation	Other confounders	Sample size	Intelligence assessment and dimensions
Huang et al. 2014 Cohort prospective, CPP(USA)	ND	WHO	2009 Institute of Medicine recommendations	7.1	maternal age at delivery, marital status at pregnancy, maternal race, education levels, number of previous deliveries, smoking during pregnancy, and diabetes	30212	Wechsler Intelligence Scale for Children (WISC I): Verbal IQ Performance IQ Full-Scale IQ
Kominiarek et al. 2018 Cohort prospective (Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, USA)	Ctrl:27.8 Overweight: 28.4 Obese:27.7	WHO	2009 Institute of Medicine recommendations	3 5	race– ethnicity, education, insurance type, parity, smoking and alcohol use in pregnancy, thyroid status, treatment group, gestational age at delivery, and neonatal sex	948	Differential Ability Scales-II (3y): full-scale IQ Wechsler Preschool and Primary Scale of Intelligence (5y): full-scale IQ
Gage et al. 2012 Cohort prospective, ALSPAC (UK)	Inadequate: 29 Adequate: 28.7 Excessive: 27.9	ND	2009 Institute of Medicine recommendations	8	mode of delivery, and the child's sex, maternal education, parity and maternal smoking in pregnancy	3340	Wechsler Intelligence Scale for Children: Verbal IQ Performance IQ Full-Scale IQ
Keim et al. 2011 Cohort prospective, CPP(USA)	ND	ND	2009 Institute of Medicine recommendations	4 7	pre-pregnancy BMI, maternal age, race, parity, smoking, SES index and child sex	31968	Stanford–Binet Intelligence Scale (4y) Wechsler Intelligence Scales for Children (WISC) (7y)
Hinkle et al. 2016 Cohort prospective, NICHD(Norway and Sweden)	29	ND	2009 Institute of Medicine recommendations	5.2	maternal education, marital status, economic situation, parity, pre-pregnancy smoking, cigarettes, alcohol use during pregnancy	344	Wechsler Preschool and Primary Scales of Intelligence (WPPSI-R): Verbal IQ Performance IQ Full-Scale IQ
ALSPAC,Avon Longitudinal Study of Parents and Children; ND, Not defined; Ctrl,Control;BMI, Body Mass Index; WHO (World Health Organization): normal (18.5 to 24.9); overweight (25.0 to 29.9);and obese (30 to 39.9);MHPCD, The Maternal Health Practices and Child Development; DNBC, Danish National Birth Cohort; CPP, The Collaborative Perinatal Project.							

Quality assessment

The mean value of the included 6 studies was 7.5 stars, ranging from 6 to 8, and 5 studies were considered high quality, according to the NOS scale (Additional file 2). Among them, only one study had a secure record of prepregnancy weight[29], and three other studies described subjects lost to follow-up or had a small number of subjects lost to follow-up (<20%)[28, 30, 39]. However, one cohort study was only of African-American women of low income, which has a high level of ethnic bias[33].

Meta-analysis

A pooled analysis of 7 studies that assessed the association between prepregnancy BMI and FIQ in offspring was performed by using a fixed-effects model. (Figure 2) There was a significant FIQ reduction in children of overweight and obese women, with WMDs of -3.25 (95% CI: -4.07, -2.42) and -4.85 (95% CI: -5.93, -3.76), respectively. Heterogeneity estimates were $I^2=6.2%$ ($p=0.377$) and $I^2=0.0%$ ($p=0.838$) for prepregnancy overweight and obesity, respectively. Two studies also evaluated the association between OWO and PIQ, and 4 studies explored the relationship between OWO and VIQ. We noticed that both the PIQ and VIQ of the OWO group were significantly lower than those of the controls, with WMDs of -2.40 (95% CI: -3.45, -1.34) and -5.28 (95% CI: -7.22, -3.34), respectively, for PIQ, and -3.47 (95% CI: -4.38, -2.56) and -5.71 (95% CI: -7.13, -4.29), respectively, for VIQ, suggesting a potential adverse effect of maternal prepregnancy weight status on the offspring's intellectual function in many dimensions (Figure 3 and Figure 4). Heterogeneity estimates were $I^2=39.8%$ ($p=0.197$) and $I^2=16.2%$ ($p=0.275$) in the PIQ group and $I^2=19.0%$ ($p=0.295$) and $I^2=34.5.0%$ ($p=0.205$) in the VIQ group for prepregnancy overweight and obesity, respectively. To reduce variability, two groups of FIQ were meta-analysed according to the age of the child at evaluation (whether or not the child was younger than 5 years). In both the overweight and obesity groups, we did not find any significant heterogeneity between the two groups based on age. (Additional file 4a and b)

Four studies reported the association between gestational weight gain and intelligence in offspring. However, compared with adequate gestational weight gain, excessive weight gain did not show a significant reduction in children's full-scale intelligence scores, with a WMD of -0.14 (95% CI: -0.92, 0.65), suggesting a weak association between GWG and children's intelligence (Figure 2). The heterogeneity I^2 was 0.0% ($p=0.482$), which suggests low heterogeneity. In the subgroup analysis, we did not find any significant difference in full-scale intelligence level between children <5 years and ≥ 5 years. (Additional file 4c)

Sensitivity analysis

Sensitivity analysis showed no relevant changes in overall WMD and heterogeneity when either included cohort was removed, which was the same for all three groups.

Publication bias

Publication bias was not found with either the Egger's or Begg's test for small-study effects, with $P=0.796$, 0.501, and 0.561 for prepregnancy overweight, obesity and excessive GWG, respectively, with Egger's test and $P=1.000$, 0.707, and 0.734 for prepregnancy overweight, obesity and excessive GWG with Begg's test, respectively. A review of the funnel plots showed no evidence of publication bias (Additional file 5a-c).

Discussion

With the increasing number of overweight and obese women of child-bearing age, the long-term effect of maternal prepregnancy weight status is drawing more attention. In this meta-analysis, we found a significantly lower general IQ score in children of both overweight and obese women. Our studies are consistent with most of related studies, which also found a somewhat adverse influence of prepregnancy obesity on children's intelligence levels. Additionally, most of the studies evaluated children's intelligence at the ages of 3–8 years; although the intelligence level is still developing at these ages, a longer follow-up time is needed. It is true that many factors may affect one's intelligence, such as parental education and intelligence levels. The prediction model proposed by Eriksen et al. suggested that parity, maternal breastfeeding and birth weight may affect children's intelligence, while maternal prepregnancy obesity is a minor predictor[32]. Coo et al. also paid attention to paternal weight status and found that paternal obesity had less to do with children's intelligence than maternal obesity[28]. Zhu et al. studied children born to fertile women through assisted reproductive technology and found that prepregnancy obesity increased the risk of preeclampsia, gestational diabetes and preterm delivery, which may contribute to impaired cognitive function, highlighting the complicated network involved in intelligence development[29]. Because it covers more studies, our meta-analysis is helpful in revealing the association between maternal OWO and offspring intelligence.

In contrast, our data showed no influence of GWG on children's intelligence. Neither inadequate weight gain nor excessive weight gain had a significant association with children's intelligence according to all the included cohorts due to the limited number of cohort studies that focused on this issue. Two of the studies also examined trimester-specific associations, but they did not observe a significant association. Both inadequate and excessive GWG may have an adverse effect on offspring, considering the possible lack of nutrients or overnutrition for foetal nervous system development[40]. Although we found little variation in intelligence level between children born to mothers who gained excessive and inadequate weight, we should pay attention to the potential adverse long-term effect of intrauterine adiposity exposure[41], as further research based on more samples is needed and additional cofounders need to be taken into consideration.

Epigenetic regulation has been shown to be involved in neural development. In animal models, the amniotic fluid of obese mothers has lower levels of folic acid, an important donor of methyl groups; thus, the regulation of developmental genes is disrupted[42]. Animal studies also showed that intrauterine adiposity exposure influenced serotonin and dopamine pathways, lipid peroxidation, and the expression of corticosteroid receptors via epigenetic regulation[7]. In the brains of offspring from mothers fed a high-fat diet (HFD) prepregnancy, DNA methylation in the promotor regions of opioid receptors and dopamine transporters decreased, while global hypermethylation was observed in brain regions associated with reward responses, such as the ventral tegmental area (VTA) and prefrontal cortex (PFC) [43]. Edlow et al. found that maternal prepregnancy obesity contributed to gene dysregulation and that dietary changes during pregnancy led to more dysregulated genes in foetal brains[44]. However, the epigenetic mechanism of the association between gestational weight gain and nervous system development in offspring has rarely been studied. Clearly, more studies are required to reveal how maternal prepregnancy obesity modifies epigenetic regulation, thus influencing the child's nervous system.

Factors other than epigenetics are also involved in this process. Maternal obesity can increase the circulating level of leptin, which induces cytokine secretion and may also indirectly impair nervous system development. Indeed, obesity can induce chronic activation of the innate immune system, leading to systemic inflammation, which theoretically affects neural development and intelligence. For example, Monthé-Drèze et al. found that prepregnancy obesity is associated with systemic inflammation and that a higher CRP level is linked to lower scores in intelligence tests[31]. Other inflammatory biomarkers, such as TNF- α and IL-1 β , are linked to neurodevelopmental disorders[45]; elevated IFN- γ , IL-4 and IL-5 may predict a higher risk of autism spectrum disorders (ASDs)[46]. Some inflammatory cytokines, such as IL-6, can pass into the human placenta[47], leading to upregulation of IL-1 β , TNF- α and other cytokines. This inflammatory environment in the foetal brain[48] can result in foetal microglia being activated and producing reactive oxygen species and chemokines, which may damage neurons and oligodendrocytes.

Strengths And Limitations

The foetal origins of adult disease have attracted increasing attention due to their long-term effects on public health, and it is understandable that additional studies are emerging. Recently, several studies have evaluated the impact of maternal prepregnancy obesity on children's cognitive development, the prevalence of ADHD, autism, behaviour problems and intellectual disability. Based on updated literature, our study first analysed the effect of GWG and prepregnancy BMI on children's intelligence together by providing a statistical assessment. Our meta-analysis confirms that prepregnancy obesity and overweight, rather than excessive GWG, have a stronger relationship with worse IQ levels in children. Thus, we provide valuable information for weight management; for childbearing-aged women, weight control is important before pregnancy for the child's long-term health status.

However, this study has some shortcomings. First, in addition to having possible publication bias, this study is not comprehensive due to the limited accessibility of data in the studies we covered here. Second, only 6 articles were available for quantitative analysis due to the lack of data, and more studies are needed to better analyse the association between maternal obesity and children's intelligence. Third, although the included studies took many covariates into consideration, most of them did not measure maternal intelligence, an important confounder. Moreover, two studies did not use the WHO criteria for OWO, leading to potential bias in this meta-analysis. Additionally, since the intelligence assessment covered many dimensions, such as verbal and nonverbal intelligence, a subgroup analysis was recommended. Due to the negligible number of study samples in each subgroup, the analysis could not be performed in the GWG group.

Conclusions

In this meta-analysis, we provide supporting evidence that prepregnancy OWO may have adverse effects on children's intelligence, but we observed no significant difference in children's intelligence scores between excessive and adequate GWG. At the population level, it is advisable to take measures to prevent obesity in childbearing-aged women to reduce the risk of intelligence problems. It is worthwhile to mention that weight status before pregnancy is more important than that during pregnancy in terms of children's intelligence. For childbearing-aged women, measures to control weight should be taken not only during pregnancy but also before pregnancy.

Abbreviations

OWO: Overweight and obesity; GWG: Gestational weight gain; ADHD: Attention deficit hyperactivity; BMI: Body mass index; WMD: Weight mean difference; CI: Confidence intervals; FIQ: Full scale intelligence quotient; VIQ: Verbal intelligence quotient; nVIQ: Non-verbal intelligence quotient; PIQ: Performance intelligence quotient; ASDs: Autism spectrum disorders; HFD: High fat diet; VTA: Ventral tegmental area; PFC: Prefrontal cortex

Declarations

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author contributions

Simeng Zhu and Yichen He are considered co-first authors. SMZ, YCH, and CZ researched, extracted, and evaluated the data, SMZ and YCH performed the data analyses, SMZ wrote the manuscript, and YTW and HFH critically revised the manuscript. YTW and HFH provided the idea and contributed to the discussion. All authors reviewed and approved the article before publication.

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Figures

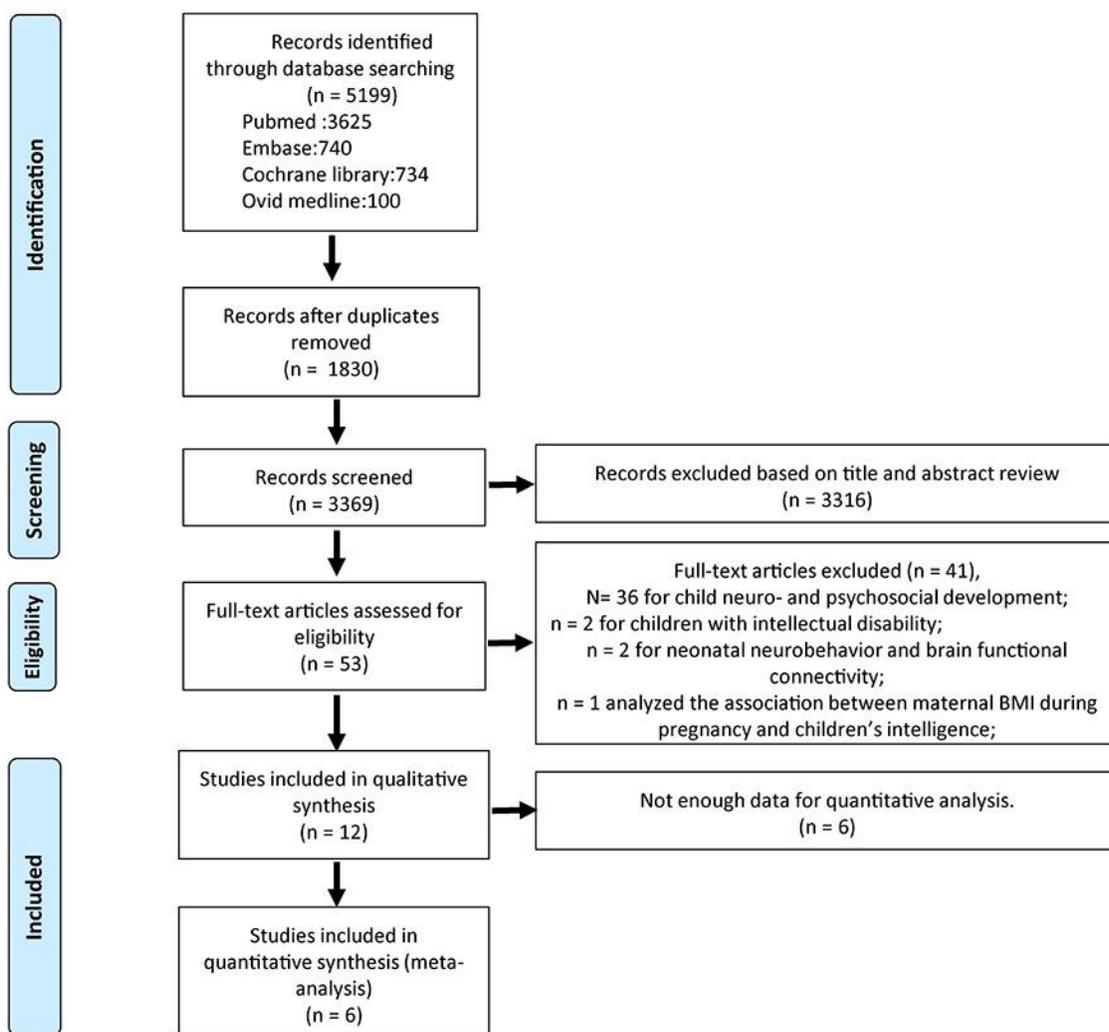


Figure 1

Flowchart of study selection process

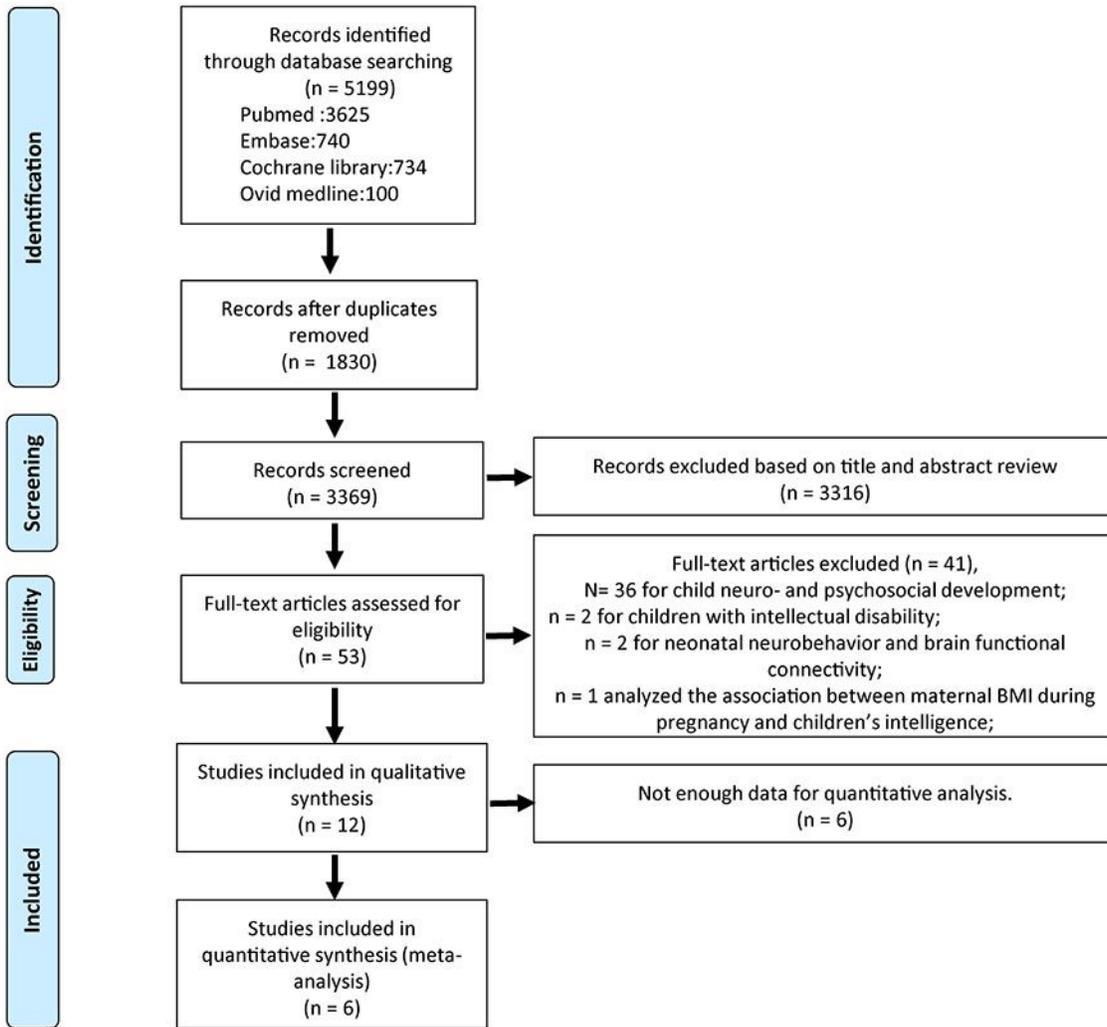


Figure 1

Flowchart of study selection process

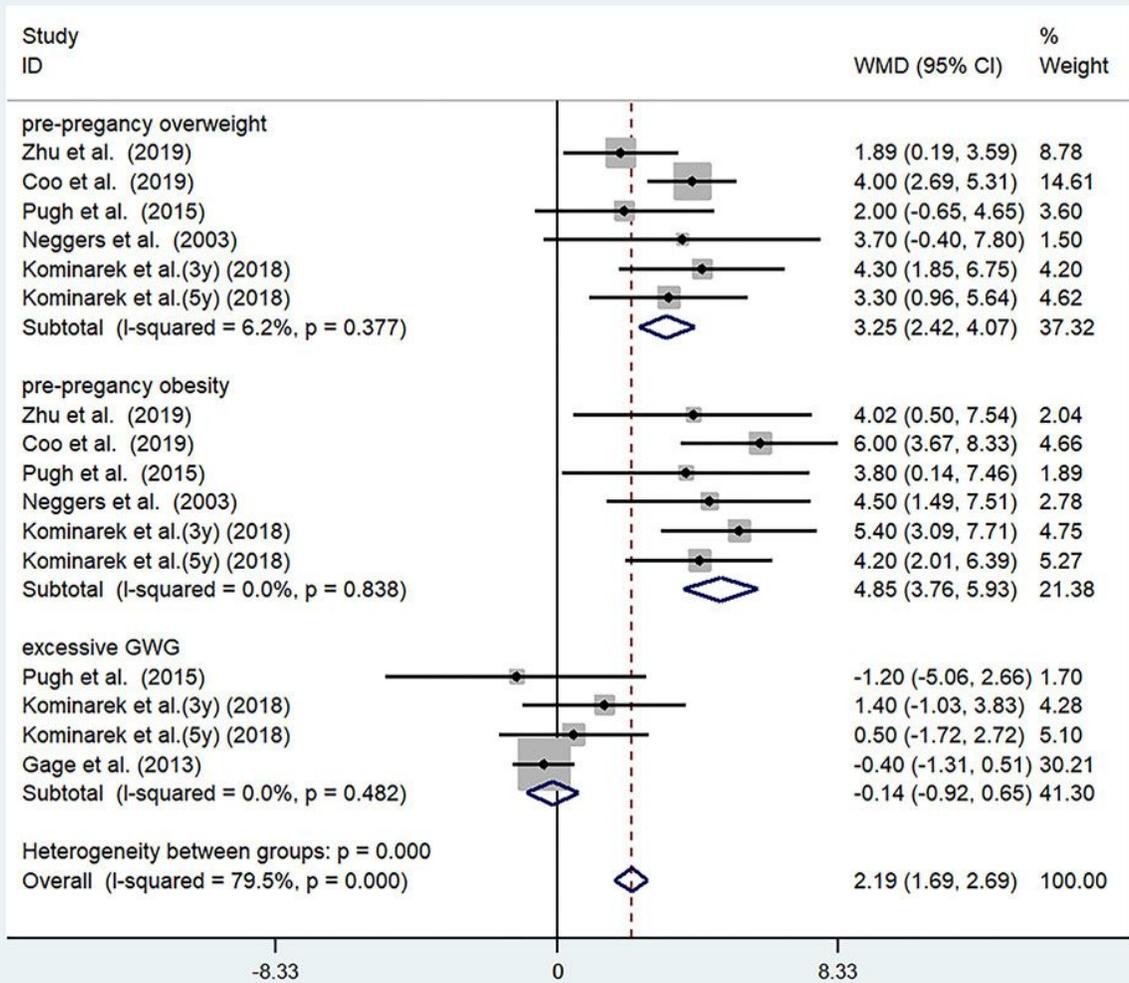


Figure 2
 Forest plots comparing the difference of full-scale intelligence quotient scores between children of pre-pregnancy overweight and normal weight mother, pre-pregnancy obese and normal weight mother and children of mother who gained excessive weight and adequate weight during pregnancy

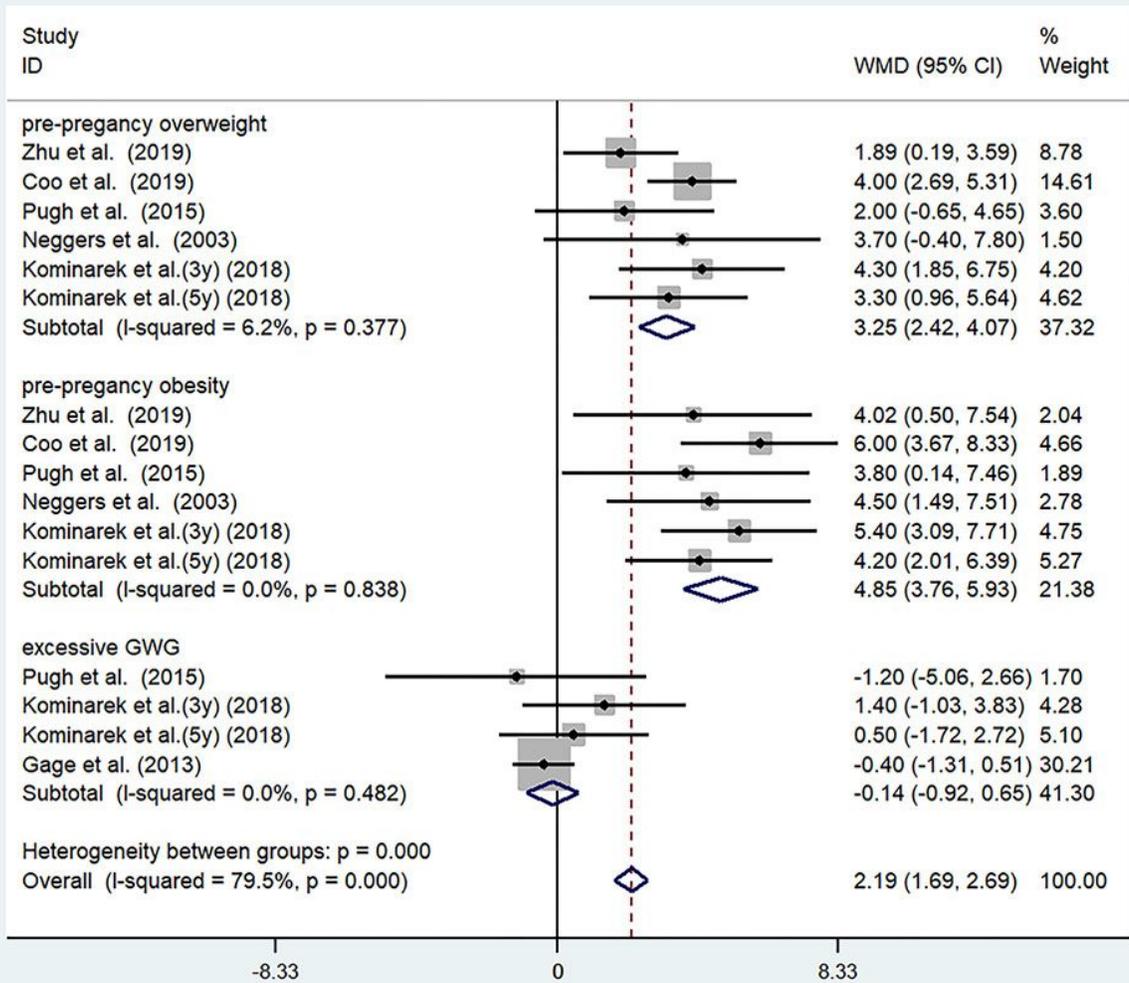


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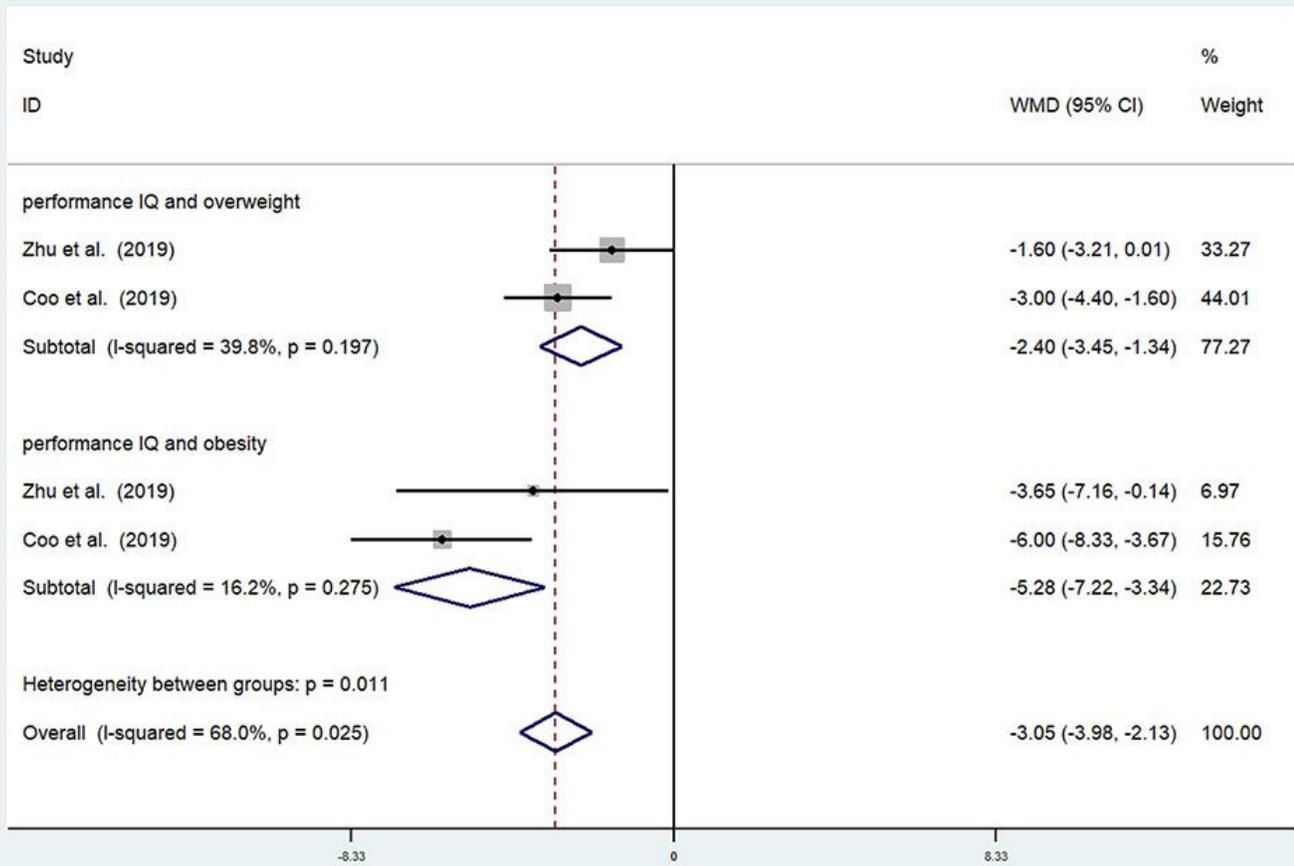


Figure 3

Forest plots comparing performance IQ level in children of pre-pregnancy overweight and obesity mother between normal weight.

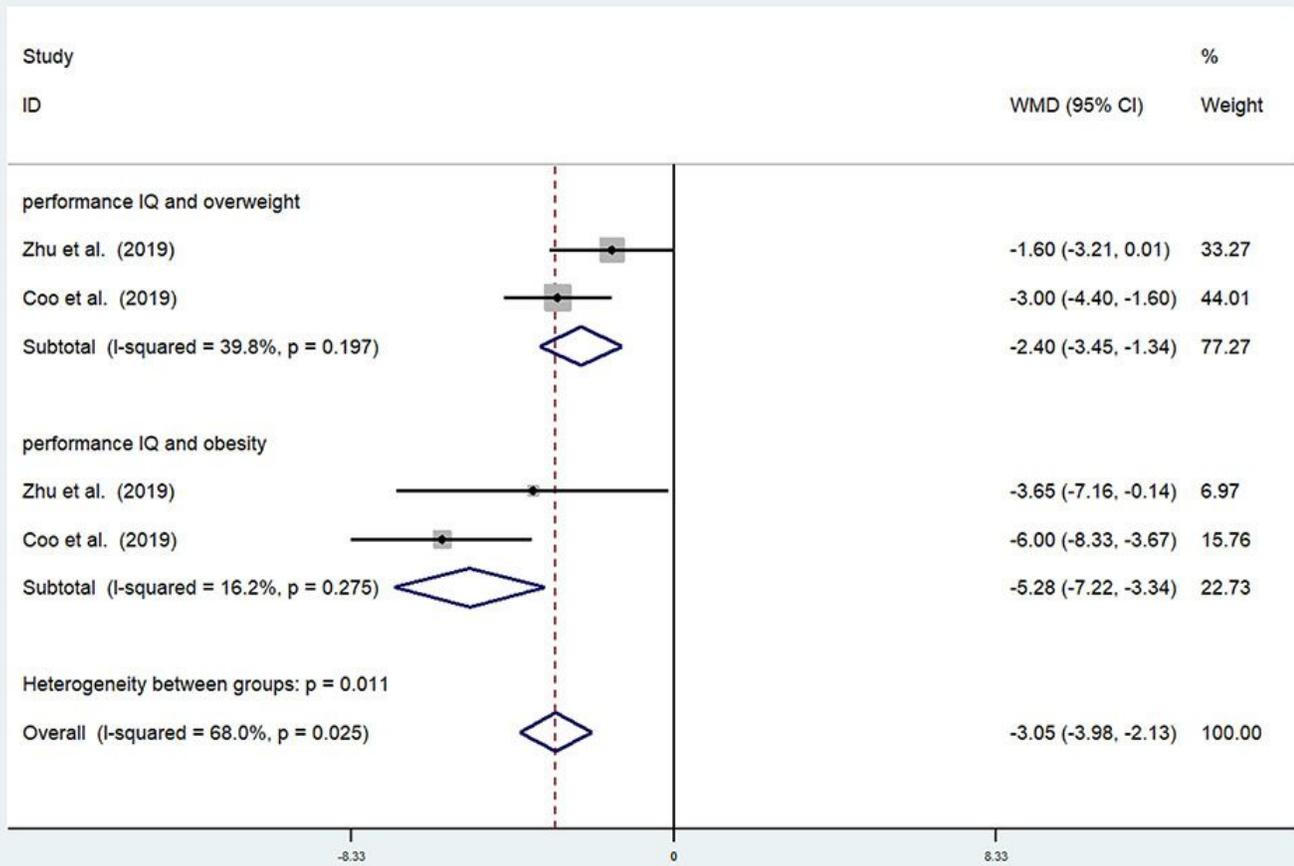


Figure 3

Forest plots comparing performance IQ level in children of pre-pregnancy overweight and obesity mother between normal weight.

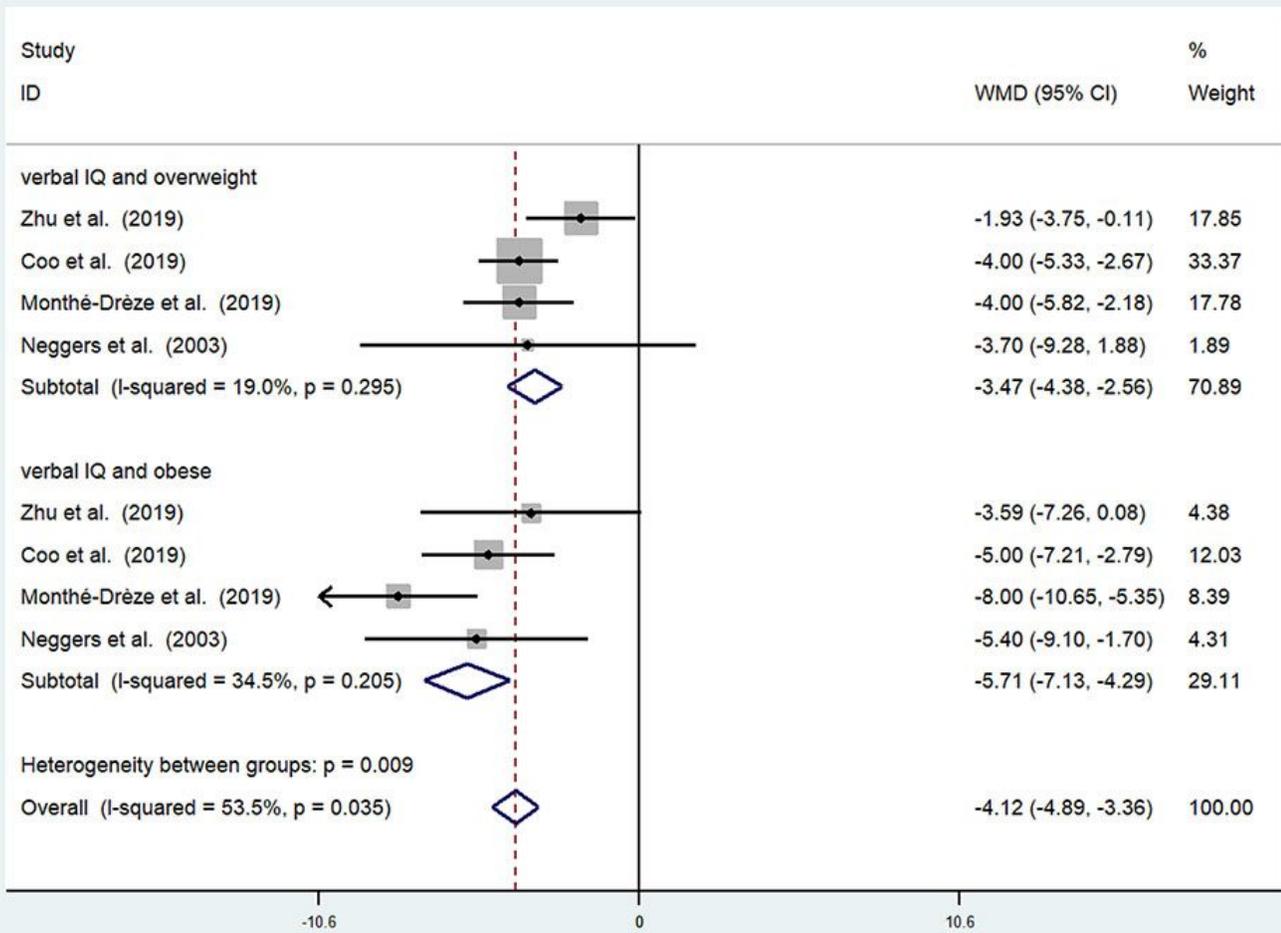


Figure 4

Forest plots comparing verbal IQ level in children of pre-pregnancy overweight and obesity mother between controls.

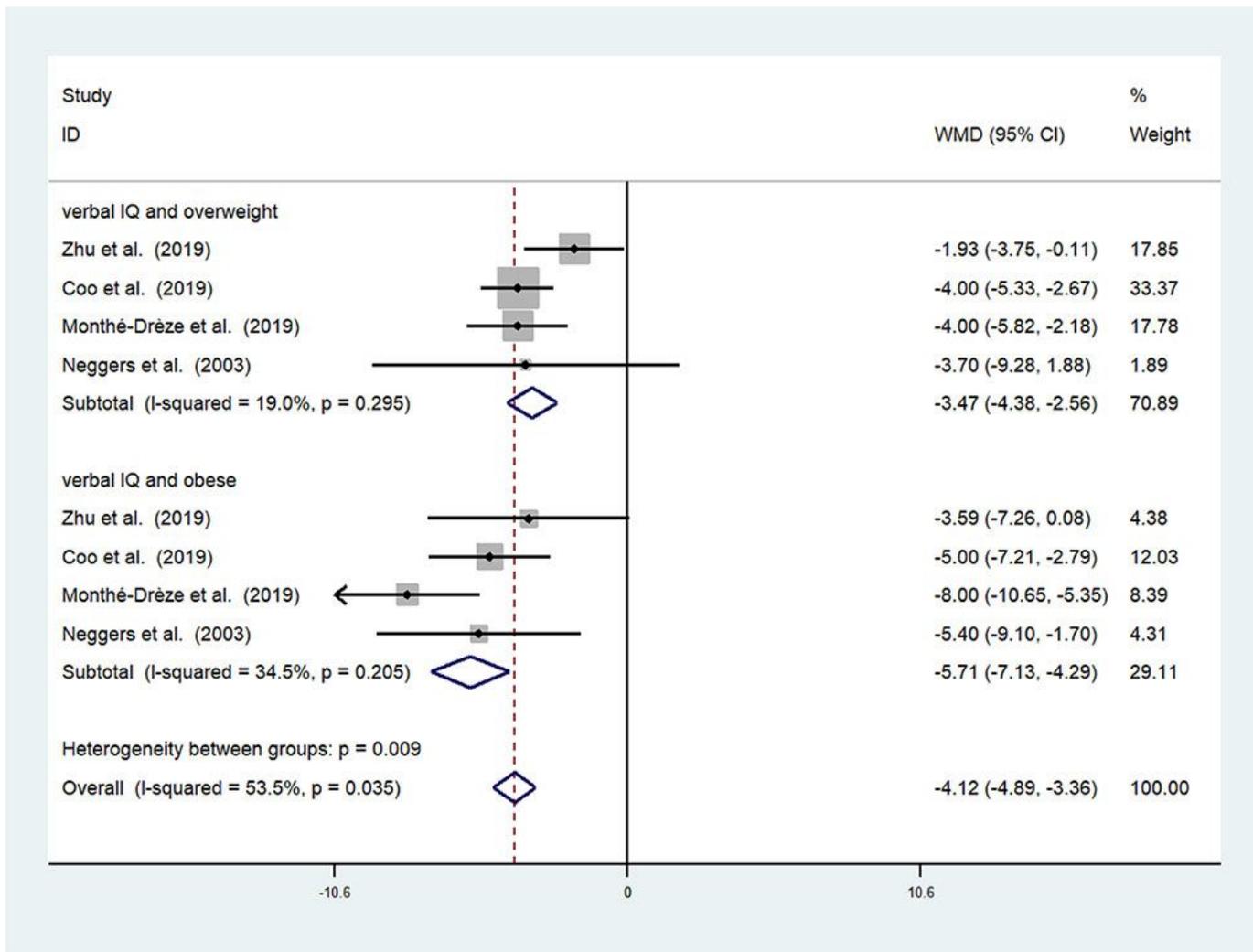


Figure 4

Forest plots comparing verbal IQ level in children of pre-pregnancy overweight and obesity mother between controls.

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