

# Association of Gestational Weight Gain With Maternal and Infant Outcomes

## A Systematic Review and Meta-analysis

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**IMPORTANCE** Body mass index (BMI) and gestational weight gain are increasing globally. In 2009, the Institute of Medicine (IOM) provided specific recommendations regarding the ideal gestational weight gain. However, the association between gestational weight gain consistent with the IOM guidelines and pregnancy outcomes is unclear.

**OBJECTIVE** To perform a systematic review, meta-analysis, and metaregression to evaluate associations between gestational weight gain above or below the IOM guidelines (gain of 12.5-18 kg for underweight women [BMI <18.5]; 11.5-16 kg for normal-weight women [BMI 18.5-24.9]; 7-11 kg for overweight women [BMI 25-29.9]; and 5-9 kg for obese women [BMI ≥30]) and maternal and infant outcomes.

**DATA SOURCES AND STUDY SELECTION** Search of EMBASE, Evidence-Based Medicine Reviews, MEDLINE, and MEDLINE In-Process between January 1, 1999, and February 7, 2017, for observational studies stratified by prepregnancy BMI category and total gestational weight gain.

**DATA EXTRACTION AND SYNTHESIS** Data were extracted by 2 independent reviewers. Odds ratios (ORs) and absolute risk differences (ARDs) per live birth were calculated using a random-effects model based on a subset of studies with available data.

**MAIN OUTCOMES AND MEASURES** Primary outcomes were small for gestational age (SGA), preterm birth, and large for gestational age (LGA). Secondary outcomes were macrosomia, cesarean delivery, and gestational diabetes mellitus.

**RESULTS** Of 5354 identified studies, 23 (n = 1309 136 women) met inclusion criteria. Gestational weight gain was below or above guidelines in 23% and 47% of pregnancies, respectively. Gestational weight gain below the recommendations was associated with higher risk of SGA (OR, 1.53 [95% CI, 1.44-1.64]; ARD, 5% [95% CI, 4%-6%]) and preterm birth (OR, 1.70 [1.32-2.20]; ARD, 5% [3%-8%]) and lower risk of LGA (OR, 0.59 [0.55-0.64]; ARD, -2% [-10% to -6%]) and macrosomia (OR, 0.60 [0.52-0.68]; ARD, -2% [-3% to -1%]); cesarean delivery showed no significant difference (OR, 0.98 [0.96-1.02]; ARD, 0% [-2% to 1%]). Gestational weight gain above the recommendations was associated with lower risk of SGA (OR, 0.66 [0.63-0.69]; ARD, -3% [-4% to -2%]) and preterm birth (OR, 0.77 [0.69-0.86]; ARD, -2% [-2% to -1%]) and higher risk of LGA (OR, 1.85 [1.76-1.95]; ARD, 4% [2%-5%]), macrosomia (OR, 1.95 [1.79-2.11]; ARD, 6% [4%-9%]), and cesarean delivery (OR, 1.30 [1.25-1.35]; ARD, 4% [3%-6%]). Gestational diabetes mellitus could not be evaluated because of the nature of available data.

**CONCLUSIONS AND RELEVANCE** In this systematic review and meta-analysis of more than 1 million pregnant women, 47% had gestational weight gain greater than IOM recommendations and 23% had gestational weight gain less than IOM recommendations. Gestational weight gain greater than or less than guideline recommendations, compared with weight gain within recommended levels, was associated with higher risk of adverse maternal and infant outcomes.

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Excessive and insufficient gestational weight gain have been associated with adverse pregnancy outcomes, including small for gestational age (SGA), large for gestational age (LGA), macrosomia, cesarean delivery, gestational diabetes mellitus (GDM), preeclampsia, postpartum weight retention, and offspring obesity.<sup>1-4</sup> The Institute of Medicine (IOM; now known as the National Academy of Medicine) recommendations regarding gestational weight gain were developed in 1990 to guide clinical practice.<sup>5</sup> These aimed to reduce the incidence of low-birth-weight babies and were based on a 1980 National Natality Survey of a largely white population. The updated IOM guidelines in 2009<sup>6</sup> incorporated World Health Organization (WHO) categories of maternal body mass index (BMI; calculated as weight in kilograms divided by height in meters squared; BMI for underweight, <18.5; normal weight, 18.5-24.9; overweight, 25-29.9; and obese, ≥30)<sup>7</sup> and recommended less gestational weight gain for obese women (Table 1). The 2009 guidelines identified maternal and infant relationships with gestational weight gain but were based on lower general population BMI with limited ethnic diversity. The 2009 IOM guidelines are endorsed by the American College of Obstetricians and Gynecologists, although they are not universally implemented.<sup>8</sup>

The prevalence of obesity and excess gestational weight gain are increasing. The US female obesity prevalence was 40% in 2013-2014.<sup>9</sup> More than 50% of obese pregnant women gained gestational weight greater than the IOM gestational weight gain recommendations in a US study that collected data from 2002 through 2008.<sup>10</sup>

The purpose of this review and meta-analysis was to compare gestational weight gain with IOM guidelines from diverse international cohorts and to evaluate associations between gestational weight gain above and below guidelines with maternal and infant outcomes.

## Methods

This systematic review, meta-analysis, and metaregression was prospectively registered with PROSPERO International Prospective Register of Systematic Reviews (PROSPERO identifier CRD42015023325).

### Search Strategy

A systematic search string of relevant terms was developed (eAppendix 1 in the Supplement). Searched databases in Ovid included EMBASE, all Evidence-Based Medicine Reviews, MEDLINE, and MEDLINE In-Process from January 1, 1999, to January 28, 2016 (Figure 1). The search was limited to articles from 1999 onward to represent more current populations. The search was later updated to February 7, 2017. Of 7 newly identified studies, 4 were included in the analyses. Three studies were excluded because the data were not in the required format, and there was insufficient time to obtain data from the authors. Bibliographies of included studies were reviewed to identify additional studies. Details of the search strategy and data extraction are shown in eAppendix 2 in the Supplement.

## Key Points

**Question** What is the association between gestational weight gain above or below the Institute of Medicine guidelines and maternal and infant outcomes?

**Findings** In this systematic review and meta-analysis of 1 309 136 pregnancies, gestational weight gain below recommendations (in 23% of women) was associated with higher risk of small for gestational age (odds ratio [OR], 1.53) and preterm birth (OR, 1.70) and lower risk of large for gestational age (OR, 0.59) and macrosomia (OR, 0.60). Gestational weight gain above recommendations (47%) was associated with lower risk of small for gestational age (OR, 0.66) and preterm birth (OR, 0.77) and higher risk of large for gestational age (OR, 1.85), macrosomia (OR, 1.95), and cesarean delivery (OR, 1.30).

**Meaning** Gestational weight gain below or above the Institute of Medicine guidelines was associated with higher risk of some adverse maternal and infant outcomes.

## Study Eligibility Criteria

Observational studies published in English and assessing singleton pregnancies in women aged 18 years or older were included. Study sample sizes larger than 500 women were required to identify outcomes present across the BMI categories. We postulated that small studies would have insufficient sample size to detect outcomes within each BMI group. Studies were included if they presented data examining women by prepregnancy BMI category, stratified by the total gestational weight gain. Studies that categorized by mean weight gain per week were excluded. Only studies presenting odds ratios (ORs) stratified by maternal BMI and gestational weight gain were included. Studies that simultaneously adjusted for categories of BMI and gestational weight gain to estimate the independent associations of weight change with outcomes were excluded because the aim of this review was to assess the association of gestational weight gain (specific for each BMI category) and outcomes.

Studies meeting these criteria used different BMI categories (eg, Metropolitan Life Insurance Tables, WHO classifications, or Chinese classifications<sup>11</sup> [BMI for underweight, <18.5; normal weight, 18.5-23.9; overweight, 24-28; and obese, ≥28]) and gestational weight gain categories (eg, 1990 IOM, 2009 IOM, population-specific, or study-specific categories) to classify participants. Additionally, some studies used a reference of normal gestational weight gain within each BMI group, whereas others used a reference of normal-weight women with normal weight gain.

In this review, BMI was defined by WHO categories and/or Chinese BMI categories. Gestational weight gain was defined by 2009 IOM criteria; thus, authors of identified studies were contacted to reanalyze data using these categories. The ORs were calculated using recommended gestational weight gain within each BMI category as the reference.

Gestational weight gain was defined as the difference between the final weight and the prepregnancy weight and was classified as below, within, or above the 2009 IOM guidelines. The prepregnancy weight was either self-reported (which correlates well with measured weight<sup>12,13</sup>) or measured at first antenatal visits. Final pregnancy weight was measured at the

Table 1. Recommendations for Gestational Weight Gain During Pregnancy<sup>a</sup>

Recommendation	Prepregnancy Weight			
	Underweight	Normal Weight	Overweight	Obese
BMI	<18.5	18.5-24.9	25-29.9	≥30
Total weight gain range, kg	12.5-18	11.5-16	7-11.5	5-9
Total weight gain range, lbs	28-40	25-35	15-25	11-20

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

<sup>a</sup> Adapted from 2009 Institute of Medicine guidelines.<sup>6</sup>

last antenatal visit or the time of delivery or was self-reported within 1 year of delivery.

Primary outcomes were the following: (1) SGA, indicated by birth weight less than the 10th percentile for gestational age; (2) preterm birth, indicated by spontaneous birth before 37 weeks' gestation; and (3) LGA, indicated by birth weight greater than the 90th percentile for gestational age. Secondary outcomes were the following: (1) macrosomia, indicated by birth weight greater than 4000 g; (2) cesarean delivery; and (3) GDM. Outcomes were selected based on the original IOM studies,<sup>6</sup> and end points were determined on a 2-round Delphi survey of experienced clinicians that was used to rank clinically important outcomes in a meta-analysis of lifestyle interventions to reduce weight gain in pregnancy.<sup>14</sup>

### Risk of Bias Appraisal

Two authors assessed risk of bias (R.F.G. and S.K.A.). Discrepancies were resolved by consensus in discussion with a third reviewer (M.M.). Methodological quality of included studies was assessed using the Monash Centre for Health Research and Implementation evidence synthesis appraisal assessment tool.<sup>15,16</sup> Individual quality items were assessed using a descriptive approach including exposure and outcome measures, reporting bias, confounding, and conflict of interest. Each study was classified as low, medium, or high risk of bias.

### Data Synthesis Strategy

Findings were synthesized by target population characteristics, study type, and outcome. Outcome measures were produced for each study by calculating ORs and 95% confidence intervals, using recommended gestational weight gain within each BMI category as the reference. When 2 or more studies assessed the same outcome, results were pooled using both fixed- and random-effects meta-analysis. There were no significant differences between fixed- and random-effects analyses. Random effects are presented given heterogeneity among studies. Extracted pooled ORs for individual outcomes were combined to construct summary pooled ORs. Crude data were used where possible, given variable control for confounding factors. However, some articles presented adjusted ORs only.<sup>17-24</sup> Absolute risk differences (ARDs) per live birth were calculated from event rates (available for a subset of studies) using random-effects meta-analysis.

Heterogeneity was assessed using the  $I^2$  statistic, where  $I^2 > 50\%$  indicated substantial heterogeneity.<sup>25</sup> Metaregression was performed to investigate sources of heterogeneity (percentage of smokers during pregnancy, mean age, and percentage of nulliparous women). Race/ethnicity data were not available for the metaregression. Where 5 or more studies were available, publication bias was assessed using Egger test

plots.<sup>26,27</sup> Statistical significance was defined as 2-sided  $P < .05$ . Statistical analysis used Stata software version 14 (StataCorp LP).

A subgroup analysis was performed in specific population groups identified a priori (studies using Chinese or Korean BMI categories, not presented herein). Obesity subclasses were included after reviewing studies that stratified by obesity class. Tests for trend based on the Cochran-Armitage test in Stata were used to assess trends in this subgroup analysis.

## Results

### Study Selection

Of 5874 studies identified by the initial search, 302 were selected for full-text review; 261 of these were excluded, leaving 41 (Figure 1). These studies grouped women by prepregnancy BMI category, stratified by total gestational weight gain. One study<sup>28</sup> did not meet inclusion criteria as published; however, prior collaboration had made data available in the required format. Of 41 identified studies, 18 were excluded because data could not be obtained in the required format. Of these 18 studies, authors of 15 were contacted and unable to reanalyze and authors of 3 were not contacted from the updated search because of insufficient time prior to publication (eAppendix 2 in the Supplement). Overall, 23 cohort studies<sup>17-24,28-42</sup> were included, involving 1309 136 women. Of these 23 studies, 7 were included without contacting the authors because data were in the required format. Of 16 authors contacted, 13 reanalyzed data and were included; 3 provided additional information, thereby avoiding reanalysis.

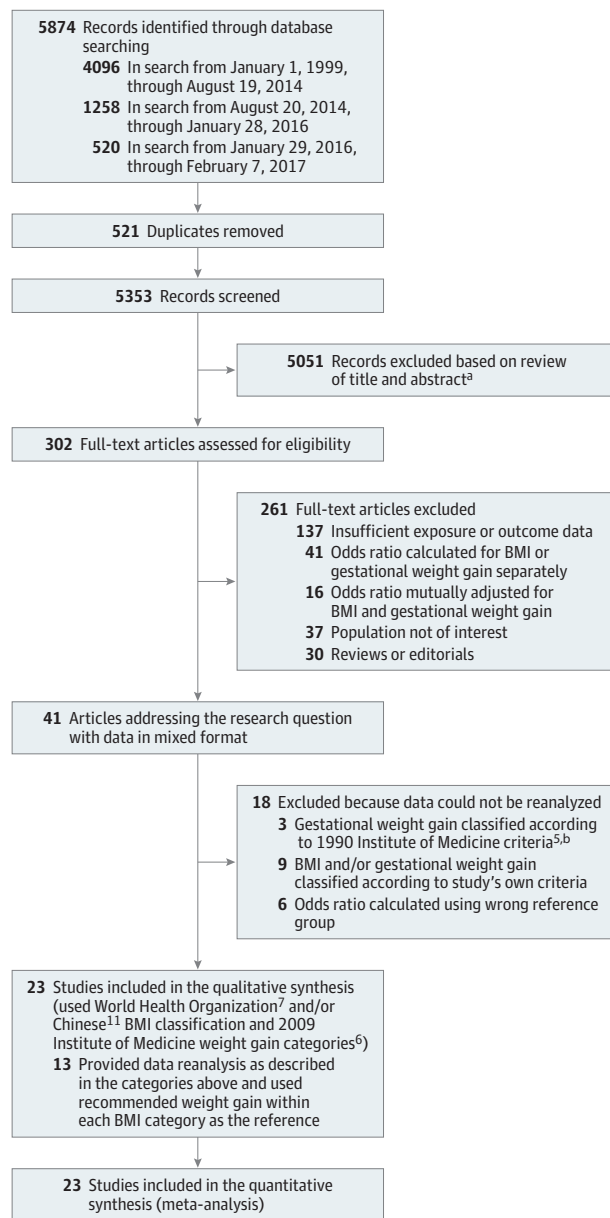
### Study Characteristics

Table 2 and Table 3 list characteristics of the studies (descriptive characteristics are shown in eTable 1 in the Supplement). Eighteen studies were retrospective, and 5 were prospective.<sup>20,29,32,33,42</sup> Ten were from the United States,<sup>18-20,23,28,31,35,38,40,41</sup> 8 were from Asia (4 from China,<sup>21,29,32,36</sup> 2 from Korea,<sup>34,39</sup> and 1 each from Taiwan<sup>24</sup> and Japan<sup>22</sup>), and 5 were from Europe (1 each from Norway,<sup>33</sup> Belgium,<sup>30</sup> Italy,<sup>37</sup> Denmark,<sup>42</sup> and Sweden<sup>17</sup>). Sample sizes ranged from 1034 to 570 672 women.

Underweight women composed 7% ( $n = 94\ 399$ ); normal-weight women, 55% ( $n = 720\ 456$ ); overweight women, 18% ( $n = 235\ 295$ ); and obese women, 20% ( $n = 258\ 986$ ). Gestational weight gain was below, within, or above guidelines in 23% ( $n = 300\ 723$ ), 30% ( $n = 387\ 409$ ), and 47% ( $n = 621\ 004$ ), respectively.

Figure 2 shows pooled ORs for primary and secondary outcomes. eFigure 1 in the Supplement shows pooled ORs for individual outcomes. eTable 2 in the Supplement reports

Figure 1. Flow Diagram of Study Selection Process



<sup>a</sup> Exact breakdown for exclusion not documented.

<sup>b</sup> The Institute of Medicine 1990 guidelines differ from the 2009 guidelines. In the 1990 guidelines, the recommended weight gain range was 12.5 to 18 kg for women with a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) less than 19.8; 11.5 to 16 kg for women with a BMI of 19.8 to 26.0; 7 to 11.5 kg for women with a BMI between 26.0 and 29.0; and at least 6.8 kg for women with a BMI higher than 29.0.

event rates. eTable 3 and eFigure 2 in the Supplement report ARDs and P values. The ARDs are expressed as percentage difference per live birth.

### Primary Outcomes

#### Small for Gestational Age

Eleven studies assessed SGA, defined as birth weight less than the 10th percentile for gestational age in 5 studies.<sup>22,31,36,39,40</sup>

Four studies defined SGA by additionally accounting for sex,<sup>24,28,33,38</sup> 1 for sex and race/ethnicity,<sup>41</sup> and another for sex, race, and parity.<sup>23</sup>

Across BMI categories, gestational weight gain below guidelines was associated with higher risk for SGA than gestational weight gain within guidelines (OR, 1.53 [95% CI, 1.44 to 1.64];  $I^2 = 82.8\%$ ; ARD, 5% [95% CI, 4% to 6%]). This association was greatest in lower prepregnancy BMI (underweight: OR, 1.89 [95% CI, 1.67 to 2.14]; ARD, 8% [95% CI, 6% to 11%]; normal weight: OR, 1.63 [95% CI, 1.54 to 1.71]; ARD, 5% [95% CI, 4% to 6%]; overweight: OR, 1.34 [95% CI, 1.24 to 1.44]; ARD, 3% [95% CI, 3% to 4%]; and obese: OR, 1.24 [95% CI, 1.06 to 1.45]; ARD, 2% [95% CI, 2% to 3%]).

Compared with gestational weight gain within guidelines, gain above guidelines was associated with lower risk for SGA (OR, 0.66 [95% CI, 0.63 to 0.69];  $I^2 = 56\%$ ; ARD, -3% [95% CI, -4% to -2%]). The association was similar across BMI categories (underweight: OR, 0.62 [95% CI, 0.53 to 0.72]; ARD, -6% [95% CI, -8% to -3%]; normal weight: OR, 0.65 [95% CI, 0.62 to 0.68]; ARD, -2% [95% CI, -3% to -1%]; overweight: OR, 0.65 [95% CI, 0.59 to 0.71]; ARD, -3% [95% CI, -4% to -2%]; and obese: OR, 0.72 [95% CI, 0.65 to 0.80]; ARD, -2% [95% CI, -3% to -1%]).

#### Preterm Birth

Four studies assessed preterm birth (<37 weeks' gestation). Of these, 3 did not specify whether the preterm birth was spontaneous or induced<sup>28,31,36</sup> and 1 specified spontaneous and induced combined.<sup>22</sup>

Compared with gestational weight gain within guidelines, weight gain below guidelines was associated with higher risk for preterm birth (OR, 1.70 [95% CI, 1.32 to 2.20];  $I^2 = 97.3\%$ ; ARD, 5% [95% CI, 3% to 8%]). This association was greatest with lower BMI (underweight: OR, 2.41 [95% CI, 1.01 to 5.73]; ARD, 8% [95% CI, 1% to 15%]; normal weight: OR, 1.96 [95% CI, 1.17 to 3.29]; ARD, 6% [95% CI, 0% to 11%]; overweight: OR, 1.55 [95% CI, 1.10 to 2.19]; ARD, 4% [95% CI, -1% to 9%]; and obese: OR, 1.20 [95% CI, 1.03 to 1.40]; ARD, 3% [95% CI, 1% to 5%]).

Gestational weight gain above guidelines was associated with lower risk for preterm birth (OR, 0.77 [95% CI, 0.69 to 0.86];  $I^2 = 78.7\%$ ; ARD, -2% [95% CI, -2% to -1%]). This association was significant for normal-weight and overweight women (underweight: OR, 0.80 [95% CI, 0.50 to 1.28]; ARD, -1% [95% CI, -3% to 0%]; normal weight: OR, 0.76 [95% CI, 0.59 to 0.97]; ARD, -1% [95% CI, -2% to 0%]; overweight: OR, 0.70 [95% CI, 0.53 to 0.93]; ARD, -3% [95% CI, -5% to -1%]; and obese: OR, 0.76 [95% CI, 0.62 to 0.93]; ARD, -2% [95% CI, -5% to 2%]).

#### Large for Gestational Age

Thirteen studies assessed LGA, defined as birth weight greater than the 90th percentile for gestational age in 6 studies.<sup>22,31,34,36,39,40</sup> Four defined LGA by additionally accounting for infant sex,<sup>24,28,33,38</sup> 1 for sex and race/ethnicity,<sup>41</sup> 1 for sex, race, and parity,<sup>23</sup> and 1 for sex, parity, and study center.<sup>20</sup>

Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup>

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category <sup>b</sup>	
							Below Guidelines	Above Guidelines
Durst et al. <sup>23</sup> 2016 (United States)	2000-2014, Retrospective	5651	University of Alabama at Birmingham	SGA, LGA, cesarean delivery, macrosomia	Overweight	5651	NR	NR
Enomoto et al. <sup>22</sup> 2016 (Japan)	2013, Retrospective	97 157	Japan Society of Obstetrics and Gynecology Registry system with 280 participating hospitals	SGA	Underweight	17724	2032/13 529 (15.0)	286/3783 (7.6)
					Normal weight	69 126	4575/44 189 (10.4)	1254/20 835 (6.0)
					Overweight	7502	275/2990 (9.2)	179/2810 (6.4)
					Obese	2805	112/1297 (8.6)	48/853 (5.6)
				LGA	Underweight	17724	518/13 529 (3.8)	388/3783 (10.3)
					Normal weight	69 126	3322/44 189 (7.5)	2754/20 835 (13.2)
					Overweight	7502	363/2990 (12.1)	489/2810 (17.4)
					Obese	2805	213/1297 (16.4)	206/853 (24.2)
				Preterm birth	Underweight	17724	1979/13 529 (14.6)	167/3783 (4.4)
					Normal weight	69 126	5891/44 189 (13.3)	994/20 835 (4.8)
					Overweight	7502	508/2990 (17.0)	240/2810 (8.5)
					Obese	2805	199/1297 (15.3)	95/853 (11.1)
				Cesarean delivery	Underweight	17724	3174/13 539 (23.4)	739/3783 (19.5)
					Normal weight	69 126	12 446/44 189 (28.2)	5062/20 835 (24.3)
					Overweight	7502	1151/2990 (38.5)	991/2810 (35.3)
					Obese	2805	542/1297 (41.8)	367/853 (43.0)
				Macrosomia	Underweight	17724	16/13 529 (0.1)	20/3783 (0.5)
					Normal weight	69 126	149/44 189 (0.3)	214/20 835 (1.0)
					Overweight	7502	34/2990 (1.1)	35/2810 (1.3)
					Obese	2805	21/1297 (1.6)	37/853 (4.3)

(continued)



Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup> (continued)

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category <sup>b</sup>	Above Guidelines	
							Below Guidelines	Within Guidelines	
Hung and Hsieh, <sup>24</sup> 2016 (Taiwan)	2009-2015, Retrospective	10 973	Taipei Chang Gung Memorial Hospital	SGA	Underweight	1556	117/691 (16.9)	63/718 (8.8)	10/147 (6.8)
					Normal weight	8247	199/2304 (8.7)	233/3827 (6.1)	90/2116 (4.3)
					Overweight + obese	1170	121/161 (75.2)	23/403 (5.7)	24/606 (4.0)
					Underweight	1556	8/691 (1.2)	34/718 (4.7)	18/147 (12.2)
					Normal weight	8247	103/2304 (4.5)	306/3827 (8.0)	274/2116 (12.9)
					Overweight + obese	1170	18/161 (11.2)	61/403 (15.1)	107/606 (17.7)
Xiong et al., <sup>29</sup> 2016 (China) <sup>c</sup>	2012-2013, Prospective	57 891	Hospitals and community centers	Cesarean delivery	Underweight	10 121	143/691 (20.7)	151/718 (21.0)	54/147 (36.7)
					Normal weight	8247	412/2304 (17.9)	882/3827 (23.1)	644/2116 (30.4)
					Overweight + obese	1170	34/161 (21.1)	89/403 (22.1)	197/606 (32.5)
					Underweight	1556	3/691 (0.4)	4/718 (0.6)	5/147 (3.4)
					Normal weight	8247	17/2304 (0.7)	63/3827 (1.7)	74/2116 (3.5)
					Overweight + obese	1170	6/161 (3.7)	9/403 (2.2)	30/606 (5.0)
Shin and Song, <sup>31</sup> 2015 (United States)	2004-2011, Retrospective	219 868	Pregnancy Risk Assessment Monitoring System	SGA, preterm birth, LGA	Underweight	11 865	NR	NR	NR
					Normal weight	1 135 523	NR	NR	NR
					Overweight	51 517	NR	NR	NR
					Obese	42 963	NR	NR	NR
					Underweight	0	NR	NR	NR
					Normal weight	13 776	NR	NR	NR
Wen and Lv, <sup>21</sup> 2015 (China) <sup>c</sup>	2009-2013, Retrospective	13 776	Jishuitan Hospital	Preterm birth	Underweight	0	NR	NR	NR
					Normal weight	13 776	NR	NR	NR
					Overweight	0	NR	NR	NR
Yang et al., <sup>32</sup> 2015 (China) <sup>c</sup>	2011-2013, Prospective	85 765	Wuhan Women and Children Health Care Center	Macrosomia	Underweight	14 477	13/158 (8.2)	93/4723 (2.0)	449/7139 (6.3)
					Normal weight	65 536	361/11627 (3.1)	623/14 103 (4.4)	3387/33 647 (10.1)
					Overweight + obese	5752	35/573 (6.1)	79/982 (8.0)	551/3299 (16.7)
Badon et al., <sup>20</sup> 2014 (United States)	2000-2006, Prospective	5297	North American Field Centers, HAPO Study	LGA	Underweight	179	NR	NR	NR
					Normal weight	3013	NR	NR	NR
					Overweight	1322	NR	NR	NR
					Obese	783			

(continued)

Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup> (continued)

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category <sup>b</sup>		
							Below Guidelines	Within Guidelines	Above Guidelines
Chihara et al, <sup>19</sup> 2014 (United States)	2003-2005, Retrospective	19 130	Hawaii's Special Supplemental Nutrition Program for Women, Infants, and Children	Macrosomia	Underweight	1153			
					Normal weight	9291			
					Overweight	4391	NR	NR	NR
					Obese	4295			
Haugen et al, <sup>33</sup> 2014 (Norway) <sup>d</sup>	1999-2008, Prospective	56 082	Norwegian Mother and Child Cohort Study	SGA	Underweight	1610	143/457 (31.3)	144/751 (19.2)	37/402 (9.2)
					Normal weight	37 315	1327/7798 (17.0)	1662/14 904 (11.2)	1042/14 613 (7.1)
					Overweight	12 181	156/1037 (15.0)	281/2485 (11.3)	557/8659 (6.4)
					Obese	4976	97/878 (11.1)	99/1054 (9.4)	204/3044 (6.7)
					Underweight	1610	4/457 (0.9)	21/751 (2.8)	30/402 (7.5)
					Normal weight	37 315	250/7798 (3.2)	914/14 904 (6.1)	1796/14 613 (12.3)
					Overweight	12 181	62/1037 (6.0)	212/2485 (8.5)	1370/8659 (15.8)
					Obese	4976	90/878 (10.3)	154/1054 (14.6)	676/3044 (22.2)
					Underweight	1610	44/457 (9.6)	71/751 (9.5)	47/402 (11.7)
					Normal weight	37 315	726/7798 (9.3)	1526/14 904 (10.2)	1836/14 613 (12.6)
Lee et al, <sup>34</sup> 2014 (Korea) <sup>e</sup>	2010-2012, Retrospective	16 297	Single medical center	LGA	Underweight	12 181	137/1037 (13.2)	327/2485 (13.2)	1439/8659 (16.6)
					Overweight	4976	173/878 (19.7)	227/1054 (21.5)	703/3044 (23.1)
					Obese	1610	15/457 (3.3)	68/751 (9.1)	62/402 (15.4)
					Underweight	37 315	782/7798 (10.0)	2573/14 904 (17.3)	4014/14 613 (27.5)
					Normal weight	12 181	160/1037 (15.4)	530/2485 (21.3)	2472/8659 (28.5)
					Overweight	4976	206/878 (23.5)	300/1054 (28.5)	1822/3044 (59.9)
					Obese	2655			
					Underweight	12 250			
					Normal weight	1191	NR	NR	NR
					Overweight	201			

(continued)

Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup> (continued)

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category <sup>b</sup>	Above Guidelines	
							Below Guidelines	Within Guidelines	
Black et al, <sup>28</sup> 2013 (United States)	2005-2010, Retrospective	9835	Kaiser Permanente Southern California	SGA	Underweight	179	11/55 (20.0)	9/75 (12.0)	3/51 (5.9)
					Normal weight	3805	158/1031 (15.3)	125/1388 (9.0)	114/1386 (8.2)
					Overweight	3116	58/424 (13.7)	70/815 (8.6)	119/1877 (6.3)
					Obese	2735	57/608 (9.4)	54/648 (8.3)	80/1479 (5.4)
					Underweight	179	0/55	4/73 (5.5)	2/51 (3.9)
					Normal weight	3805	2/1031 (0.2)	46/1388 (3.3)	113/1386 (8.2)
				Preterm birth	Overweight	3116	15/424 (3.5)	39/815 (4.8)	205/1877 (10.9)
					Obese	2735	32/608 (5.3)	52/648 (8.0)	235/1479 (15.9)
					Underweight	179	10/55 (18.2)	2/73 (2.7)	1/51 (2.0)
					Normal weight	3805	127/1031 (12.3)	77/1388 (5.5)	45/1386 (3.2)
					Overweight	3116	54/424 (12.7)	76/815 (9.3)	87/1877 (4.6)
					Obese	2735	53/608 (8.7)	49/648 (7.6)	80/1479 (5.4)
				Cesarean delivery	Underweight	179	6/55 (10.9)	14/73 (19.2)	13/51 (25.5)
					Normal weight	3805	219/1031 (21.2)	293/1388 (21.1)	339/1386 (24.5)
					Overweight	3116	105/424 (24.8)	200/815 (24.5)	589/1877 (31.4)
					Obese	2735	184/608 (30.3)	216/648 (33.3)	575/1479 (38.9)
Underweight	179	0/55	5/73 (6.8)		3/51 (5.9)				
Normal weight	3805	28/1031 (2.7)	63/1388 (4.5)		148/1386 (10.7)				
Macrosomia	Overweight	3116	17/424 (4.0)	46/815 (5.6)	225/1877 (12.0)				
	Obese	2735	38/608 (6.3)	65/648 (10.0)	265/1479 (17.9)				

(continued)



Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup> (continued)

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category <sup>b</sup>		
							Below Guidelines	Within Guidelines	Above Guidelines
Li et al. <sup>36</sup> 2013 (China) <sup>f</sup>	2009-2011, Retrospective	33 973	Tianjin Women's and Children's Health Center	SGA	Underweight	3732	151/733 (20.6)	323/1820 (17.7)	114/1179 (9.7)
					Normal weight	24 262	383/2777 (13.8)	817/9347 (8.7)	935/12 138 (7.7)
					Overweight	4998	6/86 (7.0)	54/665 (8.1)	277/4247 (6.5)
					Obese	981	1/16 (6.3)	6/54 (11.1)	44/911 (4.8)
					Underweight	3732	15/733 (2.0)	49/1820 (2.7)	77/1179 (6.5)
					Normal weight	24 262	15/2777 (0.5)	625/9347 (6.7)	1549/12 138 (12.8)
				LGA	Overweight	4998	32/86 (37.2)	86/665 (12.9)	741/4247 (17.4)
					Obese	981	4/16 (25.0)	10/54 (18.5)	228/911 (25.0)
					Underweight	3732	31/733 (4.2)	45/1820 (2.5)	22/1179 (1.9)
					Normal weight	24 262	142/2777 (5.1)	322/9347 (3.4)	248/12 138 (2.0)
					Overweight	4998	5/86 (5.8)	37/665 (5.6)	134/4247 (3.2)
					Obese	981	1/16 (6.3)	2/54 (3.7)	61/911 (6.7)
				Cesarean delivery	Underweight	3732	375/733 (51.2)	945/1820 (51.9)	723/1179 (61.3)
					Normal weight	24 262	1677/2777 (60.4)	5645/9347 (60.4)	8208/12 138 (67.6)
					Overweight	4998	62/86 (72.1)	480/665 (72.2)	3348/4247 (78.8)
					Obese	981	11/16 (68.8)	50/54 (92.6)	774/911 (85.0)
					Underweight	3732	141/733 (19.2)	53/1820 (2.9)	751/1179 (63.7)
					Normal weight	24 262	145/2777 (5.2)	581/9347 (6.2)	1464/12 138 (12.1)
				Macrosomia	Overweight	4998	6/86 (7.0)	71/665 (10.7)	687/4247 (16.2)
					Obese	981	4/16 (25.0)	9/54 (16.7)	203/911 (22.3)
					Underweight	89			
					Normal weight	1468			
					Overweight	493	NR	NR	NR
					Obese	175			
Di Benedetto et al. <sup>37</sup> 2012 (Italy)	2004-2009, Retrospective	2225	University hospital	Macrosomia, cesarean delivery	Underweight	89			
					Normal weight	1468			
					Overweight	493	NR	NR	NR
					Obese	175			
					Underweight	427			
					Normal weight	5707			
Simas et al. <sup>38</sup> 2012 (United States)	2006-2010, Retrospective	11 203	University hospital	SGA, LGA	Overweight	2756	NR	NR	NR
					Obese	2313			
					Underweight	385			
					Normal weight	1666			
					Overweight	221	NR	NR	NR
					Obese	39			
Park et al. <sup>39</sup> 2011 (Korea) <sup>e</sup>	2005-2007, Retrospective	2311	University hospital	SGA, LGA, macrosomia, cesarean delivery	Underweight	385			
					Normal weight	1666			
					Overweight	221	NR	NR	NR
					Obese	39			
					Underweight	385			
					Normal weight	1666			

(continued)

Table 2. Characteristics of 19 Studies That Stratified by Prepregnancy BMI Categories<sup>a</sup> (continued)

Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy BMI Category	Women, No.	No. of Events/No. of Live Births (%)	Below Guidelines	Within Guidelines	Above Guidelines
Park et al, <sup>40</sup> 2011 (United States)	2004-2007, Retrospective	560 672	Florida birth certificate data	SGA	Underweight	28 119	1815/11 676 (15.5)	1987/7555 (26.3)	1815/11 676 (15.5)	865/8888 (9.7)
					Normal weight	305 295	10 324/103 613 (10.0)	11 213/71 025 (15.8)	10 324/103 613 (10.0)	8460/130 657 (6.5)
					Overweight	135 668	3033/30731 (9.9)	2167/16 723 (13.0)	3033/30731 (9.9)	5516/88 214 (6.3)
					Obese	101 590	1501/17 350 (8.7)	2157/19 740 (10.9)	1501/17 350 (8.7)	4147/64 500 (6.4)
Vesco et al, <sup>41</sup> 2011 (United States)	2000-2005, Retrospective	2080	Kaiser Permanente group practice	SGA, LGA, macrosomia	Underweight	0	NR	NR	NR	NR
					Normal weight	0	NR	NR	NR	NR
					Overweight	0	NR	NR	NR	NR
					Obese	2080	851/16 723 (5.1)	84/7555 (1.1)	366/11 676 (3.1)	669/8888 (7.5)
Rode et al, <sup>42</sup> 2007 (Denmark)	1996-1998, Prospective	2248	University hospital	Macrosomia	Underweight	128	2329/30 731 (7.6)	1657/19 740 (83.9)	2329/30 731 (7.6)	12 417/88 214 (14.1)
					Normal weight	1654	1906/17 350 (11.0)	2479/71 025 (3.5)	6183/103 613 (6.0)	15 146/130 657 (11.6)
					Overweight	349	NR	NR	NR	NR
					Obese	117	NR	NR	NR	NR

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HAPO, Hyperglycemia and Adverse Pregnancy Outcome; LGA, large for gestational age; NR, not reported; SGA, small for gestational age.

<sup>a</sup> Unless indicated otherwise, prepregnancy categories of BMI categories were according to World Health Organization (WHO) categories as follows: BMI for underweight, less than 18.5; normal weight, 18.5 to 24.9; overweight, 25 to 29.9; and obese, 30 or higher.

<sup>b</sup> Refer to eFigure 1 in the Supplement for odds ratios.

<sup>c</sup> Data according to Chinese BMI categories only (BMI for underweight, <18.5; normal weight, 18.5-23.9; overweight, 24-28; and obese, ≥ 28).

<sup>d</sup> Sample size changed when additional data were provided.

<sup>e</sup> Data according to both Korean BMI categories (BMI for underweight, <18.5; normal weight, 18.5-22.9; overweight, 23-25; and obese ≥ 25) and WHO BMI categories (WHO reported herein).

<sup>f</sup> Data according to both Chinese and WHO BMI categories (WHO reported herein).

Table 3. Characteristics of 4 Studies That Stratified by Prepregnancy Obesity Class

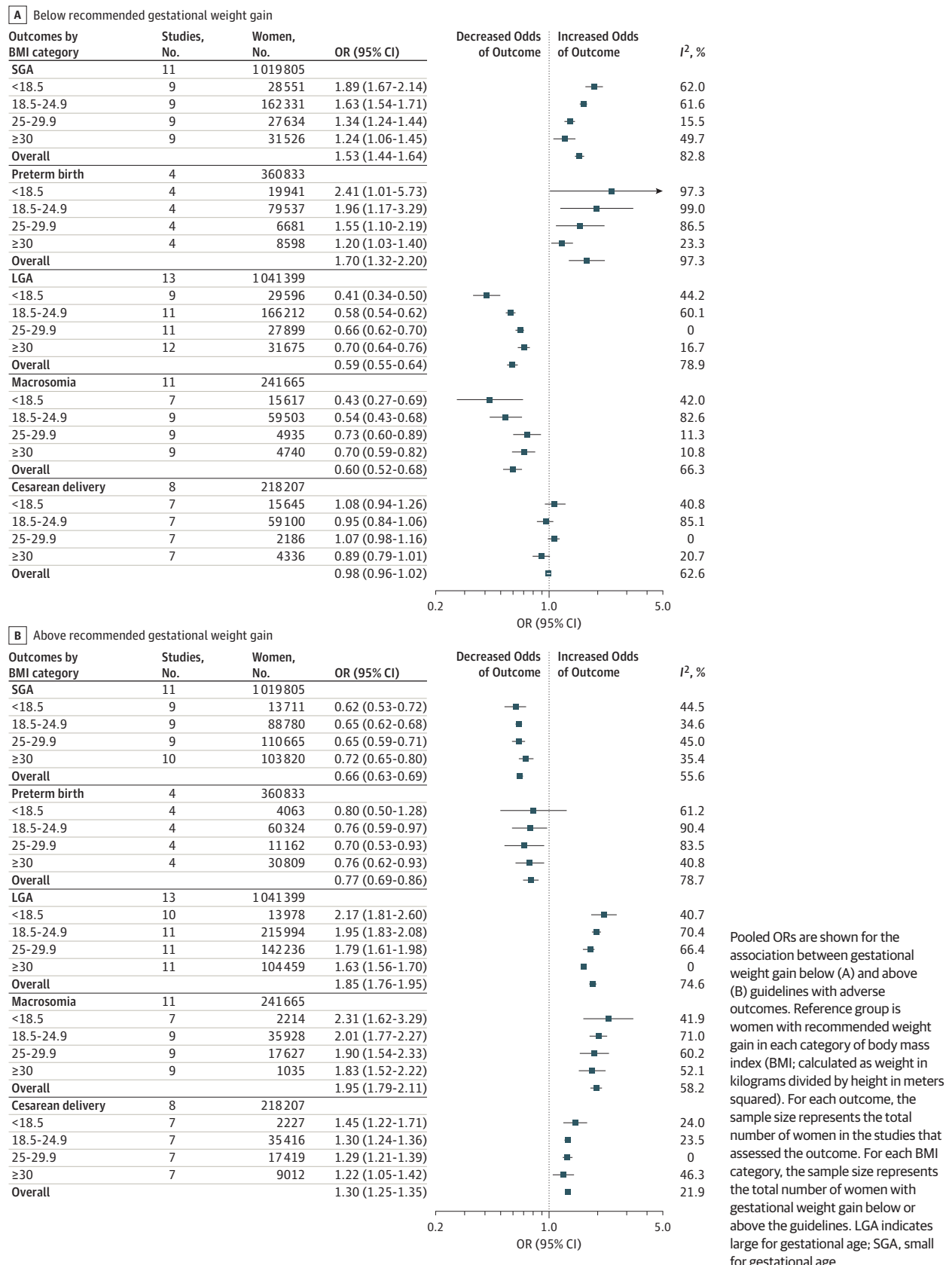
Source	Study Period, Design	Total No. of Women	Setting	Outcomes	Prepregnancy Obesity Class <sup>a</sup>	Women, No.	No. of Events/No. of Live Births (%) by Gestational Weight Gain Category			
							Loss	Gain Below Guidelines	Gain Within Guidelines	Gain Above Guidelines
Bogaerts et al., <sup>30</sup> 2015 (Belgium)	2009-2011, Retrospective	18 053	Flemish Centre for the Study of Perinatal Epidemiology	SGA	1	12 994	52/420 (12.4)	164/1554 (10.6)	316/3585 (8.8)	421/7435 (5.7)
					2	3787	32/263 (12.2)	54/648 (8.3)	80/1156 (6.9)	95/1720 (5.5)
					3	1272	16/171 (9.4)	16/291 (5.5)	22/379 (5.8)	20/431 (4.6)
					1	12 994	29/420 (6.9)	152/1554 (9.8)	474/3585 (13.2)	1468/7438 (19.7)
					2	3787	28/263 (10.6)	78/648 (12.0)	189/1156 (16.3)	409/1720 (23.8)
					3	1272	19/171 (11.1)	59/291 (20.3)	97/379 (25.6)	122/431 (28.3)
					1	12 994	101/420 (24.0)	353/1554 (22.7)	844/3585 (23.5)	2020/7435 (27.2)
					2	3787	65/263 (24.7)	153/648 (23.6)	344/1156 (29.8)	561/1720 (32.6)
					3	1272	61/171 (35.7)	98/291 (33.7)	132/379 (34.8)	168/431 (39.0)
Swank et al., <sup>35</sup> 2014 (United States)	2007, Retrospective	1034	California birth certificate data	Macrosomia	1	12 994	29/420 (6.9)	155/1554 (10.0)	435/3585 (12.1)	1384/7435 (18.6)
					2	3787	23/263 (8.7)	76/648 (11.7)	165/1156 (14.3)	366/1720 (21.3)
					3	1272	11/171 (6.4)	49/291 (16.8)	89/379 (23.5)	100/431 (23.2)
					1	1034	96/170 (56.5)	134/226 (59.3)	139/243 (57.2)	253/395 (64.1)
					2	1034	14/170 (8.2)	35/226 (15.5)	52/243 (21.4)	104/395 (26.3)
					1	12 005	66/406 (16.3)	135/1352 (10.0)	187/1931 (9.7)	549/8316 (6.6)
					2	5320	57/354 (16.1)	100/918 (10.9)	85/1018 (8.3)	193/3030 (6.4)
					3	3695	57/486 (11.7)	72/748 (10.4)	51/664 (7.7)	119/1797 (6.6)
					1	12 005	13/406 (3.2)	76/1352 (5.6)	119/1931 (6.2)	1029/8316 (12.4)
Blomberg, <sup>17</sup> 2011 (Sweden)	1993-2008, Retrospective	46 595	Swedish Medical Birth Register	LGA	1	12 005	17/354 (4.8)	67/918 (7.3)	101/1018 (9.9)	435/3030 (14.4)
					2	5320	31/486 (6.4)	77/748 (10.3)	85/664 (12.8)	315/1797 (17.5)
					3	3695	64/406 (15.8)	292/1352 (21.6)	425/1931 (22.0)	1816/8316 (21.8)
					1	12 005	86/354 (24.3)	237/918 (25.8)	277/1018 (27.2)	754/3030 (24.9)
					2	5320	144/486 (29.6)	222/748 (29.7)	233/664 (35.1)	562/1797 (31.3)
					3	3695	2/406 (0.5)	7/1352 (0.5)	15/1931 (0.8)	191/8316 (2.3)
					1	5320	1/354 (0.3)	8/918 (0.9)	13/1018 (1.3)	87/3030 (2.9)
					2	3695	7/486 (1.4)	11/748 (1.5)	19/664 (2.9)	66/1797 (3.7)
					1	32 991	51/1341 (3.8)	88/3105 (2.8)	162/8807 (1.8)	232/19738 (1.2)
Kominarek et al., <sup>18</sup> 2013 (United States) <sup>b</sup>	2002-2008, Retrospective	21 020	12 Institutions (19 hospitals)	SGA	1	10 068	13/798 (1.6)	40/1466 (2.7)	58/2927 (2.0)	70/4877 (1.4)
					2	3536	19/517 (3.7)	16/616 (2.6)	17/1002 (1.7)	27/1401 (1.9)
					1	32 991	87/1341 (6.5)	228/3105 (7.3)	757/8807 (8.6)	2674/19738 (13.5)
					2	10 068	57/798 (7.1)	142/1466 (9.7)	361/2927 (12.3)	853/4877 (17.5)
					3	3536	57/517 (11.0)	88/616 (14.3)	155/1002 (15.5)	278/1401 (19.8)
					1	32 991	206/1341 (15.4)	554/3105 (17.8)	1675/8807 (19.0)	4431/19738 (22.4)
					2	10 068	135/798 (16.9)	306/1466 (20.9)	713/2927 (24.4)	1312/4877 (26.9)
					3	3536	125/517 (24.2)	148/616 (24.0)	289/1002 (28.8)	439/1401 (31.3)

Abbreviations: LGA, large for gestational age; SGA, small for gestational age.

<sup>a</sup>Class 1 indicates a body mass index (BMI), calculated as weight in kilograms divided by height in meters squared) of 30 to 34.9; class 2, BMI of 35 to 39.9; and class 3, BMI of 40 or higher.

<sup>b</sup>Sample size changed when additional data were provided, and the odds ratios were not recalculated.

Figure 2. Summary of Pooled Odds Ratios (ORs) for the Association Between Gestational Weight Gain Below and Above Guidelines With Adverse Outcomes



Gestational weight gain below guidelines was associated with lower risk of LGA than gestational weight gain within guidelines (OR, 0.59 [95% CI, 0.55 to 0.64];  $I^2 = 78.9\%$ ; ARD,  $-2\%$  [95% CI,  $-10\%$  to  $-6\%$ ]). This was significant for underweight and normal-weight women (underweight: OR, 0.41 [95% CI, 0.34 to 0.50]; ARD,  $-3\%$  [95% CI,  $-5\%$  to  $-1\%$ ]; normal weight: OR, 0.58 [95% CI, 0.54-0.62]; ARD,  $-3\%$  [95% CI,  $-4\%$  to  $-2\%$ ]; overweight: OR, 0.66 [95% CI, 0.62 to 0.70]; ARD,  $-11\%$  [95% CI,  $-33\%$  to  $10\%$ ]; and obese: OR, 0.70 [95% CI, 0.64 to 0.76]; ARD,  $13\%$  [95% CI,  $-34\%$  to  $60\%$ ]).

Gestational weight gain above guidelines was associated with higher risk of LGA (OR, 1.85 [95% CI, 1.76 to 1.95];  $I^2 = 74.6\%$ ; ARD,  $4\%$  [95% CI,  $2\%$  to  $5\%$ ]). The association increased as BMI decreased (underweight: OR, 2.17 [95% CI, 1.81 to 2.60]; ARD,  $4\%$  [95% CI,  $4\%$  to  $5\%$ ]; normal weight: OR, 1.95 [95% CI, 1.83 to 2.08]; ARD,  $6\%$  [95% CI,  $5\%$  to  $7\%$ ]; overweight: OR, 1.79 [95% CI, 1.61 to 1.98]; ARD,  $-2\%$  [95% CI,  $-14\%$  to  $9\%$ ]; and obese: OR, 1.63 [95% CI, 1.56 to 1.70]; ARD,  $7\%$  [95% CI,  $5\%$  to  $8\%$ ]).

## Secondary Outcomes

### Macrosomia

Of 11 studies assessing macrosomia, 10 defined macrosomia as birth weight greater than 4000 g,<sup>19,22-24,28,33,36,37,39,42</sup> and 1 defined it as birth weight greater than 4500 g.<sup>41</sup>

Gestational weight gain below guidelines was associated with lower risk of macrosomia (OR, 0.60 [95% CI, 0.52 to 0.68];  $I^2 = 66.3\%$ ; ARD,  $-2\%$  [95% CI,  $-3\%$  to  $-1\%$ ]). The association was strongest in underweight women (underweight: OR, 0.43 [95% CI, 0.27 to 0.69]; ARD,  $-1\%$  [95% CI,  $-3\%$  to  $0\%$ ]; normal weight: OR, 0.54 [95% CI, 0.43 to 0.68]; ARD,  $-2\%$  [95% CI,  $-5\%$  to  $1\%$ ]; overweight: OR, 0.73 [95% CI, 0.60 to 0.89]; ARD,  $-2\%$  [95% CI,  $-6\%$  to  $2\%$ ]; and obese: OR, 0.70 [95% CI, 0.59 to 0.82]; ARD,  $-3\%$  [ $-4\%$  to  $-2\%$ ]).

Gestational weight gain above guidelines was associated with higher risk of macrosomia (OR, 1.95 [95% CI, 1.79 to 2.11];  $I^2 = 58.2\%$ ; ARD,  $6\%$  [95% CI,  $4\%$  to  $9\%$ ]). This association was strongest in underweight women according to the ORs, and all associations were significant according to the ARDs (underweight: OR, 2.31 [95% CI, 1.62 to 3.29]; ARD,  $3\%$  [95% CI,  $2\%$  to  $4\%$ ]; normal weight: OR, 2.01 [95% CI, 1.77 to 2.27]; ARD,  $10\%$  [95% CI,  $5\%$  to  $15\%$ ]; overweight: OR, 1.90 [95% CI, 1.54 to 2.33]; ARD,  $5\%$  [95% CI,  $1\%$  to  $10\%$ ]; and obese: OR, 1.83 [95% CI, 1.52 to 2.22]; ARD,  $6\%$  [95% CI,  $1\%$  to  $12\%$ ]).

### Cesarean Delivery

Eight studies assessed cesarean delivery. Seven included emergency and elective deliveries,<sup>22,28,29,33,36,37,39</sup> and 1 did not specify.<sup>24</sup> One study<sup>28</sup> included repeated cesarean delivery (total cesarean deliveries), 1 included primary cesarean delivery only,<sup>24</sup> and 6 did not distinguish these.

Gestational weight gain below guidelines was not significantly associated with cesarean delivery (OR, 0.98 [95% CI, 0.96 to 1.02];  $I^2 = 62.6\%$ ; ARD,  $0\%$  [ $-2\%$  to  $1\%$ ]).

Gestational weight gain above guidelines was associated with higher risk of cesarean delivery (OR, 1.30 [95% CI, 1.25 to 1.35];  $I^2 = 21.9\%$ ; ARD,  $4\%$  [95% CI,  $3\%$  to  $6\%$ ]). The ARD was

significant for underweight women only (underweight: OR, 1.45 [95% CI, 1.22 to 1.71]; ARD,  $6\%$  [95% CI,  $1\%$  to  $12\%$ ]; normal weight: OR, 1.30 [95% CI, 1.24 to 1.36]; ARD,  $0\%$  [95% CI,  $-4\%$  to  $3\%$ ]; overweight: OR, 1.29 [95% CI, 1.21 to 1.39]; ARD,  $1\%$  [ $0\%$  to  $3\%$ ]; and obese: OR, 1.22 [95% CI, 1.05 to 1.42]; ARD,  $-2\%$  [95% CI,  $-5\%$  to  $1\%$ ]).

### Gestational Diabetes Mellitus

Six studies assessed GDM, but they did not use consistent definitions and had different findings for gestational weight gain above guidelines and GDM risk. Black et al<sup>28</sup> defined GDM by International Association of Diabetes in Pregnancy Study Groups criteria and included only women not treated for hyperglycemia (the center used different criteria in clinical practice and excluded those treated). They found no association between weight gain above guidelines and GDM in the underweight, normal-weight, and obese groups but reported lower risk in overweight women. Enomoto et al<sup>22</sup> used International Association of Diabetes in Pregnancy Study Groups criteria, with higher risk in normal-weight women and lower risk in overweight women. Durst et al<sup>23</sup> used Carpenter-Coustan criteria and found no association. Hung and Hsieh<sup>24</sup> used Carpenter-Coustan and International Association of Diabetes in Pregnancy Study Groups criteria and found an association of gestational weight gain above guidelines with lower risk of GDM in overweight and obese women. Li et al<sup>36</sup> included both impaired glucose tolerance and type 2 diabetes by WHO criteria, with weight gain above guidelines associated with lower risk of GDM in all groups except obese women. Shin and Song<sup>31</sup> used self-reported GDM and found an association of gestational weight gain above guidelines with lower risk in all groups except underweight women.

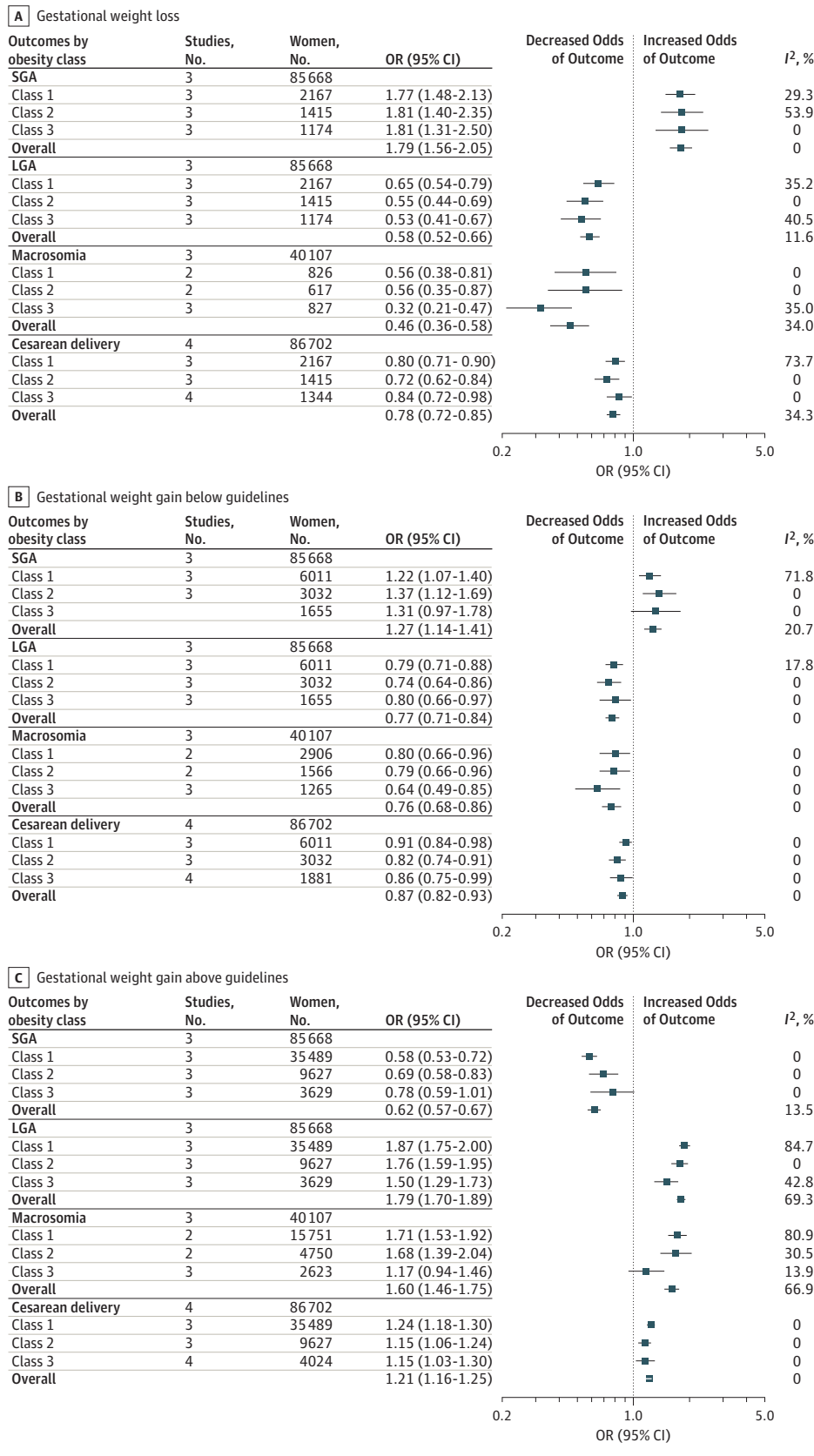
An intended meta-analysis of gestational weight gain and its relationship to GDM could not be completed because of inconsistent definitions and treatments.

### Obese Subgroup Analysis Stratified by Obesity Class

Obesity classes include the following: class 1, BMI of 30 to 34.9; class 2, BMI of 35 to 39.9; and class 3, BMI of 40 or higher. Obese studies generally included a subgroup-defined weight loss as well as gestational weight gain below, within, or above guidelines. Three studies assessed outcomes stratified by BMI classes 1 through 3.<sup>17,18,30</sup> Another study<sup>35</sup> investigated only superobese women (BMI  $\geq 50$ ) and was included in the obesity class 3 analysis. These 4 studies were included in the subgroup analysis only (not in the overall meta-analyses). Class 1 included 67% of women; class 2, 22%; and class 3, 11%. Weight loss and gestational weight gain below, within, or above recommendations occurred in 6%, 13%, 25%, and 57% of pregnancies, respectively.

Figure 3 summarizes pooled ORs for primary (SGA and LGA) and secondary (macrosomia and cesarean delivery) outcomes. eFigure 3 in the Supplement shows pooled ORs for individual outcomes. eTable 4 in the Supplement reports ARDs and *P* values. Only 1 study<sup>35</sup> assessed preterm birth and GDM in the obese subgroups, preventing meta-analysis. Komiński et al<sup>18</sup> provided separate ORs for nulliparous

Figure 3. Obese Subgroup Analysis With Summary of Pooled Odds Ratios (ORs) for the Association Between Gestational Weight Loss, Gain Below Guidelines, and Gain Above Guidelines With Adverse Outcomes





and multiparous women (multiparous values used herein), whereas other studies combined women with different parity into 1 group.

#### SGA by Obesity Class

Three studies assessed SGA. One defined SGA as birth weight less than the 10th percentile for gestational age alone,<sup>18</sup> and 2 also used sex and parity to define SGA.<sup>17,30</sup>

Weight loss and weight gain below guidelines were associated with higher SGA risk (weight loss: OR, 1.79 [95% CI, 1.56 to 2.05];  $I^2 = 0\%$ ; ARD, 3% [95% CI, 1% to 5%]; weight gain below guidelines: OR, 1.27 [95% CI, 1.14 to 1.41];  $I^2 = 20.7\%$ ; ARD, 1% [95% CI, 1% to 1%]). Gestational weight gain above guidelines was associated with lower SGA risk (OR, 0.62 [95% CI, 0.57 to 0.67];  $I^2 = 13.5\%$ ; ARD, -1% [-2% to 0%]). Weight gain in class 1 had the strongest association with lower SGA risk (lowest OR, 0.58; 95% CI, 0.53 to 0.72];  $P$  for trend < .001).

#### LGA by Obesity Class

Three studies assessed LGA. One defined LGA as birth weight greater than the 90th percentile for gestational age alone,<sup>18</sup> and 2 also used sex and parity to define LGA.<sup>17,30</sup>

Weight loss and gestational weight gain below guidelines were associated with lower LGA risk (weight loss: OR, 0.58 [95% CI, 0.52 to 0.66];  $I^2 = 11.6\%$ ; ARD, -5% [95% CI, -7% to -3%]; weight gain below guidelines: OR, 0.77 [95% CI, 0.71 to 0.84];  $I^2 = 0\%$ ; ARD, -2% [95% CI, -3% to -1%]). Weight loss in class 3 had the strongest association with lower LGA risk (lowest OR, 0.53 [95% CI, 0.41 to 0.67];  $P$  for trend < .001). Weight gain above guidelines was associated with higher LGA risk (OR, 1.79 [95% CI, 1.70 to 1.89];  $I^2 = 69.3\%$ ; ARD, 5% [95% CI, 5% to 6%]). LGA was most strongly associated with class 1 obesity compared with the other classes (highest OR, 1.87 [95% CI, 1.75 to 2.00];  $P$  for trend < .001).

#### Macrosomia by Obesity Class

Three studies assessed macrosomia, defined as birth weight greater than 4000 g in 1 study,<sup>30</sup> greater than 4500 g in 1 study,<sup>18</sup> and both greater than 4000 g and greater than 4500 g in 1 study.<sup>35</sup> Meta-analysis used data for birth weight greater than 4000 g.

Weight loss and gestational weight gain below guidelines were associated with lower macrosomia risk (weight loss: OR, 0.46 [95% CI, 0.36 to 0.58];  $I^2 = 34.0\%$ ; ARD, -5% [95% CI, -9% to -2%]; weight gain below guidelines: OR, 0.76 [95% CI, 0.68 to 0.86];  $I^2 = 0\%$ ; ARD, -2% [95% CI, -3% to 0%]). Low weight gain in class 3 had the strongest association with lower macrosomia risk (lowest OR, 0.64 [95% CI, 0.49 to 0.85];  $P$  for trend = .046). Gestational weight gain above guidelines was associated with higher risk of macrosomia (OR, 1.60 [95% CI, 1.46 to 1.75];  $I^2 = 66.9\%$ ; ARD, 3% [95% CI, 0% to 6%]).

#### Cesarean Delivery by Obesity Class

Four studies assessed cesarean delivery. They included emergency,<sup>30</sup> emergency and elective,<sup>18,35</sup> and undefined<sup>17</sup> indications for cesarean delivery.

Weight loss and gestational weight gain below guidelines were associated with lower risk of cesarean delivery (weight

loss: OR, 0.78 [95% CI, 0.72 to 0.85];  $I^2 = 34.3\%$ ; ARD, -4% [95% CI, -6% to -3%]; weight gain below guidelines: OR, 0.87 [95% CI, 0.82 to 0.93];  $I^2 = 0\%$ ; ARD, -2% [95% CI, -3% to -1%]). Gestational weight gain above guidelines was associated with higher risk of cesarean delivery (OR, 1.21 [95% CI, 1.16 to 1.25];  $I^2 = 0\%$ ; ARD, 2% [95% CI, 0% to 3%]).

#### Metaregression

Substantial heterogeneity ( $I^2 > 50\%$ ) was present for gestational weight gain below and above guidelines for SGA, preterm birth, LGA, and macrosomia and for gestational weight gain above guidelines for cesarean delivery. When sufficient data were available, metaregression analysis was performed to investigate possible sources of heterogeneity: percentage of smokers during pregnancy, mean age, and percentage of nulliparous women (eTable 5 in the Supplement). The obese subgroups had insufficient studies to perform metaregression.

Gestational weight gain above guidelines and LGA demonstrated a source for heterogeneity ( $P = .04$ ); specifically, there was an association between the treatment effect and the covariate smoking ( $P = .02$ ). For gestational weight gain below guidelines and preterm birth, mean maternal age was the only covariate associated with outcome, where the risk for preterm birth varied by maternal age due to the heterogeneity in maternal age in included studies ( $P = .03$ ); however, the overall  $P$  value was not significant ( $P = .09$ ). Heterogeneity was unexplained for remaining outcomes.

#### Publication Bias

There was no evidence of publication bias for SGA, LGA, macrosomia or cesarean delivery (eFigure 4 in the Supplement). Assessment for publication bias was not performed for preterm births (<5 studies).

#### Risk of Bias

Participants were selected from maternity clinics or from large data sets (Table 4). Apart from 3 studies,<sup>19,23,32</sup> inclusion and exclusion criteria were adequately described. Performance bias (a potential difference in the care provided between BMI groups) was difficult to assess. Very few studies provided information regarding diet and/or exercise advice given and whether this differed between groups. Overweight and obese women were possibly treated more intensively, which could introduce bias.

Three studies demonstrated moderate bias risk<sup>19,21,31</sup> and 20 demonstrated low bias risk.<sup>17,18,20,22-24,28-30,32-42</sup> Reasons for moderate bias risk included self-reported final weight (detection bias), self-reported outcome measures (detection bias), failure to report all outcomes (report bias), and insufficient adjustment for confounding variables (confounding bias). Nineteen studies reported no conflict of interest.

#### Discussion

In this analysis of 1 309 136 pregnancies from diverse international cohorts, gestational weight gain below or above 2009

Table 4. Summary of Risk of Bias Assessment

Source	Selection Bias, Exposed Cohort Representative	Detection Bias		Reporting Bias, Free of Selective Outcome Reporting	Assessment of Confounding in Original Analysis	Conflict of Interest	Overall Risk of Bias
		Adequate Exposure Measures	Adequate Outcome Measures				
Durst et al, <sup>23</sup> 2016	Yes	Yes	Yes	Yes	Yes	No	Low
Enomoto et al, <sup>22</sup> 2016	Yes	NR	Yes	Yes	Yes	No	Low
Hung and Hsieh, <sup>24</sup> 2016	Yes	Yes	Yes	Yes	Yes	No	Low
Xiong et al, <sup>29</sup> 2016	Yes	Yes	Yes	Yes	Yes	No	Low
Bogaerts et al, <sup>30</sup> 2015	Yes	Yes	Yes	Yes	Yes	No	Low
Shin and Song, <sup>31</sup> 2015	Yes	Yes	No (self-reported)	Yes	Partial (did not adjust for parity)	No	Moderate
Wen and Lv, <sup>21</sup> 2015	NR	Yes	NR	Partial (not all outcomes reported)	Partial (did not adjust for required number of confounders)	No	Moderate
Yang et al, <sup>32</sup> 2015	Yes	Yes	Yes	Yes	Yes	No	Low
Badon et al, <sup>20</sup> 2014	Yes	Yes	Yes	Yes	Yes	No	Low
Chihara et al, <sup>19</sup> 2014	Yes	Partial (self-reported final weight)	No (self-reported)	Yes	Yes	NR	Moderate
Haugen et al, <sup>33</sup> 2014	Yes	Partial (self-reported final weight)	Yes	Yes	Yes	No	Low
Lee et al, <sup>34</sup> 2014	NR	Yes	Yes	Yes	Yes	No	Low
Swank et al, <sup>35</sup> 2014	Yes	Yes	Yes	Yes	Yes	No	Low
Black et al, <sup>28</sup> 2013	Yes	Yes	Yes	Yes	Yes	No	Low
Kominiarek et al, <sup>18</sup> 2013	Yes	Yes	Yes	Yes	Yes	No	Low
Li et al, <sup>36</sup> 2013	Yes	Yes	Yes	Yes	Yes	No	Low
Di Benedetto et al, <sup>37</sup> 2012	Yes	Yes	Yes	Yes	Partial (did not adjust for parity)	No	Low
Simas et al, <sup>38</sup> 2012	Yes	Partial (some self-reported final weight)	Yes	Yes	Yes	No	Low
Blomberg, <sup>17</sup> 2011	Yes	Yes	Yes	Yes	Yes	No	Low
Park et al, <sup>39</sup> 2011	Yes	Yes	Yes	Partial (not all outcomes reported)	Yes	NR	Low
Park et al, <sup>40</sup> 2011	Partial	NR	Yes	Yes	Yes	NR	Low
Vesco et al, <sup>41</sup> 2011	Yes	Yes	Yes	Yes	Yes	No	Low
Rode et al, <sup>42</sup> 2007	NR	Partial (self-reported final weight)	Yes	Yes	Partial (did not adjust for parity)	NR	Low

Abbreviation: NR, not reported.

IOM guidelines among women across the BMI range was associated with greater risk for maternal and infant adverse outcomes. Underweight women composed 7%; normal-weight women, 55%; overweight women, 18%; and obese women, 20%. For gestational weight gain, 23% gained below and 47% gained above guidelines. Compared with recommended gestational weight gain, gain below guidelines was associated with 5% higher risk of both SGA and preterm birth and 2% lower risk of both LGA and macrosomia. Weight gain above guidelines was associated with 3% lower risk of SGA and 2% lower risk of preterm birth and 4%, 6%, and 4% higher risk of LGA, macrosomia, and cesarean delivery, respectively.

Gestational weight gain below guidelines was associated with higher SGA risk, with greatest risk in underweight women, as shown previously.<sup>43,44</sup> Obesity was associated with higher risk of SGA, with weight loss and gestational weight gain below guidelines increasing risks, similar to prior systematic reviews.<sup>26,45,46</sup> Underweight status combined with gestational weight gain below recommendations as well as obese status combined with gestational weight loss present the highest risk groups for SGA, at 8% and 3%, respectively.

Gestational weight gain below guidelines was associated with a 5% increase in preterm birth across the included populations. With 23% having weight gain below

recommendations, this could correspond to 15 000 more preterm birth events. Weight gain above guidelines was associated with lower risk of preterm birth. Prior reviews have shown similar associations, but they did not stratify by prepregnancy BMI and gestational weight gain.<sup>47,48</sup> One small systematic review in obese women did not find associations between preterm birth and weight gain outside guidelines.<sup>49</sup> With larger sample sizes and stratification by BMI and prepregnancy weight gain, the current review adds to prior work and has greater clinical applicability. Also, as maternal BMI increased, the association between gestational weight gain below guidelines and preterm birth risk was weakened, consistent with an earlier review.<sup>3</sup>

Gestational weight gain below guidelines was associated with lower risks of LGA and macrosomia. This association was lowest in underweight women. Weight gain above guidelines was associated with higher risks of LGA and macrosomia, with ARDs of 4% and 6% greater risks, respectively. Underweight status was associated with the greatest risk. This is similar to the 2009 IOM report<sup>6</sup> that stated, “the lower the prepregnancy BMI, the stronger the association between increased gestational weight gain and birthweight”; it may be related to higher absolute weight gain in underweight women.<sup>1</sup> Animal studies suggest that baseline maternal BMI and gestational weight gain are associated with changes in the hormonal milieu, including insulin resistance.<sup>50</sup> Similarly, excess weight gain in underweight women may be associated with greater changes in the hormonal milieu and placental function than in normal-weight or overweight women. Weight gain above guidelines was associated with increased risk of cesarean delivery across the BMI spectrum.

Similarly, within the obese subgroups, weight loss was associated with a 5% lower risk for both LGA and macrosomia and 4% lower risk for cesarean delivery. Weight gain below guidelines was associated with 2% lower risk across all these outcomes. Class 3 obesity combined with weight loss was associated with the greatest LGA risk reduction. Gestational weight gain above guidelines was associated with increased LGA risk. Class 1 obesity was associated with the greatest risk for LGA, which may be partly due to higher absolute weight gain in less obese women.<sup>10</sup> While other systematic reviews have assessed gestational weight gain below guidelines,<sup>26</sup> to our knowledge, this is the first review exploring relationships between weight gain above guidelines and outcomes within obesity classes.

While GDM has adverse maternal and infant outcomes<sup>51</sup> and is related to maternal BMI and possibly to gestational weight gain, associations could not be assessed because of heterogeneity of diagnosis and treatment as well as the potential effect of GDM treatment on gestational weight gain. Prior systematic reviews have not demonstrated that healthy lifestyle and gestational weight gain reduced rates of GDM,<sup>14</sup> even in high-risk populations.<sup>52</sup> Consistent diagnostic criteria and reporting of gestational weight gain at GDM diagnosis are needed to study associations between gestational weight gain and GDM.

Lifestyle interventions in pregnancy can help women attain recommended gestational weight gain.<sup>14</sup> Optimal inter-

ventions and effects on outcomes are currently being studied in a large-scale international individual patient data meta-analysis.<sup>53</sup> The WHO has prioritized achievement of ideal BMI prior to conception and prevention of excess gestational weight gain.<sup>54</sup> Identification of women prior to conception and implementing healthy lifestyle strategies before and during pregnancy have yet to be integrated into routine health care,<sup>55</sup> requiring research implementation.

Strengths of this review are the inclusion of common maternal and infant risks associated with gestational weight gain below and above the 2009 IOM guidelines in women across the prepregnancy BMI spectrum and across international cohorts. Four databases were searched, a risk of bias appraisal was performed, and reanalyses were undertaken, allowing inclusion of data from more than 1.3 million pregnant women globally. Collaboration with other authors facilitated more homogeneous data, data integration, and meta-analysis.

### Limitations

This study has limitations. It lacks studies from developing countries and excluded non-English-language articles. Fifteen of 31 authors contacted were unable to reanalyze data, so these studies were excluded from the meta-analysis. A meta-analysis could not be performed for GDM because of inconsistent primary data. Some outcomes were assessed in only 1 study, precluding meta-analysis. Inconsistent definitions of preterm birth, cesarean delivery, and macrosomia limited interpretation of findings. Study heterogeneity may have affected reliability of results, although the metaregression did not identify characteristics responsible for this heterogeneity. Studies published before 2009 IOM guidelines were included, and gestational weight gain targets before and after these guidelines may have differed. Preterm birth was not adjusted for gestational age, potentially resulting in less total gestational weight gain than would have been otherwise attained. Spontaneous and induced preterm birth were not clearly differentiated, and studies did not distinguish between emergency and elective or primary and repeated cesarean deliveries. These factors may limit interpretation and underscore the importance of improving outcome definition reporting. Event rates were not available for all studies, limiting interpretation of ARDs. Findings from this review are based on observational data and no causal links may be concluded. They may be applicable on a population level, but recommendations need to be individualized when applied clinically.

### Conclusions

In this systematic review and meta-analysis of more than 1 million pregnant women, 47% had gestational weight gain greater than IOM recommendations and 23% had gestational weight gain less than IOM recommendations. Gestational weight gain greater than or less than guideline recommendations, compared with gestational weight gain within recommended levels, was associated with higher risk of adverse maternal and infant outcomes.

## ARTICLE INFORMATION

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