

Height and Risk of Gestational Diabetes: Does Maternal Race Make a Difference?

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Abstract

Aims/hypothesis

Gestational diabetes (GDM) is a common pregnancy complication that affects women of different race/ethnicities disproportionately. Adult height, an indicator of the interplay between genetic and early-life and childhood factors, was inversely associated with the risk of GDM in most but not all studies. The current study aims to investigate the association of adult height with GDM risk and evaluate whether the association varies by race.

Methods

The Consortium on Safe Labor (CSL) is a retrospective observational study of medical data capturing 135,861 deliveries (2005-2007) including 5,567 GDM cases. Generalized estimating equations were used to estimate odds ratios (OR) and 95% confidence interval (95% CI) of GDM by quartiles of height for each race and while controlling for known risk factors. Multiplicative interaction terms in the models and stratified analyses were used to evaluate interactions. A meta-analysis of 15,761 GDM cases and 205,828 controls from 38 studies including the CSL data was conducted to estimate the pooled mean difference in height between GDM and non-GDM women.

Results

Findings of CSL deliveries suggested that height is significantly and inversely associated with GDM risk across different race/ethnicities, with the largest magnitude of association among Asians and smallest in Blacks (P for interaction between height and race <0.001). Comparing extreme quartiles of height (> 168 cm vs. <157cm), the adjusted ORs (95% CI) were 0.19 (0.10-0.38) for Asians/Pacific Islanders, 0.35 (0.30-0.40) for non-Hispanic whites, 0.42 (0.33-0.55) for Hispanics, and 0.59 (0.47-0.76) for non-Hispanic blacks. The mean differences between women with versus without GDM in centimeters by race were -1.31 for non-Hispanic whites, 0.14 for non-Hispanic blacks, -0.67 for Hispanics and -1.64 for Asian/Pacific Islanders. Meta-analysis of pooled mean difference showed that GDM women were significantly shorter than non-GDM women across all race/ethnicity groups except among women of African or African American descent.

Conclusions/interpretation

Women of high stature are at substantially lower risk of developing GDM. Across different race/ethnicities, the significant association persists although the magnitude of the association varies significantly.

Key words: height, gestational diabetes, meta-analysis,

Abbreviations: CSL-Consortium on Safe Labor; GDM-gestational diabetes mellitus; GEE-generalized estimating equations

Introduction

Gestational diabetes mellitus (GDM), a common pregnancy complication defined as glucose intolerance with onset or first recognition during pregnancy, affects approximately 7% (ranging from 1%-14%) of all pregnancies in the US [1]. The incidence is higher among Asians, Hispanics, Native Americans, and African-American women than non-Hispanic white women [2]. GDM increases risk of adverse pregnancy outcomes [3], and has substantial long-term adverse health impacts on both mothers and their offspring, including a predisposition to obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM) in later life [1, 4, 5]. Therefore it is important to understand its etiology and identify risk factors that may help identify women at high risk.

Adult height is an indicator of genetic, early-life and childhood factors and their interplay. Height varies across different populations, with Asians generally shorter than African-American or non-Hispanic white women. Height has been inversely associated with the risk of GDM in some but not all studies [6-11]. However, studies examining the association between height and GDM in heterogeneous race/ethnicity populations are sparse, and whether the inverse association of height with GDM varies across different race/ethnicities remains unclear.

The current study aimed to investigate the association between height and GDM in a nationally representative cohort of 135,861 U.S. pregnancies in 9 American College of Obstetricians and Gynecologists districts to evaluate whether the association varies across women of different races. To our knowledge, no study has achieved enough power to fully detect racial and ethnic differences in the association between height and GDM.

Methods

Description of patients

The Consortium on Safe Labor (CSL) is a nationally representative retrospective observational study conducted at 12 clinical centers (made up of 19 hospitals) in 9 American College of Obstetricians and Gynecologists districts. Each institution extracted information on maternal demographic characteristics (including height, race, educational attainment, insurance status, and age); medical, reproductive, and prenatal history; labor and delivery summary; and postpartum and newborn outcomes via electronic medical records. Determination of GDM status was recorded in the medical record. The study included 228,562 deliveries, 87 percent of which occurred between the years 2005 and 2007. Each clinical center transferred data to coordinating centers, which mapped variables to predefined common codes. Validation studies of four key outcome diagnoses were conducted by selecting eligible charts and recollecting data by hand chart abstraction and comparing it to information downloaded from electronic medical records.

Women were excluded if they experienced multiple gestation, were missing data on the primary outcome or exposure: GDM or height (~16%), were positive for or missing data for T2DM, or delivered at less than 24 weeks. In addition three sites were excluded: sites 2 and 4 (Cedars-Sinai Medical Center, Los Angeles, CA, and Indiana University School of Medicine, Indianapolis, IN) did not provide GDM data and site 12 (University of Texas Health Science Center at Houston) reported a GDM prevalence of less than 1%.

Meta-analysis

Epidemiologic studies were identified that a) were written in English, b) were population-based cohort and cross-sectional studies, c) included women aged 18 or older, d) reported height by GDM status or height was able to be calculated from body mass index (BMI) and weight, and e) defined GDM. Pubmed and Embase were searched using the MeSH headings for gestational diabetes and the following free-text words: GDM, gestational diabetes, height, body mass index, BMI, weight, obesity, observational, cohort, and cross-sectional. Additional studies and data were hand searched using references from the retrieved articles and other relevant review articles. Very few of the eligible studies aimed to examine the association of height and GDM specifically and therefore did not provide the odds ratio for the association. To maximize the number of studies included, we used mean difference between GDM and non-GDM controls as the major estimate of effect size in the meta-analysis, as the majority of eligible studies provided mean and standard deviation of mean.

Two independent reviewers (ES & EY) abstracted data from primary studies using predetermined criteria with differences arbitrated by a third independent investigator (CZ) as necessary. Information abstracted included last name of first author, publication date, study location, study period, method for GDM screening, diagnostic criteria to define GDM cases, and the sample size (cases and controls), along with age, race, BMI (SD), weight (SD), and height (SD) for each GDM category.

Statistical analysis

In the CSL, means with standard deviations for continuous baseline characteristics and proportions for categorical characteristics were calculated and compared by GDM status using unpaired t or χ^2 tests. Baseline characteristics were also compared across quartiles of height and assessed using anova or χ^2 tests. Height was assessed both as a categorical (in quartiles) and continuous variable. Linear trends were evaluated across race using the median height value analyzed as a continuous variable in multivariate models for each racial category. Generalized estimating equations (GEE) were used to estimate odds ratios (OR) and 95% confidence intervals (CI) of prevalence GDM for each height quartile and also for each centimeter increase in height. (Repeated measures were added to the GEE equation to avoid intra-person correlation as some women contributed information for more than one pregnancy.) Multiplicative interaction terms were used to identify interactions (or effect modification), and for statistically significant interactions, stratified analyses were used to estimate the effect estimates across groups. Covariates were selected a priori based on the literature and prior studies. All models adjusted for age.

In meta-analysis, the mean difference and standard error (SE) in height by GDM status was calculated for each study. Fixed-effect and random-effects models of the mean difference in height were examined weighted by the inverse variance of the height. Heterogeneity among studies was investigated using Cochran's Q-test with a significance level of an alpha of 0.1. If the studies appeared to be heterogeneous, a random-effects model was preferred. Publication bias and sensitivity analyses were performed. Race-specific pooled estimates were also calculated. The studies were not weighted by quality. MIX software, version 1.7, and SAS, version 9.2 were used for all analyses [12, 13].

Results

Consortium on Safe Labor

The final CSL sample included 135,861 pregnancies, 5,567 of which were diagnosed with GDM. The overall prevalence of GDM was approximately 4%, reflective of the US obstetric population. Prevalence of GDM varied between 2.55% and 6.14% across sites. In general, GDM women were heavier, shorter, of lower education, and older than non-GDM women. On average, women with GDM were 1.5 cm shorter than non-GDM women (Table 1). Women in the tallest quartile of height were better educated (33% had more than a high school diploma compared to 16% in the shortest quartile); predominately white (66% compared to 40% in the shortest quartile); and more often privately insured (67% compared to 52% in the shortest quartile) (Table 2).

Height was significantly and inversely associated with GDM risk. Overall, women in the highest height quartile had more than 60% lower risk of GDM when compared to women in the lowest quartile (adjusted OR 0.39; 95% CI: 0.36-0.43), even after accounting for maternal age, pre-pregnancy weight, race, insurance, and education. (**Table 2**) Similarly, every 5 centimeter increase in height was also associated with 20% significant decrease in risk (adjusted OR 0.80 (95% CI:0.30, 0.82) The association differed significantly by race/ethnicity ($p<0.001$). In addition the association varied substantially across different races/ethnicities with the magnitude of the association strongest among Asians and smallest for Blacks. (**Table 3**).For instance, among Asians, women with height >168 cm had more than 80% reduced risk for GDM as compared with women with height <157 cm. Corresponding ORs (95% CIs), were 0.18 (0.09-0.35) for Asians, 0.34 (0.29-0.38) for Whites, 0.39 (0.31-0.51) for Hispanics, and 0.59 (0.47-0.75) for Blacks (p -value for interaction for height and race <0.001).

Meta-analysis

A total of 38 studies [9, 11, 14-48] including CSL among 221,589 women (15,761 GDM women) were included in quantitative synthesis to evaluate the mean difference of height between GDM and non-GDM controls. Also presented in this table are the mean differences by race from the CSL (**Supplemental Table 1**). GDM screening methods and diagnostic criteria varied among studies. However, most studies employed universal screening or universal diagnostic testing. A random-effect models was applied due to heterogeneity (Cochran's $Q < 0.001$). In general, GDM women were significantly shorter than non-GDM women across all race/ethnicity groups except among women of African or African American descent (Table 4), among whom, although GDM women were shorter, the difference was not statistically significant. Funnel plots did not show evidence of publication bias (**Supplemental Figure 2**). Sensitivity and trim and fill analyses showed that the removal of one study did not measurably alter the mean difference estimate or 95% confidence interval.

Discussion

In a large and nationally representative cohort of U.S. women, we observed that taller adult stature was significantly associated with lower risk of GDM. The association persisted, but the magnitude of the association varied, significantly across different race/ethnicities with Asians demonstrating the strongest effect and Blacks the least effect.

Due to the small number of GDM cases, race/ethnicity specific association of height with GDM hasn't been evaluated in an ethnically heterogeneous population. Our findings, however, were generally consistent with prior studies [6-11, 48] among ethnically homogeneous population, though not all studies. For example, Ogonowski et. al [7] found women with GDM were two centimeters shorter than controls (165.7 \pm 5.6 vs 163.8 \pm 6.6 cm; $P < 0.001$) and a study in Seattle and Tacoma, Washington [6], found GDM risk in mothers taller than 170 cm was approximately 60 percent lower than in those 160 cm or shorter (RR = 0.40, 95 percent CI: 0.17, 0.95). To our knowledge, only one study examined the relationship between height and GDM and found null results [40].

The mechanisms whereby a shorter adult height is associated with a greater risk of GDM are not clear. Adult height has been regarded as an indicator of the interplay of genetic and early-life environmental factors. Growth hormones, the intrauterine environment and childhood nutrition have been previously suggested as potential pathways linking impaired peripheral growth, as indicated by short stature, to the risk of impaired glucose tolerance in adulthood [49]. For instance, low birth weight has been correlated with shorter stature later in life [50]. Low birth weight has previously been linked with increased risk for metabolic dysfunction in child-and adulthood including GDM [51]. The mechanism has been suggested to be fetal programming in response to maternal malnutrition [52]. One hypothesized pathway that this could occur is through epigenetic changes such as DNA methylation that alter expressions of growth or other metabolic factors in utero to compensate for nutritional insufficiencies that later in life leads to metabolic risk [53] when facing metabolic challenges in pregnancy. Moreover under-nourished fetuses may be born with a reduced number and function of pancreatic β -cells [54, 55], compromising insulin production and consequently resulting in a high risk for GDM. Another possible mechanism is shared genetic risk factors of short stature and related growth measures and defects in glucose metabolism. For instance, a polymorphism in the gene for IGF-I functional properties was significantly related to both shorter adult stature and an increased risk for type 2 diabetes in the Rotterdam Study [56]. Moreover, risk alleles at the *CDKAL1* and *HHEX-IDE* loci were associated with both reduced birth weight and increased risk for type 2 diabetes in four studies of European [57, 58]. Finally, an artifact may be at work, with height affecting OGTT results as shorter women have a lower mass of metabolically active tissues to respond to a standardized 75-100 gram of oral glucose compared to taller women [7]. Asians are, on average, shorter than other groups, so this may explain why they are diagnosed with GDM more often.

Our study has several unique strengths. The CSL represents a large study of heterogeneous race/ethnicity with comprehensive information on maternal, delivery, and neonatal characteristics, and reliable and uniform data collection, which together minimize measurement error and bias. The meta-analysis systematically synthesized population-based cohorts from 21 countries resulting in a large cohort of GDM and non-GDM women. It has been argued that because height is a basic anthropological measurement recorded in virtually every study, null results are unlikely to be present in the literature [40] and the height-GDM association exists due to publication bias. However, our meta-analysis, which pooled from all studies reporting height and extracting height information from BMI and weight, did not appear to confirm this hypothesis.

Several potential limitations warrant discussion. We did not have information on variables that may be significant, such as childhood SES and in-utero and early-life nutrition deficiencies (or their indicators such as maternal birth weight). The CSL study was observational so unmeasured and unknown confounders cannot be ruled out. We also found almost half of African American women gave birth at sites with GDM prevalence of less than 3%, causing African Americans to have lower odds of GDM compared to whites. This directly

contradicts established research on GDM [59], leading us to believe certain sites may have underreported more than others and that African Americans may have been unduly impacted. However because GDM prevalence for each of the other races/ethnicities in our study matched those found in the general population for those groups, we feel confident in our other estimates. Our study is limited by the absence of assessment of leg length, which Moses and Mackay [48] have previously shown to be the precise anthropometric measurement that relates height to glycemia. Another limitation of this study is the classification of race/ethnicity in CSL. Specifically, Asians and Pacific Islanders were combined.

Conclusion

In summary, our findings suggest height is significantly and inversely associated with GDM. The significant association persists across different race/ethnicity although the magnitude of the association varies by race. Adult height is an indicator of the interplay of genetic and early-life and childhood factors. Findings from the present study indicate the potential role of these factors in the etiology of GDM. Future studies investigating the underlying mechanisms are warranted.

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Duality of interest

The authors report no conflicts of interest

Tables

Table 1. Baseline characteristics of the Consortium on Safe Labor (CSL) study population women by gestational diabetes (GDM) status.

	GDM (n=5,567)	No GDM (n=138,857)	p-value
Height (cm)	161.7 (7.48)	163.2 (7.42)	<.0001
Height quartiles, n (%)			<.0001
Q1: 101 – 157.48	1,906 (34)	34,084 (26)	
Q2: 157.50 – 162.56	1,521 (27)	34,189 (26)	
Q3: 162.60 – 167.64	1,172 (21)	31,676 (24)	
Q4: 167.89 – 210.0	968 (17)	30,345 (23)	
BMI (kg/m ²), n (%)			<.0001
<18.5	91 (2.0)	5,638 (5.2)	
18.6-24.9	1,364 (29.7)	57,607 (53.5)	
25.0-29.9	1,285 (28.0)	24,802 (23.1)	
≥30	1,851 (40.3)	19,570 (18.2)	
Missing	976 (17.5)	22,677 (17.4)	
Education, n (%)			<.0001
Less than high school	655 (12)	12,263 (9)	
High school diploma	877 (16)	19,687 (15)	
More than high school	1,179 (21)	32,058 (25)	
Unknown	2,856 (51)	66,286 (51)	
Insurance, n (%)			
Private	3,290 (59)	77,566 (60)	.95
Public	1,777 (32)	40,992 (31)	
Self pay	67 (1)	1,495 (1)	
Other/unknown	433 (8)	10,241 (8)	
Pre-pregnancy weight (kg)	77.4 (21.5)	67.8 (17.2)	<.0001
Race, n (%)			<.0001
White	2,571 (46)	70,924 (54)	
Black	813 (15)	24,365 (19)	
Hispanic	1,379 (25)	22,205 (17)	
Asian/Pacific Islander	386 (7)	3,804 (3)	
Multi-racial/other/unknown	418 (8)	8,996 (7)	
Maternal age (years)	30.7 (5.8)	27.1 (5.9)	<.0001
Parity, n (%)			
0	1,823 (33)	50,721 (39)	<.0001
1	1,670 (30)	39,422 (3)	
2	1,072 (19)	22,189 (17)	
3	521 (9)	10,282 (8)	
4 or more	481 (9)	7,680 (6)	

Table 2. Baseline characteristics of the Consortium on Safe Labor (CSL) study population women by quartiles of height (cm).

Table 2.	Q1 101 – 157.48	Q2 157.50 – 162.56	Q3 162.60 – 167.64	Q4 167.89 – 210.0	p-value
Gestational Diabetes	1,906 (5.3)	1,521 (4.3)	1,172 (3.6)	968 (3.1)	<.0001
Height (cm)	154.1 (4.5)	161.3 (1.2)	166.1 (1.3)	172.8 (3.5)	<.0001
BMI (kg/m ²), n (%)					
<18.5	1176 (3.3)	1,432 (4.0)	1,471 (4.5)	1,650 (5.27)	<.0001
18.6-24.9	14,591 (40.5)	16,000 (44.8)	14,698 (44.8)	13,682 (43.7)	
25.0-29.9	7,405 (20.6)	6,506 (18.2)	6,164 (18.8)	6,012 (19.2)	
≥30	5,881 (16.3)	5,402 (15.1)	4,999 (15.2)	5,139 (16.4)	
Missing	6,937 (19.3)	6,370 (17.8)	5,516 (16.8)	4,830 (15.4)	
Education, n (%)					<.0001
Less than high school	4,945 (13.7)	3,574 (10.0)	2,786 (8.5)	1,613 (5.2)	
High school diploma	5,230 (14.5)	5,437 (15.2)	5,151 (15.7)	4,746 (15.2)	
More than high school	5,718 (15.9)	8,294 (23.2)	8,842 (26.9)	10,383 (33.2)	
Unknown	16,542 (46.0)	15,007 (42.0)	13,134 (40.0)	11,908 (38.0)	
Insurance, n (%)					<.0001
Private	18,564 (51.6)	21,455 (60.1)	19,966 (60.8)	20,871 (66.7)	
Public	13,733 (38.2)	10,531 (29.5)	9,897 (30.0)	8,648 (27.6)	
Self pay	534 (1.5)	4401 (1.1)	333 (1.0)	294 (0.9)	
Other/unknown	3,159 (8.8)	3,323 (9.3)	2,692 (8.2)	1,500 (4.8)	
Pre-pregnancy weight (kg)	61.5 (14.3)	66.0 (15.6)	70.0 (17.0)	27.7 (19.5)	<.0001
Race, n (%)					<.0001
White	14,505 (40.3)	19,377 (54.3)	18,888 (57.5)	20,725 (66.2)	
Black	5,960 (16.6)	5,933 (16.6)	6,678 (20.3)	6,607 (21.1)	
Hispanic	10,791 (30.0)	6,545 (18.3)	4,404 (13.4)	1,844 (5.9)	
Asian/Pacific Islander	1,790 (5.0)	1,285 (3.6)	723 (2.2)	392 (1.3)	
Multi-racial/other/unknown	26.7 (6.1)	2,570 (7.2)	2,155 (6.6)	1,745 (5.6)	
Maternal age (years)	26.7 (6.1)	27.3 (6.0)	27.5 (5.9)	27.7 (5.7)	<.0001
Parity, n (%)					.0007
0	14,050 (39.0)	13,800 (38.6)	12,624 (38.4)	12,070 (38.6)	
1	10,984 (30.5)	10,835 (30.3)	9,837 (30.0)	9,436 (30.1)	
2	6,065 (16.9)	6,006 (16.8)	5,789 (17.6)	5,401 (17.3)	
3	2,732 (7.6)	2,840 (8.0)	2,609 (7.9)	2,622 (8.4)	
4 or more	2,159 (6.0)	2,229 (6.2)	1,689 (6.1)	1,784 (5.7)	

Table 3. Adjusted ORs (95% CI) estimating the relationship between quartiles of height and GDM among all of the women in the Consortium on Safe Labor

	Total (n)	Cases (n)	Age-adjusted	Multivariate I	Multivariate II
			OR (95% CI)	OR (95% CI)	OR (95% CI)
Height (each 5 cm increment)	135,861	5,567	0.86 (0.84, 0.87)	0.77 (0.24, 0.78)	0.80 (0.30, 0.82)
Height quartiles: range (median)					
Q1: 101–157.48 (154.94)	34,084	1,906	1.00 (ref)	1.00 (ref)	1.00 (ref)
Q2: 157.50 – 162.56 (162)	34,189	1,521	0.75 (0.70-0.81)	0.66 (0.61-0.72)	0.72 (0.66-0.78)
Q3: 162.60 – 167.64 (165.10)	31,676	1,172	0.62 (0.57-0.67)	0.46 (0.43-0.51)	0.53 (0.49-0.58)
Q4: 167.89 – 210 (172)	30,345	968	0.53 (0.49-0.57)	0.32 (0.30-0.36)	0.39 (0.36-0.43)
p-value for trend			<0.0001	<0.0001	<0.0001
N=	135,861	5,567	135,775	112,182	112,182

Multivariate model I = age, pre-pregnancy weight

Multivariate model II= age, pre-pregnancy weight, race, insurance, education

*height and race interaction term statistically significant

Table 4. Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for the effect of height on risk of GDM stratified by race/ethnicity

	Non-Hispanic white		Non-Hispanic black		Hispanic		Asian/Pacific Islander	
	Cases (n)	OR (95% CI)	Cases (n)	OR (95% CI)	Cases (n)	OR (95% CI)	Cases (n)	OR (95% CI)
Height (each 5 cm increment)	2,571	0.78 (0.76, 0.80)	813	0.86 (0.81, 0.91)	1,379	0.83 (0.80, 0.86)	386	0.76 (0.70, 0.83)
Height quartiles: range (median)								
Q1: 101–157.48 (154.94)	682	1.00 (ref)	183	1.00 (ref)	678	1.00 (ref)	199	1.00 (ref)
Q2: 157.50 – 162.56 (162)	704	0.65 (0.57, 0.74)	213	0.99 (0.79, 1.24)	379	0.75 (0.65, 0.87)	120	0.72 (0.54, 0.96)
Q3: 162.60 – 167.64 (165.10)	590	0.47 (0.41, 0.54)	205	0.68 (0.54, 0.86)	236	0.61 (0.51, 0.72)	49	0.41 (0.27, 0.64)
Q4: 167.89 – 210 (172)	595	0.35 (0.30, 0.40)	212	0.59 (0.47, 0.76)	86	0.42 (0.33, 0.55)	18	0.19 (0.10, 0.38)
p-value for trend		<0.0001		<0.0001		<0.0001		<0.0001

Models adjust for age, pre-pregnancy weight, race, insurance, education

Table 5. Race stratified mean differences in the Consortium on Safe Labor cohort and by meta-analysis

Race/Ethnicity	No. of Studies	No. of GDM Women	No. of NGT Women	Mean Difference (95% Confidence Interval)	P-Value
<u>Consortium on Safe Labor</u>					
Non-Hispanic white	n/a	2,571	70,924	-1.31 (-1.03, -1.59)	0.0001
Non-Hispanic black	n/a	813	24,365	0.14 (-0.37, 0.64)	0.58
Hispanic	n/a	1,379	22,205	-0.67 (-0.29, -1.05)	0.0006
Asian/Pacific Islander	n/a	386	3,804	-1.64 (-0.91, -2.36)	<0.0001
Overall	n/a	5,567	138,857	-1.54 (-1.34, -1.74)	P<0.0001
<u>Meta-analysis</u>					
European Caucasian	9	5276	83278	-1.00 (-1.57, -0.43)	0.0006
African/Afr. American	5	1466	26170	-0.29 (-1.15, 0.57)	0.50
Hispanic	7	4304	34271	-1.22 (-1.72, -0.71)	<0.0001
Asian	10	2083	42791	-0.94 (-1.43, -0.45)	0.0002
ALL	38	15761	205828	-1.13 (-1.49, -0.78)	<0.0001

Supplemental materials

Supplemental Table S1. Summary of meta-analysis of 38 studies with information on height by GDM status

<u>Author (Date)</u>	<u>Country (Period)</u>	<u>Screening Method</u>	<u>GDM Dx Criteria</u>	<u># Participants</u>	
Al-Shawaf (1988)	Saudi Arabia (N/A)	Universal 75g GCT	WHO	1089	1
Anastasiou (1998)	Greece (1990-1996)	None (all OGTT)	NDDG	1787	68
Bell (1990)	US (1983+)	N/A	N/A	606	34
Bo (2003)	Italy (1999-2001)	Universal 50g GCT	C&C	700	250
Catalano (2009)	US (1990-1999)	Universal 50g GCT	NDDG	89	3
Caudana (2011)	Mexico (2006-2007)	None (all OGTT)	C&C	450	4
Corcoy (2004)	Spain (1986-1992)	Universal 50g GCT	ADA	2552	16
de Santis (2010)	Italy (2000-2004)	Universal 50g GCT	C&C	214	17
DiCianni (2007)	Italy (2001-2005)	Universal 50g GCT	C&C	4053	72
Gonzalez-Clemente (2007)	Spain (2001-2002)	Universal 50g GCT	NDDG	335	4
Hill (2005)	South India (1997-1998)	None (all OGTT)	C&C	785	4
Iqbal (2007)	Pakistan (2002-2004)	Universal 75g GCT	ADA	612	49
Jang (1995)	Korea (1991-1993)	Universal 50g GCT	NDDG	3512	8
Jang (1998)	Korea (1991-1994)	Universal 50g GCT	NDDG	8863	17
Jimenez-Moleon (2002)	Spain (1995)	Universal 50g GCT	ADA	1962	6
Kale (2005)	India (1998-2003)	High Risk: 75g GCT	WHO	350	16
Katzuky-Willer (2008)	Austria (2001-2004)	None (all OGTT)	Modified C&C	1466	672
Keshavarz (2005)	Iran (1999-2001)	Universal 50g GCT	C&C	1310	6
Lao (2003)	Hong Kong (N/A)	High Risk or IGT: OGTT	WHO	2149	1155
Magee (1993)	US (1985-1986)	None (all OGTT)	C&C or NDDG	886	10
Mambolo (2007)	South Africa (1999-2000)	None (all OGTT)	WHO	262	23
Mello (1997)	Italy (1989-1992)	Universal 50g GCT	C&C	1615	17
Meza (1995)	Mexico (1991-1992)	None (all OGTT)	O'Sullivan	519	5
Moses (2004)	Australia (2003)	None (all OGTT)	ADIPS	222	6
Naylor (1996)	Canada (1989-1992)	None (all OGTT)	C&C or NDDG	3778	25
Phaloprakarn (2008)	Thailand (2005-2006)	Universal 50g GCT	NDDG	909	15
Pirkola (2010)	Finland (1985-1986)	None (all OGTT)	Custom	6574	12
Rey (1996)	Canada (1992)	Universal 50g GCT	Custom	528	17
Ricart (2005)	Spain (2002)	Universal 50g GCT	ADA or NDDG	9270	10
Saisho (2010)	Japan (2004-2009)	Universal 50g GCT	JSOG	277	5
Saldana (2004)	US (1995-2000)	None (all OGTT)	C&C	1698	8
Seyoum (1999)	Ethiopia (N/A)	None (all OGTT)	WHO	890	3
Sugaya (2000)	Japan (1991-1995)	None (all OGTT)	WHO or JSOG	416	13
Tabak (2002)	Hungary (1999-2000)	None (all OGTT)	WHO	611	9

Tan (2007)	Malaysia (2006)	Universal 50g GCT	WHO	521	18
Yang (2002)	China (1998-1999)	Universal 50g GCT	WHO	9286	177
Yang (2009)	China (2006)	Universal 50g GCT	ADA	16286	70
Current study	US (2002-2007)	Site specific	Site specific	138857	55

Abbreviations:

GCT = glucose challenge test (i.e. glucose screen), OGTT = oral glucose tolerance test

GDM diagnostic criteria: ADA = American Diabetes Association (ADA), C&C = Carpenter & Coustan, NDDG = National Diabetes Data Group, WHO = World Health Organization

GDM = gestational diabetes mellitus, IGT = impaired glucose tolerance

Figure S1. Study specific and pooled mean difference (95% confidence interval) in height comparing women with GDM and women without GDM in 38 studies

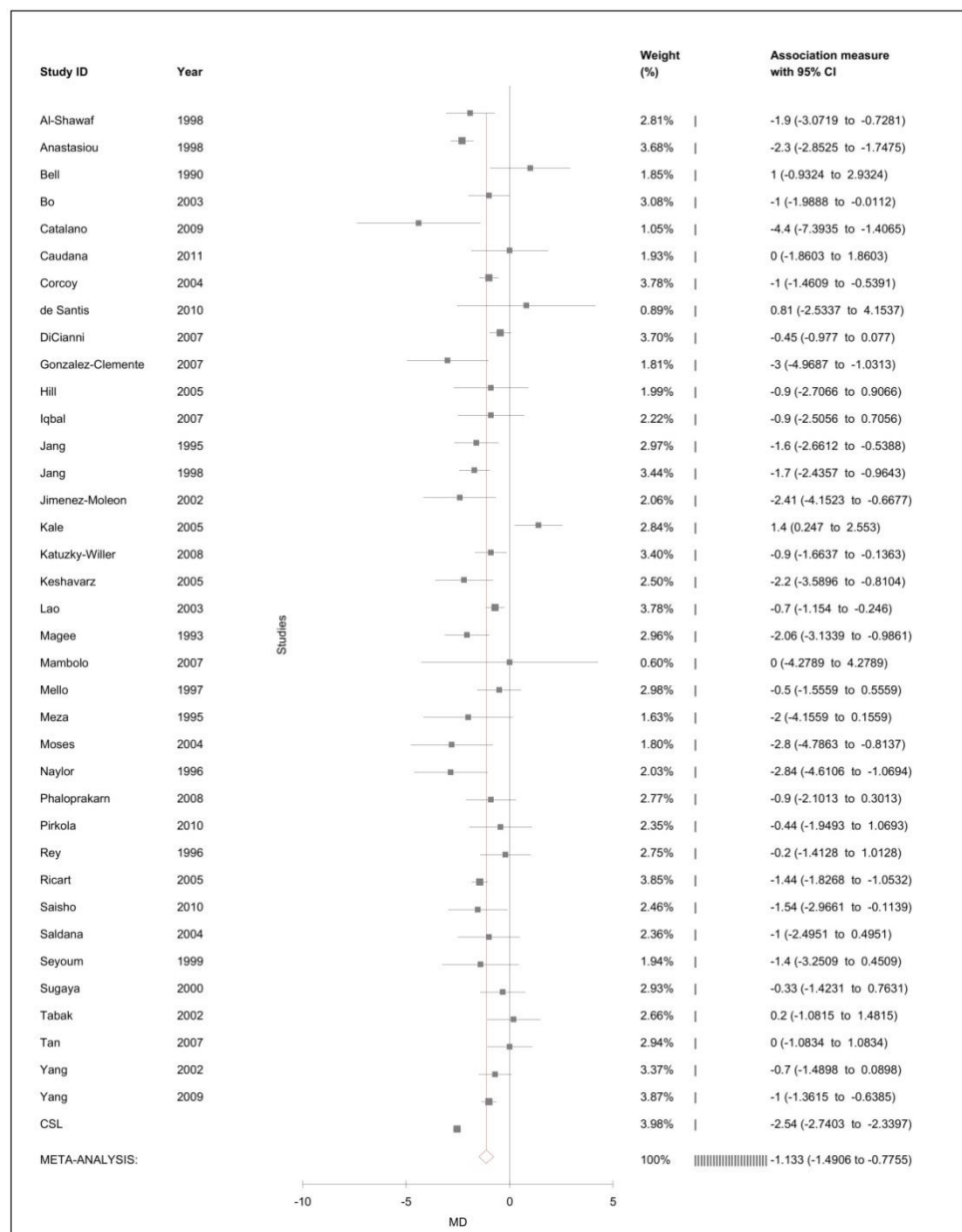
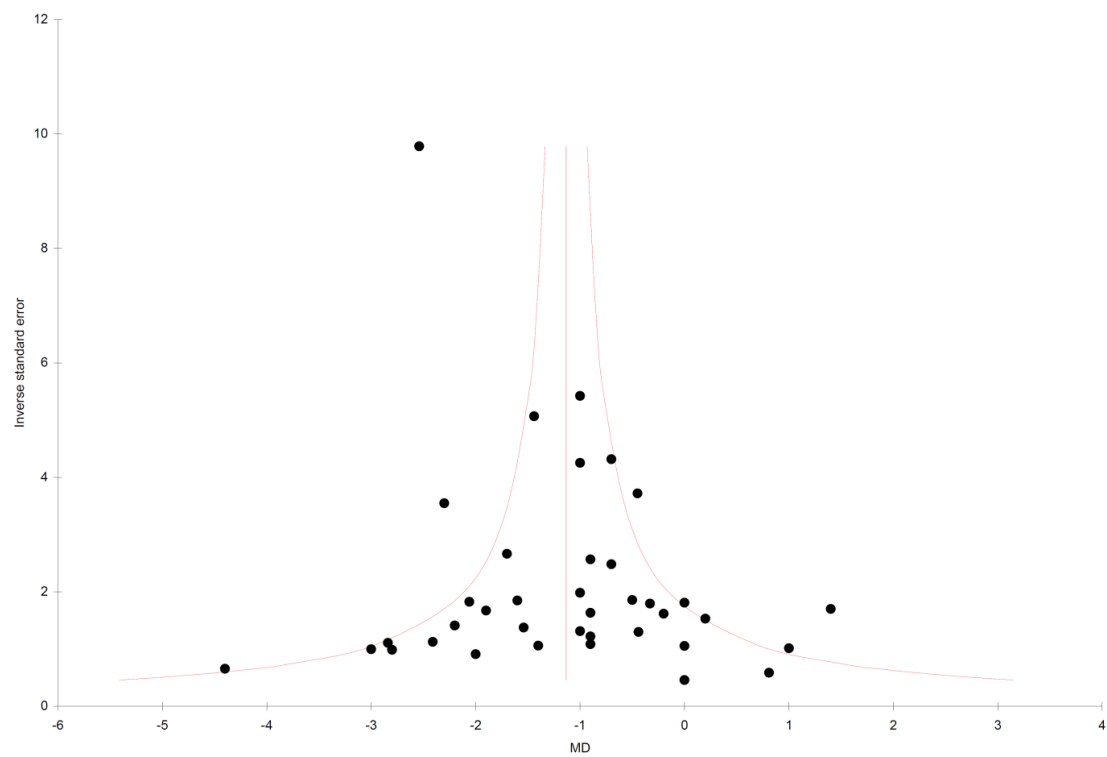


Figure S2. Funnel plot examining publication bias of included studies of height and GDM



References

1. American Diabetes, A., *Gestational diabetes mellitus*. Diabetes Care, 2004. **27 Suppl 1**: p. S88-90.
2. Ferrara, A., *Increasing prevalence of gestational diabetes mellitus: a public health perspective*. Diabetes Care, 2007. **30 Suppl 2**: p. S141-6.
3. Group, H.S.C.R., et al., *Hyperglycemia and adverse pregnancy outcomes*. N Engl J Med, 2008. **358**(19): p. 1991-2002.
4. Reece, E.A., G. Leguizamon, and A. Wiznitzer, *Gestational diabetes: the need for a common ground*. Lancet, 2009. **373**(9677): p. 1789-97.
5. Bellamy, L., et al., *Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis*. Lancet, 2009. **373**(9677): p. 1773-9.
6. Rudra, C.B., et al., *Weight characteristics and height in relation to risk of gestational diabetes mellitus*. Am J Epidemiol, 2007. **165**(3): p. 302-8.
7. J., O., *Are short women at risk for gestational diabetes mellitus?* . European Journal of Endocrinology, 2010. **165**(3): p. 302-308.
8. Kousta, E., et al., *Women with a history of gestational diabetes of European and South Asian origin are shorter than women with normal glucose tolerance in pregnancy*. Diabet Med, 2000. **17**(11): p. 792-7.
9. Jang, H.C., et al., *Short stature in Korean women: a contribution to the multifactorial predisposition to gestational diabetes mellitus*. Diabetologia, 1998. **41**(7): p. 778-83.
10. Branchtein, L., et al., *Short stature and gestational diabetes in Brazil*. Brazilian Gestational Diabetes Study Group. Diabetologia, 2000. **43**(7): p. 848-51.
11. Anastasiou, E., et al., *Decreased stature in gestational diabetes mellitus*. Diabetologia, 1998. **41**(9): p. 997-1001.
12. Bax, L., et al., *Development and validation of MIX: comprehensive free software for meta-analysis of causal research data*. BMC Med Res Methodol, 2006. **6**: p. 50.
13. *Statistical Analysis Software*, 2008, SAS Institute Inc: Cary, NC.
14. Al-Shawaf, T., A. Akiel, and S.A. Moghraby, *Gestational diabetes and impaired glucose tolerance of pregnancy in Riyadh*. Br J Obstet Gynaecol, 1988. **95**(1): p. 84-90.
15. Bell, D.S., et al., *Risk factors for gestational diabetes in black population*. Diabetes Care, 1990. **13**(11): p. 1196-201.
16. Bo, S., et al., *Obesity or diabetes: what is worse for the mother and for the baby?* Diabetes Metab, 2003. **29**(2 Pt 1): p. 175-8.
17. Catalano, P.M., et al., *Perinatal risk factors for childhood obesity and metabolic dysregulation*. Am J Clin Nutr, 2009. **90**(5): p. 1303-13.
18. Corcoy, R., et al., *Is selective screening for gestational diabetes mellitus worthwhile everywhere?* Acta Diabetol, 2004. **41**(4): p. 154-7.
19. Di Cianni, G., et al., *Normal glucose tolerance and gestational diabetes mellitus: what is in between?* Diabetes Care, 2007. **30**(7): p. 1783-8.
20. Gonzalez-Clemente, J.M., et al., *Increased cholesterol intake in women with gestational diabetes mellitus*. Diabetes Metab, 2007. **33**(1): p. 25-9.

21. Hill, J.C., et al., *Glucose tolerance in pregnancy in South India: relationships to neonatal anthropometry*. Acta Obstet Gynecol Scand, 2005. **84**(2): p. 159-65.
22. Iqbal, R., et al., *Increased body fat percentage and physical inactivity are independent predictors of gestational diabetes mellitus in South Asian women*. Eur J Clin Nutr, 2007. **61**(6): p. 736-42.
23. Jang, H.C., et al., *Screening for gestational diabetes mellitus in Korea*. Int J Gynaecol Obstet, 1995. **51**(2): p. 115-22.
24. Jimenez-Moleon, J.J., et al., *Impact of different levels of carbohydrate intolerance on neonatal outcomes classically associated with gestational diabetes mellitus*. Eur J Obstet Gynecol Reprod Biol, 2002. **102**(1): p. 36-41.
25. Kautzky-Willer, A., et al., *The impact of risk factors and more stringent diagnostic criteria of gestational diabetes on outcomes in central European women*. J Clin Endocrinol Metab, 2008. **93**(5): p. 1689-95.
26. Keshavarz, M., et al., *Gestational diabetes in Iran: incidence, risk factors and pregnancy outcomes*. Diabetes Res Clin Pract, 2005. **69**(3): p. 279-86.
27. Lao, T.T. and L.F. Ho, *Does maternal glucose intolerance affect the length of gestation in singleton pregnancies?* J Soc Gynecol Investig, 2003. **10**(6): p. 366-71.
28. Magee, M.S., et al., *Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity*. JAMA, 1993. **269**(5): p. 609-15.
29. Mamabolo, R.L., et al., *Prevalence of gestational diabetes mellitus and the effect of weight on measures of insulin secretion and insulin resistance in third-trimester pregnant rural women residing in the Central Region of Limpopo Province, South Africa*. Diabet Med, 2007. **24**(3): p. 233-9.
30. Mello, G., et al., *Anthropometric characteristics of full-term infants: effects of varying degrees of "normal" glucose metabolism*. J Perinat Med, 1997. **25**(2): p. 197-204.
31. Meza, E., et al., *Gestational diabetes in a Mexican-U.S. border population: prevalence and epidemiology*. Rev Invest Clin, 1995. **47**(6): p. 433-8.
32. Naylor, C.D., et al., *Cesarean delivery in relation to birth weight and gestational glucose tolerance: pathophysiology or practice style?* Toronto Trihospital Gestational Diabetes Investigators. JAMA, 1996. **275**(15): p. 1165-70.
33. Phaloprakarn, C. and S. Tangjitgamol, *Diagnosis of gestational diabetes mellitus using a modified 100 g oral glucose tolerance test*. J Perinatol, 2008. **28**(1): p. 7-11.
34. Pirkola, J., et al., *Prepregnancy overweight and gestational diabetes as determinants of subsequent diabetes and hypertension after 20-year follow-up*. J Clin Endocrinol Metab, 2010. **95**(2): p. 772-8.
35. Rey, E., D. Monier, and M.C. Lemonnier, *Carbohydrate intolerance in pregnancy: incidence and neonatal outcomes*. Clin Invest Med, 1996. **19**(6): p. 406-15.
36. Ricart, W., et al., *Potential impact of American Diabetes Association (2000) criteria for diagnosis of gestational diabetes mellitus in Spain*. Diabetologia, 2005. **48**(6): p. 1135-41.
37. Saldana, T.M., A.M. Siega-Riz, and L.S. Adair, *Effect of macronutrient intake on the development of glucose intolerance during pregnancy*. Am J Clin Nutr, 2004. **79**(3): p. 479-86.

38. Seyoum, B., et al., *Prevalence of gestational diabetes mellitus in rural pregnant mothers in northern Ethiopia*. Diabetes Res Clin Pract, 1999. **46**(3): p. 247-51.
39. Sugaya, A., et al., *Comparison of the validity of the criteria for gestational diabetes mellitus by WHO and by the Japan Society of Obstetrics and Gynecology by the outcomes of pregnancy*. Diabetes Res Clin Pract, 2000. **50**(1): p. 57-63.
40. Tabak, A.G., et al., *Height and gestational diabetes mellitus*. Diabet Med, 2002. **19**(4): p. 344-5.
41. Tan, P.C., L.P. Ling, and S.Z. Omar, *Screening for gestational diabetes at antenatal booking in a Malaysian university hospital: the role of risk factors and threshold value for the 50-g glucose challenge test*. Aust N Z J Obstet Gynaecol, 2007. **47**(3): p. 191-7.
42. Yang, H., et al., *Risk factors for gestational diabetes mellitus in Chinese women: a prospective study of 16,286 pregnant women in China*. Diabet Med, 2009. **26**(11): p. 1099-104.
43. Yang, X., et al., *Gestational diabetes mellitus in women of single gravidity in Tianjin City, China*. Diabetes Care, 2002. **25**(5): p. 847-51.
44. Saisho, Y., et al., *Beta cell dysfunction and its clinical significance in gestational diabetes*. Endocr J, 2010. **57**(11): p. 973-80.
45. de Santis, M.S., et al., *Growth of fetal lean mass and fetal fat mass in gestational diabetes*. Ultrasound Obstet Gynecol, 2010. **36**(3): p. 328-37.
46. Lopez Caudana, A.E., et al., *Prediction of alterations in glucose metabolism by glucose and insulin measurements in early pregnancy*. Arch Med Res, 2011. **42**(1): p. 70-6.
47. Kale SD, K.S., Lubree HG, Meenakumari K, Deshpande VU, Rege SS, et al., *Characteristics of gestational diabetic mothers and their babies in an Indian diabetes clinic*. Journal of the Association of Physicians of India, 2005. **53**: p. 857-863.
48. Moses, R., *Is there a relationship between leg length and glucose tolerance?*. Diabetes Care, 2004. **27**(5): p. 1033-1035.
49. Wang, Z., et al., *Anthropometric indices and their relationship with diabetes, hypertension and dyslipidemia in Australian Aboriginal people and Torres Strait Islanders*. Eur J Cardiovasc Prev Rehabil, 2007. **14**(2): p. 172-8.
50. Srensen, H., *Birth weight and length as predictors for adult height*. American Journal of Epidemiology, 1999. **149**(8): p. 726-729.
51. Yeung, E.H., et al., *Life-course weight characteristics and the risk of gestational diabetes*. Diabetologia, 2010. **53**(4): p. 668-78.
52. Barker, D.J., *The developmental origins of insulin resistance*. Horm Res, 2005. **64 Suppl 3**: p. 2-7.
53. Gallou-Kabani, C. and C. Junien, *Nutritional epigenomics of metabolic syndrome: new perspective against the epidemic*. Diabetes, 2005. **54**(7): p. 1899-906.
54. Inoue, T., et al., *Effect of intrauterine undernutrition during late gestation on pancreatic beta cell mass*. Biomed Res, 2009. **30**(6): p. 325-30.
55. Portha, B., A. Chavey, and J. Movassat, *Early-life origins of type 2 diabetes: fetal programming of the beta-cell mass*. Exp Diabetes Res, 2011. **2011**: p. 105076.
56. Vaessen, N., et al., *A polymorphism in the gene for IGF-I: functional properties and risk for type 2 diabetes and myocardial infarction*. Diabetes, 2001. **50**(3): p. 637-42.
57. Hattersley, A.T., et al., *Mutations in the glucokinase gene of the fetus result in reduced birth weight*. Nat Genet, 1998. **19**(3): p. 268-70.
58. Freathy, J., *Type 2 diabetes risk alleles are associated with reduced size at birth*. Diabetes, 2009. **58**(6): p. 1428-1433.

59. Hunsberger, M., *Racial/ethnic disparities in gestational diabetes mellitus: findings from a population-based survey*. Women's health issues, 2010. **20**(5): p. 323-8.

