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Systematic Review

Risk of type 2 diabetes mellitus after gestational diabetes mellitus: A systematic review & meta-analysis

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***Background &objectives*: Women with gestational diabetes are at an increased risk of being diagnosed as type 2 diabetes, but the postpartum screening rate is low. To provide evidence-based data for health providers and promote postpartum screening, this systematic review and meta-analysis was conducted to access the risks of type 2 diabetes mellitus (T2DM) diagnosis after gestational diabetes mellitus (GDM) in different demographic and maternal subgroups.**

***Methods*: MEDLINE, Embase and Cochrane Library were searched systematically. Unadjusted relative risks (RRs) and 95 per cent confidence intervals (CIs) were calculated and pooled using a random-effects model. Heterogeneity was assessed with Cochrane's *Q* text and by calculating I^2 values. Subgroup analyses were conducted to address the disparities of type 2 diabetes conversion after gestational diabetes in different demographic and maternal subgroups.**

***Results*: 1809 publications were screened and 39 cohort studies including 2,847,596 women were selected. In these studies, 78,893 women were diagnosed as T2DM at six weeks or later after delivery. The unadjusted RRs of women diagnosed T2DM at six weeks or later after delivery ranged from 1.32 (95% CI, 0.46-3.37) to 47.25 (95% CI, 2.95-758.01) with a pooled unadjusted RR of 8.92 (95% CI, 7.84-10.14). Older women, women with a family history of diabetes, Black and non-Hispanic White women and women living in Europe and South-East Asia had a higher risk of developing T2DM after GDM.**

***Interpretation & conclusions*: It is suggested that healthcare providers may focus on older women with GDM and women with GDM and a family history of diabetes. Black and non-Hispanic White women with GDM may receive more attention, and healthcare providers, especially those in Europe and South-East Asia, may pay more attention to preventive measures for postpartum T2DM.**

Key words Blood glucose - gestational diabetes mellitus - OGTT screening - postpartum - type 2 diabetes mellitus

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first detected during pregnancy. The prevalence of GDM has increased more than 30 per cent over the past two decades[1]. As reported, the median prevalence of GDM globally ranges from 1.8 to 22.3 per cent[2]. GDM is associated with short and long-term adverse outcomes of both mothers and their respective offsprings, and is a well - known risk factor

for developing type 2 diabetes mellitus (T2DM) after delivery. The rates of T2DM diagnosis after GDM range from two to 70 per cent, from six weeks to 28 yr postpartum[3]. Increasing prevalence of GDM and T2DM and their related complications lead to huge healthcare and economic costs[4,5].

In light of these risks and the opportunity for preventive intervention, women with GDM are advised to have oral glucose tolerance test (OGTT) assessed at 6-12 wk postpartum[6]. However, studies reported that postpartum screening rates range from 13 to 82 per cent varying across geography, ethnicity and practice patterns. and is underused[7-9]. Furthermore, while there are various barriers of postpartum diabetes screening patient compliance with diabetes screening recommendations are inadequate[10]. Systematic review and meta-analysis previously showed that women with a history of GDM have a sevenfold risk of being diagnosed as T2DM than those without although the results of this study were synthesized despite heterogenous differences[11]. In the present study the relative risks (RRs) among all selected studies were included and sensitivity and subgroup analyses were conducted to identify the sources of the heterogeneity. Moreover, risks of being diagnosed as T2DM vary widely[2], and therefore the disparities of T2DM diagnosis after GDM in different demographic subgroups to help health providers focus on the high-risk patient were assessed.

Material & Methods

Literature search and inclusion criteria: Twenty studies were hand-searched from the previous systematic review[11] and did an electronic search of MEDLINE and Embase from January 1, 2009 to July 31, 2019 and did not apply any restrictions. The search of the Cochrane Library was from inception to July 31, 2019, without restrictions. Search terms were a combination of 'gestational diabetes mellitus', 'pregnancy diabetes mellitus', 'diabetes, gestational', 'type 2 diabetes mellitus', 'diabetes mellitus, type 2' and 'non-insulin dependent diabetics mellitus'. In addition to the electronic search, reference lists and citations of relevant reviews and articles were hand-searched.

Prospective and retrospective cohort studies (PCS and RCS) in which women were diagnosed with GDM and normal blood glucose were searched for. The outcome was the diagnosis of T2DM at six weeks or later after delivery. The criteria of GDM and T2DM were not restricted. Studies of women with pre-existing diabetes mellitus were excluded.

Methodological quality assessment: The quality of included studies was assessed by a standardized checklist based on the Newcastle–Ottawa Scale (NOS)[12]. The NOS is a star rating system (0-9 stars) used for observational studies. For cohort studies, the criteria cover three domains: selection of participants, between-group comparability and ascertainment of outcome. Each item can get one star in selection and outcome domains and two stars in comparability domain if appropriate methods were reported[12,13]. According to the final score, studies were classified as high (c7-9 stars), medium (5-6 stars) or low (0-4 stars) quality. Low quality (c7) study might reduce the credibility of results, so we excluded low quality studies in this meta-analysis.

Data abstraction: Participant and study characteristics and cumulative incidences of T2DM in the GDM and non-GDM groups were independently extracted by two authors using standardized tables. Disagreements were solved by discussion with the third author. If more than one report based on the same population was identified, the one with the most relevant and complete information was selected.

Statistical analysis: A Meta-analysis was carried out using Stata/MP (Version 14.0, StataCorp LLC, Texas, USA). Unadjusted, pooled relative risks (RRs) and 95 per cent confidence intervals (CIs) were calculated. Heterogeneity was assessed with Cochrane's Q text and by calculating I^2 values. High heterogeneity was defined by either $P \leq 0.10$ or $I^2 \geq 60$ per cent, median heterogeneity was defined by either $P \leq 0.10$ or 30 per cent $\leq I^2 <$ 60 per cent and little or no heterogeneity was defined by either $P > 0.10$ or $I^2 <$ 30 per cent[14]. In cases of high heterogeneity, a random-effects model was used. Sensitivity analyses were conducted to identify the outliers by testing the outcome robustness after one study was removed. Subgroup analyses were performed to explore the sources of heterogeneity among studies by stratification according to mean maternal age, body mass index (BMI) at follow up, race/ethnicity, region, family history of diabetes mellitus, time interval of postpartum OGTT performed, GDM criteria, T2DM criteria and number of confounders matched. Begg's test and Egger's test were performed to investigate small sample bias and publication bias. A $P<0.05$ was considered statistically significant.

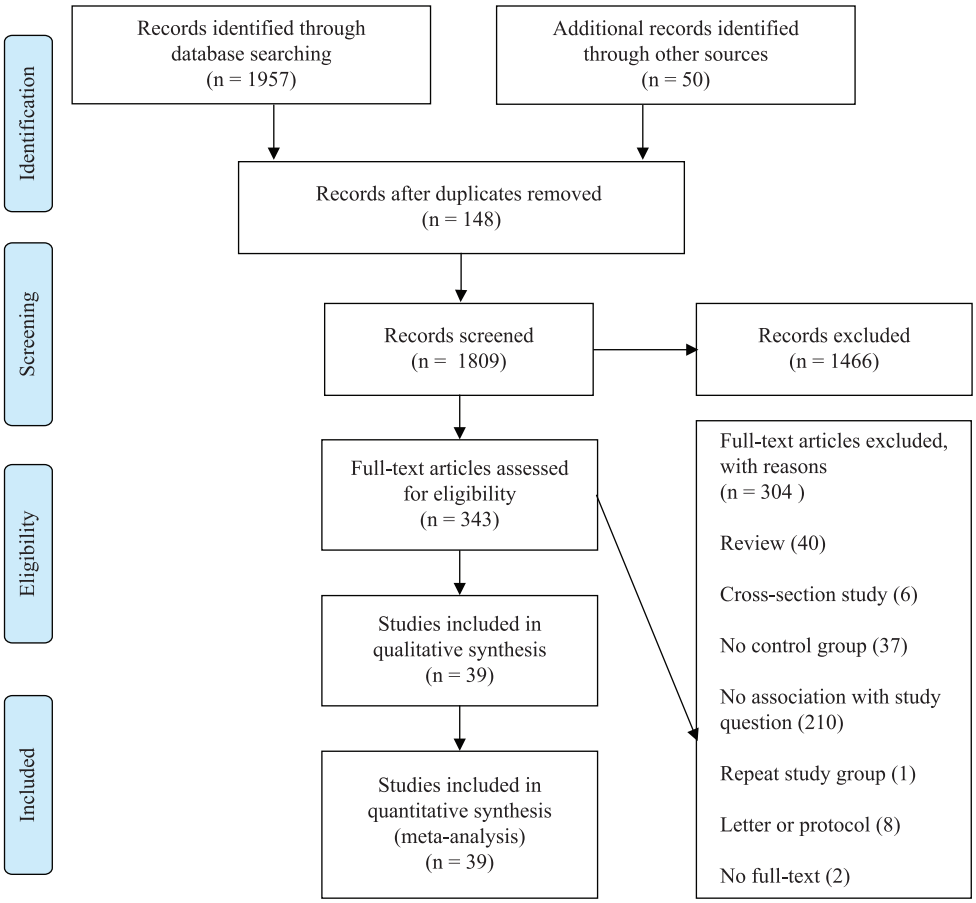

Fig. 1. PRISMA flow diagram showing literature search.

Results

Selection of studies: In total, 1957 records were identified through electronic database searching, 30 additional publications were identified through reference lists and 20 publications were included from a previous systematic review. Altogether,1809 titles and abstracts were screened after 198 duplicates were removed. Of 343 publications that were selected for full-text review, 304 were excluded for various reasons. Finally, 39 cohort studies involving 2,847,596 women were included in this meta-analysis. In these studies, 78,893 women were diagnosed as T2DM at six weeks or later after delivery (Fig. 1).

Characteristics of the studies: A total of 26 retrospective[4,15-39] and 13 prospective cohort studies[5,40-51] conducted in different countries were considered for this meta-analysis. The participants varied widely in maternal age, BMI, family history of diabetes mellitus, ethnicity, length of follow up and time interval of postpartum OGTT performed. Moreover, diagnostic criteria of GDM and T2DM varied by country as well. In 15.4 per cent (6/39) of studies, the dropout rate was under 30 per cent. In 5.1 per cent (2/39) of studies, the dropout rate is between 30 and 60 per cent. In 38.5 per cent (15/39) of studies, none of the women dropped out. In 41.0 per cent (16/39) studies, the dropout rate was not recorded. In 76.9 per cent (30/39) of studies, women in two groups were matched by different confounders. In 23.1 per cent (9/39) of studies, confounders adjustment was not recorded (Table).

As per the NOS scores as shown in Fig. 2, 87 per cent (34/39) of studies included in this meta-analysis were of high quality, and 13 per cent (5/39) studies were of medium quality. The unadjusted RRs of women diagnosed as T2DM at six weeks or later after delivery ranged from 1.32 (95% CI, 0.46-3.37) to 47.25 (95% CI, 2.95-758.01), with a pooled unadjusted RR of 8.92 (95% CI, 7.84-10.14).The heterogeneity was defined as high with $P<0.01$, and $I^2=94.1$ per cent (Fig. 3). Sensitivity analyses were conducted by recalculating the pooled RRs with included studies removed one by one. The results indicated that the pooled RRs were

Table. Characteristics of 39 studies included in the meta-analysis

Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Daly *et al*[15], 2018	RCS	Europe	Other	33/33	Not recorded	Not recorded	Three years	Not recorded	Clinical codes	Not recorded	Age
Shen *et al*[40], 2018	PCS	Western Pacific	Asian	29.7/30.1	22.9/24.2	27.1/35.7	4.4 yr	WHO, 1999	ADA, 2018	Not recorded	Smoking exposure
Herath *et al*[16], 2017	RCS	South-East Asia	Other	31.7/27.7	Not recorded	Not recorded	One year	WHO, 1999	WHO, 1999	Not recorded	Ethnicity, education, family income per month, sex of infant, exclusive breastfeeding duration
Ajala *et al*[17], 2015	RCS	North America	Other	32.1/31.4	28.9/26.6	52.2/52.5	One year	CDA, 2008	Local	None	Age, ethnicity, BP, smoking exposure, amount of alcohol consumed and time of physical activity
Cormier *et al*[4], 2015	RCS	North America	Other	36.4/35.6	27.7/25.6	Not recorded	Three-four years	Not recorded	CDA, 2013	None	Age, parity, time to follow up after delivery
Hakkarainen *et al*[5], 2015	PCS	Europe	Non-Hispanic White	30.8	26.88/28.38	Not recorded	Not recorded	Local	ADA, 2011	Not recorded	Infant birth weight
Pintaudi *et al*[41], 2015	PCS	Europe	Hispanic	35.7	Not recorded	Not recorded	Not recorded	ADA, 2004	Local	Not recorded	Propensity score

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Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Mai *et al*[18], 2014	RCS	Western Pacific	Asian	30.6/27.2	22.7/21.5	19.5/6.3	Six months	ADA, 2004	ADA, 2010	None	Family history, parity, length of follow up, DBP and hip circumference
Barden *et al*[42], 2013	PCS	Western Pacific	Non-Hispanic White	32.9/32.6	Not recorded	60.70/53.4	Six months	Australasian diabetes, 1998	Local	27.90	Not recorded
Feig *et al*[19], 2013	RCS	North America	Other	28.8	Not recorded	Not recorded	5.4 yr	Canadian Institute for Health Information Discharge Abstract Database	Ontario Diabetes Database	Not recorded	Not recorded
Hummel *et al*[20], 2013	RCS	Europe	Non-Hispanic White	Not recorded	Not recorded	Not recorded	Not recorded	German Diabetes Association, 2001	German Diabetes Association, 2011	None	Not recorded
Anderberg *et al*[21], 2012	RCS	Europe	Non-Hispanic White	Median 32	Not recorded	Not recorded	Not recorded	Local	Not recorded	None	Age, year of delivery and residence
Mukerji *et al*[22,] 2012	RCS	North America	Other	20-49	Not recorded	Not recorded	Not recorded	Ontario Ministry of Health and Long-Term Care, Registered Persons Database	Ontario Diabetes Database	Not recorded	Not recorded

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Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Tam *et al*[43], 2012	PCS	Western Pacific	Asian	28.8/28.2	24.7/24.4	Not recorded	Not recorded	WHO, 1999	WHO, 1999	31.50	Age, parity, smoking exposure, BMI, waist-hip ratio, fat (%), LDL, HDL, cholesterol and metabolic syndrome
Tehrani *et al*[23], 2012	RCS	Middle East	Other	33.6/33.7	30.0/29.8	37.9/34.5	Not recorded	WHO, 1998	ADA, 2009	Not recorded	Age, BMI, parity, family history, BP, blood glucose, cholesterol, LDL and HDL
Wang *et al*[44], 2012	PCS	North America	Other	26.8/24.3	Not recorded	Not recorded	Not recorded	ADA, 2004 or WHO, 1998	ADA, 2004 or WHO, 1998	Not recorded	Postpartum DBP, current smoker and annual family income
Akinci *et al*[24], 2011	RCS	Europe	Non-Hispanic White	31.9/31.4	26.51/21.79	46.7/26.8	One year	Carpenter and Coustan	ADA, 2009	None	Age and length of followup
Ramezani *et al*[45], 2011	PCS	Middle East	Other	36.3	Not recorded	Not recorded	Not recorded	ADA, 2009	ADA, 2009	None	Not recorded
Xiang *et al*[25], 2011	RCS	North America	Other	32.4/32.3	Not recorded	Not recorded	Not recorded	Carpenter and Coustan	ADA, 2010	4.82	Ethnicity
Feig *et al*[26], 2008	RCS	North America	Non-Hispanic White	29.3	Not recorded	Not recorded	Six months	Canadian Institute for Health Information Discharge Information	Ontario Diabetes Database	3.90	Not recorded

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Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Lee *et al*[27], 2008	RCS	Western Pacific	Asian	33.6	23.5/22.5	36.5/11.9	Six weeks	NDDG, 1979	Local	Not recorded	Age, smoking exposure, hip circumference and DBP
Madarász *et al*[28], 2008	RCS	Europe	Non-Hispanic White	33.1/30.0	Not recorded	Not recorded	Not recorded	WHO, 1999	WHO, 1999	Not recorded	Not recorded
Vambergue *et al*[29], 2008	RCS	Europe	Other	27.0/28.8	Not recorded	Not recorded	Six years	Carpenter and Coustan	ADA, 1997	29	Pregnancy-induced hypertension and caesarean section
Ferraz *et al*[46], 2007	PCS	South America	Hispanic	26.9/25.1	26.34/25.33	Not recorded	6.2 yr	WHO, 1999	WHO, 1999	None	BMI, BP and blood glucose at follow up
Gunderson *et al*[47], 2007	PCS	North America	Other	18-30	24.45	Not recorded	5-20 yr	Obstetric Laboratory Reports	ADA, 1997	28	Age, smoking exposure and marital status
Krishnaveni *et al*[48], 2007	PCS	South-East Asia	Other	19.6/33.1	25.5/23.5	57.1/27.2	Six months	Carpenter and Coustan	WHO, 1999	None	Parity, BMI at follow up, height, family history and waist-hip ratio
Lee *et al*[30], 2007	RCS	Western Pacific	Other	30.7/30.5	Not recorded	16.7/24.0	Six weeks	Australian Diabetes in Pregnancy Society Guidelines	WHO, 1998	56.20	Height, parity and Infant birth weight
Morimitsu *et al*[49], 2007	PCS	South America	Other	32/27	29.6/24.4	Not recorded	Four-six months	ADA, 1997	ADA, 1997	Not recorded	Age, LDL and HDL
Järvelä *et al*[31], 2006	RCS	Europe	Non-Hispanic white	31.6/31.3	Not recorded	Not recorded	Not recorded	Finnish Diabetes Association	Medication for T2DM linked to database 13	Not recorded	Age, parity and date of delivery

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Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Albareda *et al*[50], 2003	PCS	Europe	Hispanic	30.7/30.4	24.5/24.8	53.7/43.9	Six weeks	Second and Third Workshop-Conferences on Gestational Diabetes	WHO, 1998	Not recorded	Family history, subsequent pregnancies and BMI at followup
Aberg *et al*[32], 2002	RCS	Europe	Hispanic	35.7	Not recorded	Not recorded	One year	ADA, 2004	Local	Not recorded	Age, parity, pregnancy weight, pregnancy duration and infant birth weight
Linné *et al*[33], 2002	RCS	Europe	Non-Hispanic white	32.6/30.6	25.7/24.7	Not recorded	Not recorded	Local	Local	None	Age, weight before first pregnancy, fat (%), BP, cholesterol, LDL, HDL and number of children
Bian *et al*[34], 2000	RCS	Western Pacific	Asian	29	Not recorded	Not recorded	5-10 yr	NDDG, 1979	WHO, 1985	None	Age, social background and Ga of birth
Ko *et al*[35], 1999	RCS	Western Pacific	Asian	34.0/34.4	22.7/24.8	Not recorded	Six weeks	Local	WHO, 1985	None	Age
Osei *et al*[36], 1998	RCS	North America	Black	31.3/36.0	34/27.0	Not recorded	Not recorded	NDDG, 1979	NDDG, 1979	None	Age, BMI, fat (%) and lean body mass
Damm *et al*[37], 1994	RCS	Europe	Non-Hispanic white	30.1/26.7	21.0/23.1	Not recorded	Two months	Local	WHO, 1985	19.90	Not recorded

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Author	Study type	Region	Race/ ethnicity	Mean maternal age (yr; overall or GDM/non-GDM)	BMI at followup (kg/m^2; overall or GDM/non-GDM)	Family history (GDM/ non-GDM, %)	Time interval of postpartum OGTT performed	GDM criteria	T2DM criteria	Dropout rate (%)	Confounders matched
Benjamin *et al*[38], 1993	RCS	North America	Other	27.2/26.5	Not recorded	Not recorded	1-10 yr	Local	NDDG, 1979	None	Age, BMI, parity and length of follow up
O'Sullivan *et al*[51], 1984	PCS	North America	Other	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	WHO, 1985	Not recorded	Not recorded
Persson *et al*[39], 1991	RCS	Europe	Non-hispanic white	31/30	24.18/21	Not recorded	Not recorded	WHO, 1985	WHO, 1985	None	Pre-pregnancy weight, Ga at OGTT and Infant birth weight

Ga, gestational age; RCS, retrospective cohort studies; PCS, prospective cohort studies; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; BMI, body mass index; T2DM, type 2 diabetes mellitus; NDDG, national diabetes data group; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; DBP, diastolic blood pressure; ADA, age discrimination Act; CDA, Canadian diabetes association

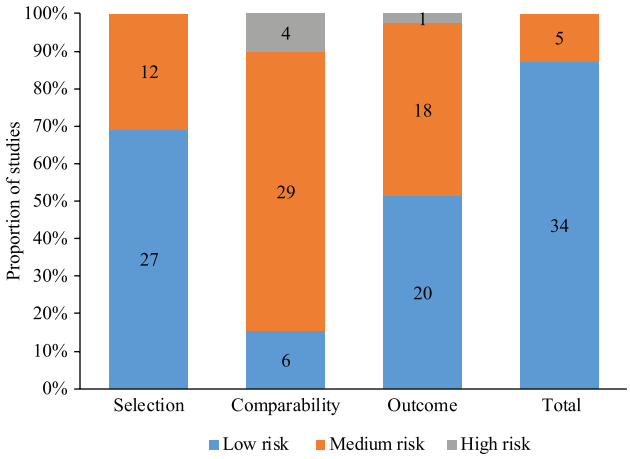

Fig. 2. Newcastle–Ottawa Scale scores of 39 included studies in meta-analysis.

not affected by the exclusion of any individual study (Fig. 4).

Subgroup analyses indicated that maternal characteristics and the time interval of postpartum OGTT performed was associated with the RR of T2DM onset after GDM. Older maternal age and family history of diabetes mellitus increased the risk of T2DM after GDM. The incidence of T2DM after GDM is the highest within the first year after delivery. The RR of diagnosing T2DM after GDM is variable when studies were grouped according to race/ethnicity and geographic region. The RR of diagnosing T2DM after GDM was lower when more confounders were matched (Fig. 5).

These results suggest that race/ethnicity, region, family history and time interval of postpartum OGTT performed could explain the reason behind the heterogeneity among studies. However, mean maternal age, BMI at follow up, GDM criteria, T2DM criteria and number of confounders matched could not explain the same.

Publications bias: No apparent asymmetry was observed in the Begg's funnel plot (Fig. 6) and Egger's publication bias plot (Fig. 7). Results of the Begg's test (P=0.200) and Egger's test (P=0.380) were not significant.

Discussion

This meta-analysis indicates that women with a history of GDM have near nine fold increased risk of being diagnosed as T2DM in the future compared with those without GDM. The magnitude of the association

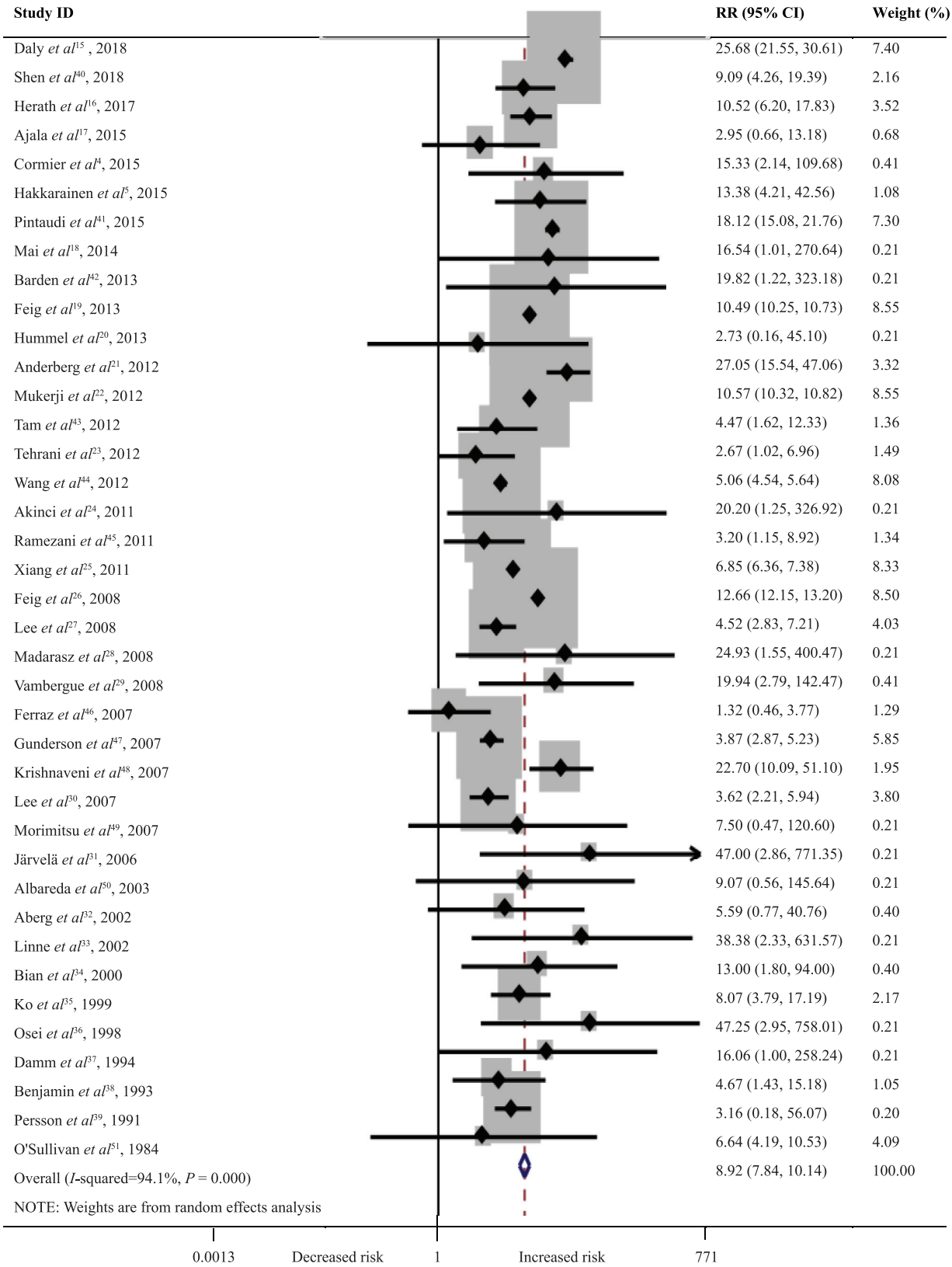

Fig. 3. Forest plot of the risk of women diagnosed as type 2 diabetes mellitus (DM) after gestational DM. X-axis is plotted in log scale. Solid squares and horizontal lines indicate relative ratios and 95 per cent confidence intervals. The diamond represents the pooled relative risk (RR).

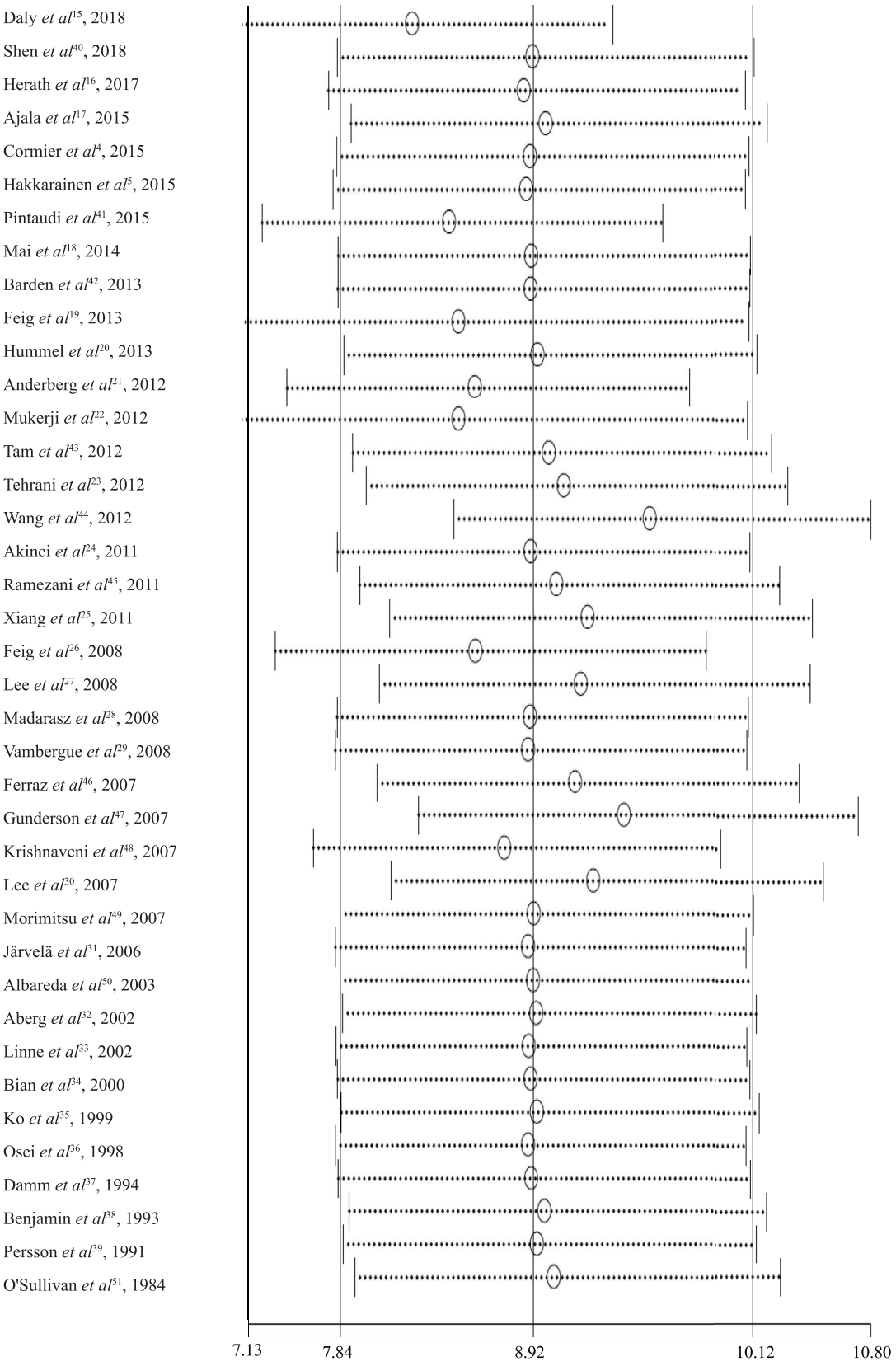

Fig. 4. Sensitivity analysis of women diagnosed as type 2 DM after gestational DM. Three vertical lines indicate the pooled RR and 95 per cent CI of all studies. Circles and horizontal dashed lines indicate recalculated RRs and 95 per cent CIs.

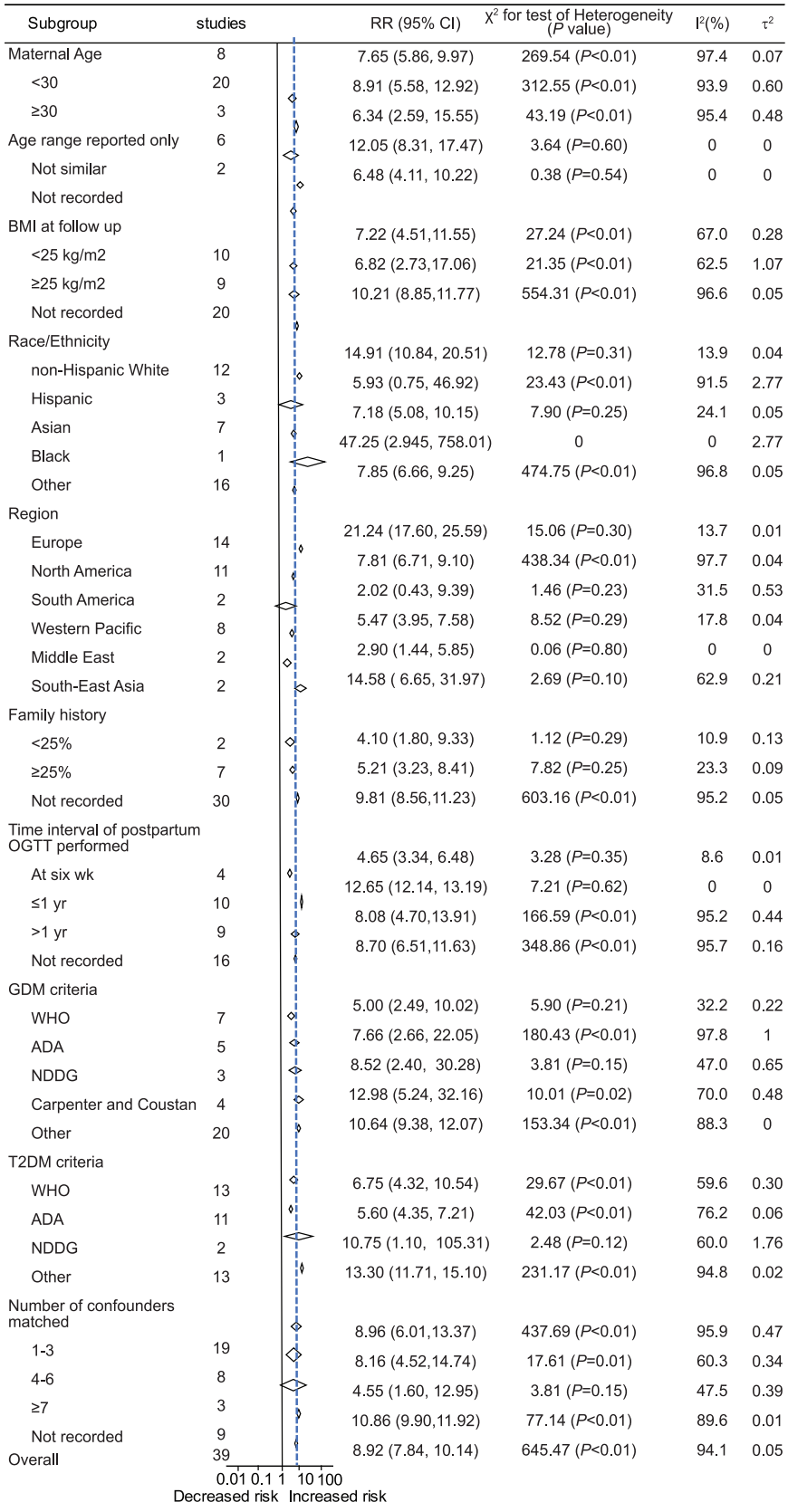

Fig. 5. Risk of women diagnosed as type 2 DM after gestational diabetes mellitus grouped by maternal characteristics, study characteristics and diagnostic criteria. The diamond represents the subtotal relative risk.

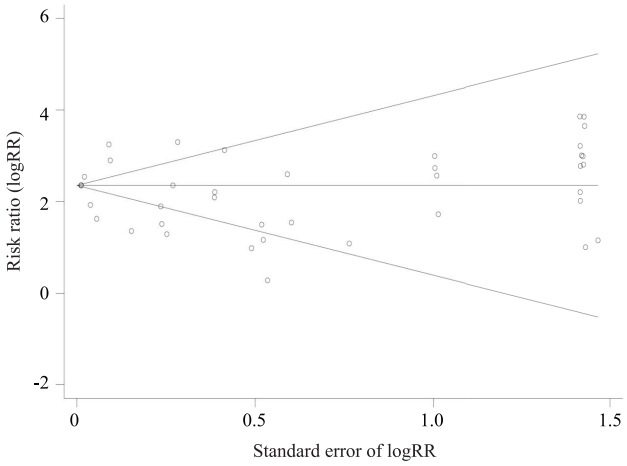

Fig. 6. Begg's funnel plot of 39 publications.

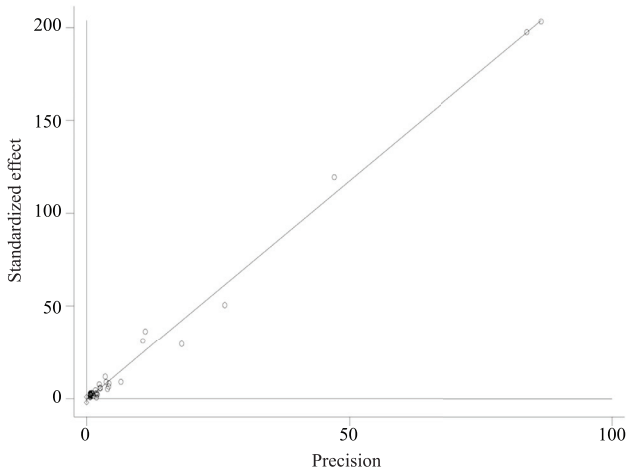

Fig. 7. Egger's publication bias plot of 39 publications.

between GDM and T2DM suggests that more frequent assessment and effective interventions targeting eligible women are needed. American Diabetes Association and other professional organizations recommend diabetes screening at 6-12 wk postpartum for women with GDM[52,53]. Despite the emphasis of multiple guidelines, the postpartum screening compliance rates are still typically low[54,55]. In addition, from the present study it was evident that within the first year after delivery, the progression of T2DM increased steeply. So, healthcare providers should emphasize the importance of continuity in treatment and healthcare and women with GDM should attend the follow up programmes earlier and conduct OGTT at 6-12 wk postpartum. Furthermore, later long-time screening strategies and optimal screening frequency may be needed further studies to explore.

Maternal age, BMI, race/ethnicity and family history are associated with the prevalence of GDM and T2DM[11]. In this meta-analysis, the results of subgroup analyses corroborated that maternal age and family history of diabetes might be the risk factors for T2DM after GDM. Thus, older women or those with a family history should value antepartum counselling and postpartum diabetes screening more than other women with GDM.

It has been suggested previously that the prevalence of GDM varies with race/ethnicity[2,25], with Asians and Hispanics reported to have a higher GDM prevalence than non-Hispanic Whites and Blacks[56,57]. In the present study it was observed that Blacks and non-Hispanic Whites had a higher RR of developing T2DM after GDM than Hispanics and Asians, which was consistent with a large multi-ethnic cohort study[25]. Another study reported that Hispanics and Asians had the highest RR of T2DM after GDM[44] however, the sample size was small and CIs were wide[44]. This inconsistency could be attributed to the sample size. Large multi-ethnic cohort studies are needed to verify that conjecture.

Besides race/ethnicity, regional disparity (geographic level) is an important influence factor of GDM prevalence. The Middle East and North Africa had the highest prevalence of GDM, followed by South-East Asia, Western Pacific, South America, Africa and North America, whereas Europe had the lowest prevalence[2]. Despite the relatively high prevalence, no eligible studies from North Africa or Africa were identified in our search, and only two studies from South-East Asia were included. The subgroup analysis indicated that the RR of T2DM after GDM in Europe and South-East Asia was higher than other geographic regions. Although the GDM prevalence in Europe was the lowest, the RR of T2DM after GDM in Europe was the highest. Moreover, RRs in South America and Middle East were relatively low. Taken together, the RR of T2DM after GDM was not associated with GDM prevalence.

In this meta-analysis (P<0.01, I^2=94.1%) high heterogeneity was noted similar to a previous study[10] (P<0.01, I^2=85%). In this meta-analysis, sensitivity analysis indicated that no individual study contributed to the heterogeneity and the subgroup analyses, indicated that maternal age, BMI at follow up, GDM and T2DM criteria, and number of confounders matched could not explain the heterogeneity. Nevertheless, race/ethnicity, region, family history and time interval of postpartum OGTT performed might have contributed to the

same. In subgroup analysis based on race/ethnicity, no significant evidence of heterogeneity was found in group 'non-Hispanic White' and 'Asian', but significant evidence of heterogeneity was found in group 'Other' and 'Hispanic'. In group 'Other', most studies included mixed population and their racial/ethnic composition was different, which was considered the cause of the subgroup heterogeneity. In group 'Hispanic', two studies were carried out in Europe and one in South America; it was thus inferred that regional disparity might cause subgroup heterogeneity. In the results of subgroup analyses based on geographic regions, we only observed significant evidence of heterogeneity in the group 'North America'. Such heterogeneity might be attributed to diversity in race/ethnicity, because the degree of diversification among population in North America was higher than that among the population of other geographic regions and most studies on this group included mixed population. In subgroup analysis based on family history, no heterogeneity was found in the group '<25 per cent' and '>25 per cent'. In addition, in subgroup analysis based on time interval of postpartum OGTT performed, no heterogeneity was found in the groups 'at six weeks' and '<one year' and high heterogeneity was seen in group '>one year'. Therefore, it was inferred that the family history of diabetes and time interval of postpartum OGTT performed might be the source of heterogeneity. Meanwhile, 76.9 per cent (30/39) studies did not record the family history information and 41.0 per cent (16/39) studies did not record the time interval of postpartum OGTT performed. Such absence of information might have caused a bias.

There were, however, two limitations in the present study. The RR was synthesized regardless of the huge variance in diagnostic criteria and screening protocol for GDM and T2DM. However, the diagnose criteria have been constantly changing over the last four decades. In 1997, the T2DM diagnosis threshold was reduced[58]. Moreover, recent studies using the new International Association of Diabetes and Pregnancy Study Group criteria show a higher prevalence of GDM[58]. Therefore, the inclusion of old studies might have caused the underestimation of the risk of having T2DM after GDM. Secondly, the main source of heterogeneity in this study could not be identified. Such heterogeneity in the present study might have been caused by the number of included studies and the differences in the participant characteristics.

In summary, the high risk of diagnosing T2DM after GDM suggests that healthcare providers need postpartum screening and follow up programmes, both of which are convenient and economic methods for early treatment of T2DM, thereby reducing the prematurity of cardiovascular, renal and retinal diseases[59-62]. Continuous assessment and effective interventions targeting eligible women are needed, in particular, older women with GDM or women with GDM and a family history of diabetes should value antepartum consulting and postpartum followup programmers more than other women with GDM only. Blacks and non-Hispanic Whites could receive more attention, and healthcare providers, especially those in Europe and South-East Asia, could pay more attention to preventive measures. Overall, it is concluded that the RR of diagnosing T2DM after GDM is not directly proportional to GDM prevalence among racial/ethnic groups or geographic regions. Whether the difference is due to lifestyle, genetics or environment needs to be investigated further.

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