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TYPE 2 DIABETES MELLITUS AFTER GESTATIONAL DIABESTES: A META ANALYSIS STUDY

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Abstract:

Increased risk of developing type 2 diabetes in women with who had gestational diabetes. A comprehensive systematic review and meta-analysis to assess the strength of association between these conditions and the effect of factors that might modify the risk. It is identified that cohort studies in which women who had developed type 2 diabetes after gestational diabetes were followed up from Embase and Medline. 20 studies were included in study that met our inclusion criteria. Included studies with 675 455 women and 10 859 type 2 diabetic events. Calculated and pooled unadjusted relative risks (RRs) with 95% CIs for each study using a random-effects model. Number of cases of type 2 diabetes, ethnic origin, and duration of follow-up, maternal age, body-mass index, and diagnostic criteria were analyzed as subgroup. In conclusion, gestational diabetes had an increased risk of developing type 2 diabetes AS compared with those who had a normoglycaemic pregnancy (RR 7·43, 95% CI 4·79–11·51) . Although the largest study (659 164 women; 9502 cases of type 2 diabetes) had the largest RR (12·6, 95% CI 12·15–13·19), RRs were generally consistent among the subgroups assessed.

Key Words: *Gestational Diabetes, Type 2 Diabetes, Diabetes Mellitus*.

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INTRODUCTION:

Gestational diabetes mellitus (GDM), or impaired glucose intolerance first diagnosed during pregnancy [1], affects 14% of pregnancies, or 135,000 women a year in the U.S., and is a risk factor for type 2 diabetes in the mother [2]. It is not clear that how much of the variation is reported by changing in ethnicity, length of follow-up, selection criteria, and tests for GDM and type 2 diabetes [3-5]. Screening protocols for type 2 diabetes could be affected by the basic understanding in risk differences in women with a history of GDM.

Gestational diabetes mellitus is defined as glucose intolerance that is first detected during pregnancy. Shortly after delivery, glucose homoeostasis is restored to non-pregnancy levels, but affected women remain at high risk of developing type 2 diabetes mellitus in the future.[6, 7] For any population and ethnic group, the risk of gestational diabetes indicates the underlying frequency of type 2 diabetes.[8] The incidences of gestational diabetes and type 2 diabetes are rising throughout the world, with huge health-care and economic costs. [9[9, 10]

Women who have had gestational diabetes are advised to have their glucose tolerance assessed 6 weeks after delivery.[11] However, low rates of attendance at the 6-week follow-up, [12] suggest that health-care professionals, women with gestational diabetes, or both, do not realize the importance of this disorder as an early warning sign of the susceptibility to develop type 2 diabetes in the future; therefore an opportunity to promote health and prevent disease is missed. Moreover, no consensus exists on how and whether mothers should continue to be monitored after this period. The association between gestational diabetes and type 2 diabetes mellitus has implications for the elucidation of the causes of these disorders, and for the prediction and possible prevention or delay of the development of type 2 diabetes in women.

METHOD:

Electronic databases were used .search of Embase from 1974 to 2018, and Medline search term combinations were “gestational diabetes”, “diabetic pregnancy”, “diabetes mellitus”, “type 2 diabetes mellitus”, “NIDDM”, and “non-insulin dependent diabetes mellitus”. All reference lists were hand searched manually for additional eligible studies. We identified retrospective and prospective cohort studies, in which pregnant women of any parity or ethnic origin were identified as having gestational diabetes (exposed group) and normoglycaemic pregnancies (control group). The outcome studied was the development of type 2 diabetes at least 6 weeks after the end of the index pregnancy, and was defined with an oral glucose tolerance test or fasting plasma glucose concentration, or both, Cohort studies of women with diabetes mellitus before the index pregnancy were excluded. If there was more than one report relating to the same cohort, the report with the information most relevant to our analysis was included. We used RevMan (version 5) to calculate unadjusted summary relative risks (RRs) with 95% CIs, using a random-effects model for all analyses We investigated potential sources of identified heterogeneity among studies by stratification according to the number of cases of type 2 diabetes (500); ethnic origin (white, non-white, and mixed race populations); average follow-up (30 kg/m²); study design (prospective and retrospective); and variation in criteria used in each study to diagnose gestational diabetes and type 2 diabetes.

RESULTS:

Figure 1 shows the study selection process (reasons for exclusion are listed in web appendix pp 1–13). 48 of 68 full-text reports meeting all the inclusion criteria were subsequently excluded because of the absence of an appropriate control or reference population. The 20 remaining studies (table), contributed 675 455 women with type 2 diabetes to the meta-analysis, and 31 867 of these had previous pregnancies affected by gestational diabetes with a total of 10 859 incident cases of type 2 diabetes. Figure 2 shows the overall RR of women developing type 2 diabetes after a pregnancy complicated by gestational diabetes with evidence of heterogeneity in the risk estimate. Generally, small studies had large effect estimates (fi gure 3), but the largest study18 included in the meta-analysis had the largest effect estimate (fi gure 2). Figure 4 shows the potential sources of heterogeneity by study characteristics, participant characteristics, and diagnostic criteria for gestational diabetes and type 2 diabetes. Effect estimates were broadly consistent in all the subgroups analyzed (figure 4B; figure 4C). There was some heterogeneity in effect estimates when studies were grouped according to the number of cases of type 2 diabetes (500; figure 4A). Heterogeneity was reduced by exclusion of the largest study (χ^2=1·48, df=1, p=0·22, I^2=32·2%).

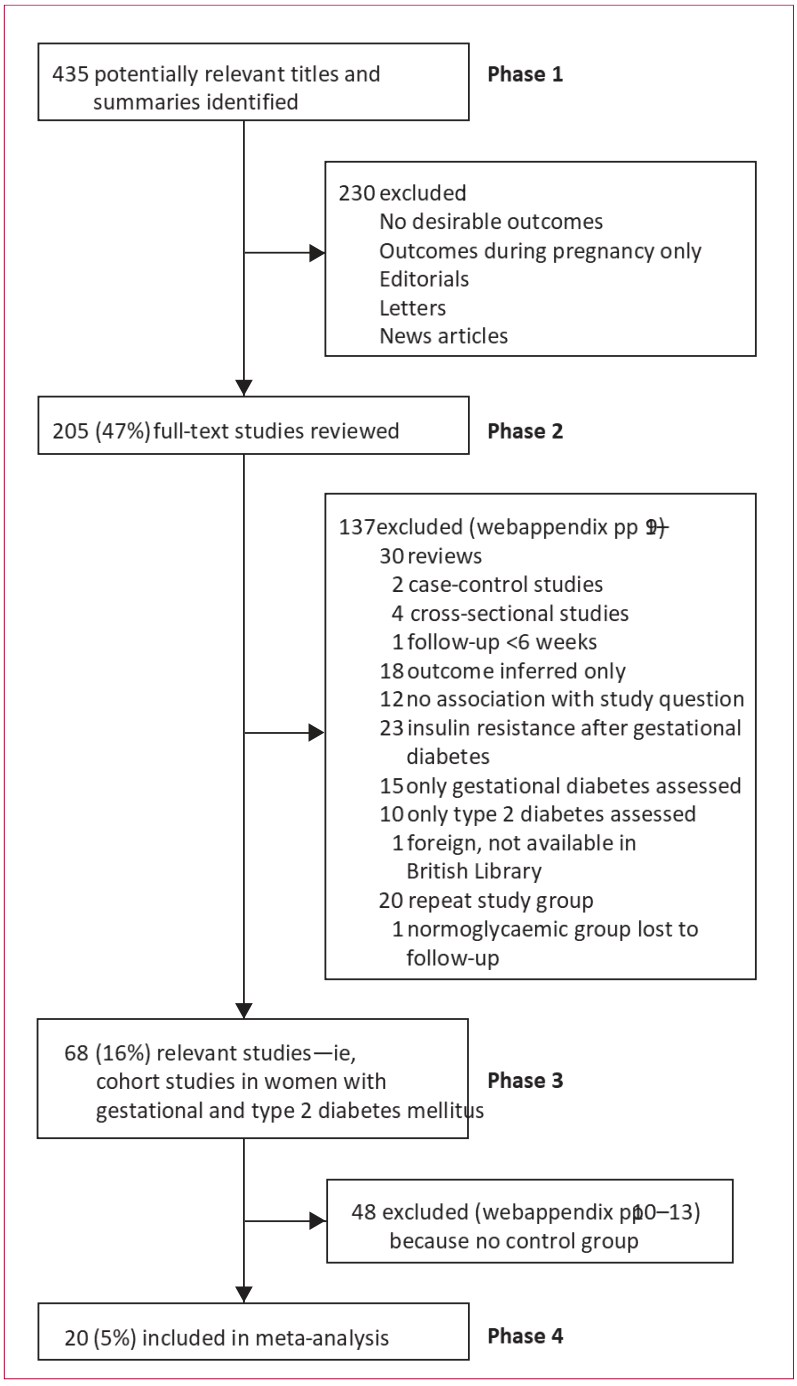

Figure 1 **Study selection process**

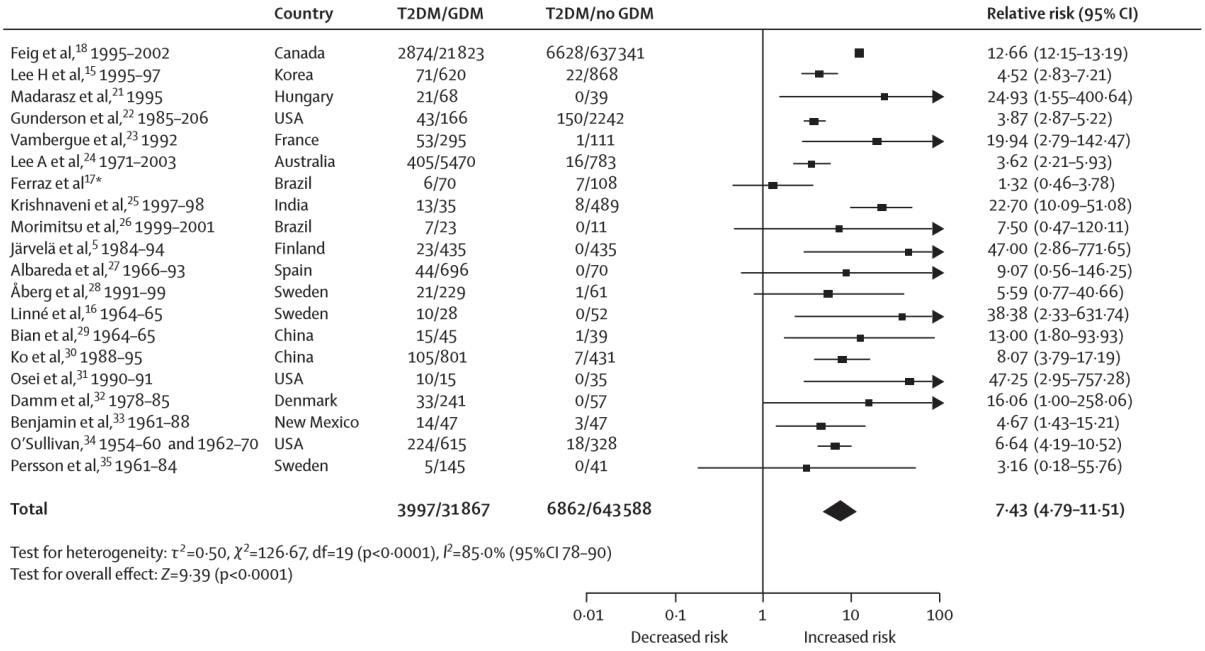

***Figure 2*: Risk of type 2 diabetes mellitus (T2DM) after gestational diabetes mellitus (GDM)**

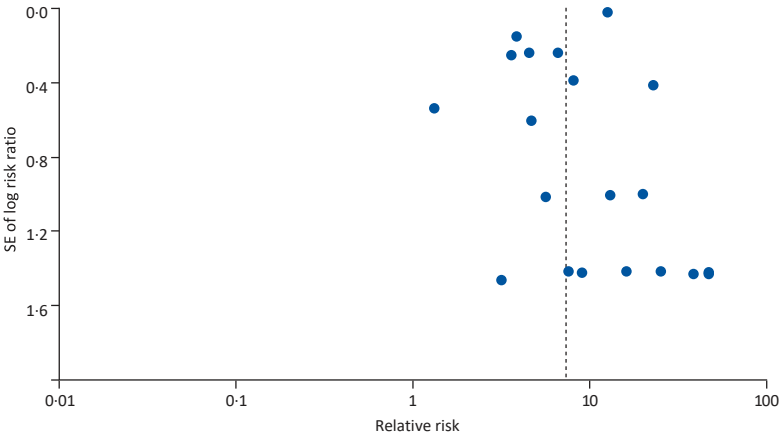

***Figure 3*: Funnel plot of 20 cohort studies included in meta-analysis**

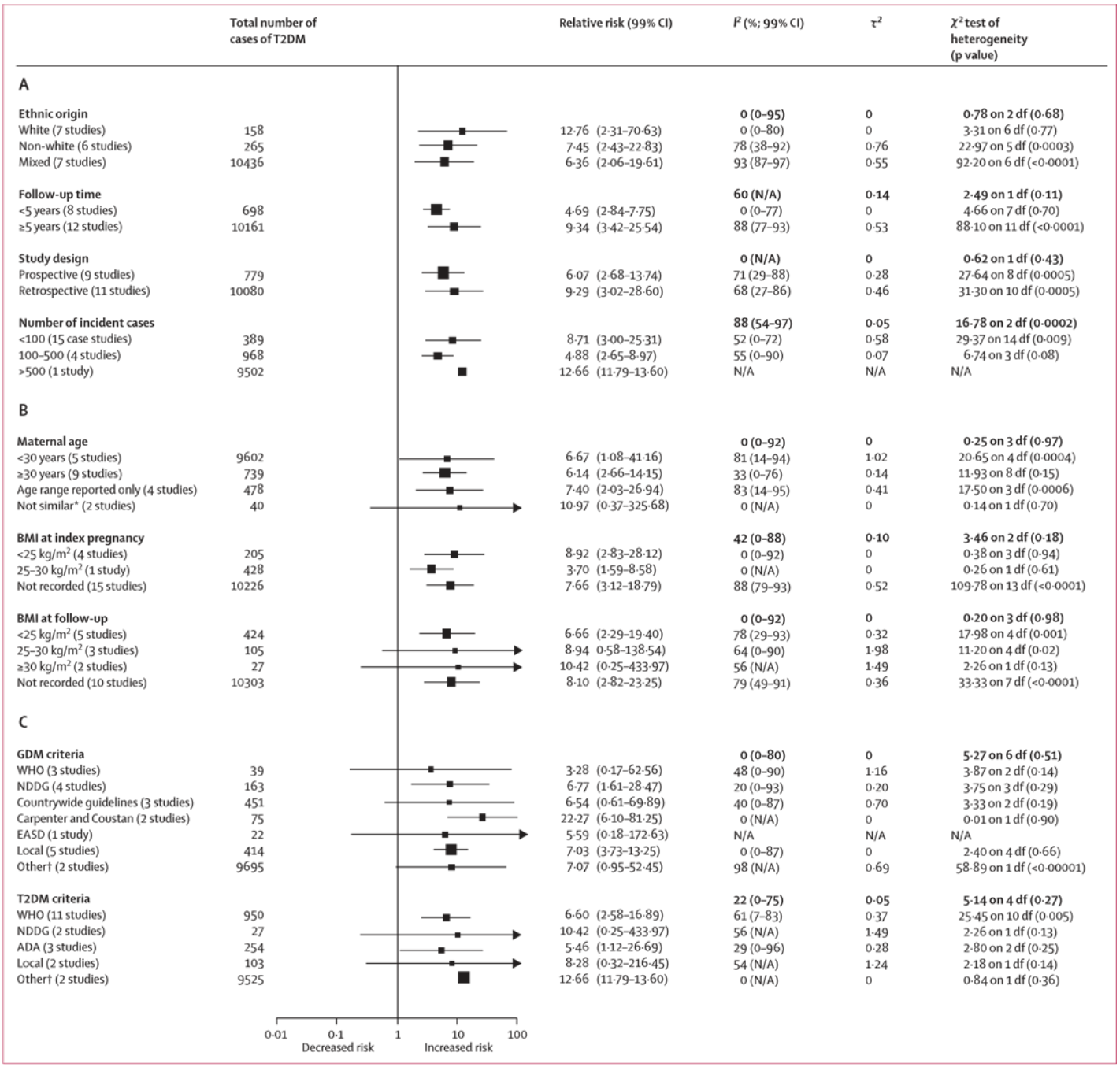

Figure 4: **Risk of type 2 diabetes mellitus (T2DM) grouped by study characteristics (A), participant characteristics (B), and diagnostic criteria (C)**

	Study type, year, country	Ethnic origin	Mean maternal age (years; SD or 95% CI) of women with GDM/non-GDM	GDM criteria	Total women studied (degree of matching GDM/ non–GDM)	Mean follow-up (SD or 95% CI)	Defi nition of T2DM
Feig et al[18]	Retrospective cohort, 2008, Canada	Mixed	29·3 (5·5)	Canadian Institute for Health Information (discharge summary)[36]	659 164	5·2 years[i]	Ontario Diabetes Database[ii,37]
Lee H et al[15]	Prospective cohort[iii], 2008, Korea	Non-white	33·6 (4·8)	National Diabetes Data Group, 1979[iv,38]	1736[v] (248 IGT)	2·1 years[i]	Local[vi]
Madarász et al[21]	Retrospective cohort[iii], 2008, Hungary	White	33·1/30·0 (5·9)	WHO, 1999[vii,39]	107	3·6 years (GDM; 0·8)/ 8·1 years (non-GDM; 5·1)	WHO, 1999[viii,40]
Gunderson et al[22]	Prospective cohort, 2007, USA	Mixed	Matched range 18–30	Obstetric laboratory reports	2408	Total 20 year follow-up (72% followed for entire time)	American Diabetes Association, 1997[ix]/diabetes medication/self report
Vambergue et al[23]	Prospective cohort, 2007, France	Mixed	27·0 (5·2)/28·8 (5·8)	Carpenter and Coustan[x,41]	581[xi,xii] (175 AGT)	6·75 years (0·8)	American Diabetes Association, 1997[ix]
Lee A et al[24]	Retrospective cohort, 2007, Australia	Mixed	30·7 (5·1)/30·5 (4·6)	Australian Diabetes[xiii,42] (pregnancy guidelines)	6253[xiv]	2·2 years (GDM), [i] 8·6 years (non-GDM)[i]	WHO, 1998[viii,40]
Ferraz et al[17]	Prospective cohort, 2007, Brazil	Non-white	26·9/25·1	WHO, 1999[xv,43]	178xvi	6·2 years (0·8)	WHO, 1999[viii,40]
Krishnaveni et al[25]	Prospective cohort, 2007, India	Non-white	Matched age range	Carpenter and Coustan[x,41]	524	5 years	WHO, 1999[viii,40]

Morimitsu et al[26]	Prospective cohort, 2007, Brazil	Mixed	32/27 (7)	American Diabetes Association, 1997[xvii,14]	34xviii	16–24 weeks	American Diabetes Association, 1997[ix]
Järvelä et al[5]	Retrospective cohort[iii], 2006, Finland	White	31·6 (17·7–46·5)/31·3 (18·8–46·0)	Finnish Diabetes Association[xix,44]	870v,xii,xiv	5·7 years (GDM; 1·0–11·6) 6·1 (non-GDM; 1·5–13·1)	Medication for T2DM linked to database[xx,45]
Albareda et al[27]	Prospective cohort, 2003, Spain	White	30·7/30·4	Second and third GDM workshop conference[xxi,46,47]	766xiv	6·16 years (0·05–13·73)	WHO, 1998[viii,40]
Åberg et al[28]	Retrospective cohort, 2002, Sweden	White	Matched range 20–45	European Association for Study of Diabetes[xxii,48]	290	1 year	WHO, 1985[xxiii]
Linné et al[16]	Retrospective cohort [iii], 2002, Sweden	White	32·6/30·6	Local[xxiv]	80v,xvi,xxv	15 years	Local[xxvi]
Bian et al[29]	Retrospective cohort, 2000, China	Non-white	29/29 (23–40)	National Diabetes Data Group, 1979[iv]	84v,xiv,xviii,xxvi	5–11 years	WHO, 1985[xxiii]
Ko et al[30]	Prospective cohort, 1999, China	Non-white	34·0 (4·1)/34·4 (6·4)	Localxxviii	1232[v]	6 weeks	WHO, 1985[xxiii]
Osei et al[31]	Retrospective cohort, 1998, USA	Non-white	31·3 (2·0)/36·0 (0·9)	National Diabetes Data Group, 1979[iv]	65xxix	7 years	National Diabetes Data Group, 1979[xxx,49]
Damm et al[32]	Retrospective cohort, 1994, Denmark	White	30·1/26·7	Local[xxxi]	298xiv	7·5 years[i]	WHO, 1985[xxiii]
Benjamin et al[33]	Retrospective cohort, 1993, New Mexico	Mixed	27·2/26·5	Localxxxii,50	94v,xii,xvi,xxxiii,51	4·8 years (GDM)/ 5·5 years (non-GDM)	National Diabetes Data Group, 1979[xxx,49]
O'Sullivan[34]	Prospective cohort, 1991, USA	Mixed	··	Localxxxii	943	22–28 years	WHO, 1985[xxiii]

DISCUSSION:

Women who have had gestational diabetes have at least a seven-fold increased risk of developing type 2 diabetes mellitus in the future compared with those who have had a normoglycaemic pregnancy. The strength of the association between gestational diabetes and type 2 diabetes, and the knowledge that many of the risk factors are the same suggest that the two disorders might have an overlapping cause. Results of candidate gene studies, giving support to this hypothesis, show that frequency of some alleles associated with the increased risk of development of type 2 diabetes were increased in women who had gestational diabetes. Irrespective of the precise biological link between these two disorders, the development of gestational diabetes might help to identify women at high risk of developing type 2 diabetes.

Although women who have had gestational diabetes are recommended to have a glucose tolerance test at 6 weeks postpartum, most do not attend.11 The increased risk of type 2 diabetes reported in this meta-analysis might help to motivate mothers to attend screening programs, and health-care professionals to increase uptake to these programs or perhaps suggest the best time for reassessment. Since the risk of type 2 diabetes seems to be maintained for several years, consideration of whether any form of continuous assessment would lead to health gains is important. Women who have had gestational diabetes also have increased lipid concentrations and blood pressure, and type 2 diabetes is estimated to confer an equivalent risk of ageing 15 years. Early identification and treatment of these factors could also help to reduce premature cardiovascular and renal diseases in this group of individuals.

Suggesting that much of the heterogeneity was unexplained. The effect estimates reported in studies in which different criteria were used for the diagnosis of gestational diabetes mellitus and type 2 diabetes mellitus were similar. The number of cases of type 2 diabetes included in our analysis contributed to the heterogeneity, which was reduced by exclusion of the largest study. However, this study was of high quality and resulted in an effect size that was larger, instead of smaller, than the estimates from small studies. Although we did not identify the main sources of heterogeneity of effect size, a meta-analysis of summary data from reported studies has little capacity to do so.

CONCLUSION:

Magnitude and timing of the risk of type 2 diabetes after gestational diabetes have increased awareness among patients and clinicians could provide an opportunity to test and use dietary, lifestyle, and pharmacological interventions that might prevent or delay the onset of type 2 diabetes in affected women.

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