Identifying women with gestational diabetes based on maternal characteristics: An analysis of four Norwegian prospective studies

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Research Article

Keywords: Gestational diabetes mellitus, pre pregnancy BMI, pregnancy, screening, diagnostic criteria

Posted Date: April 7th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-379289/v1

Abstract

Background There is still no worldwide agreement on the best diagnostic thresholds to define gestational diabetes (GDM) or the optimal approach for identifying women with GDM. Should all pregnant women perform an oral glucose tolerance test (OGTT) or can easily available maternal characteristics, such as age, BMI and ethnicity, indicate which women to test? The aim of this study was to assess the prevalence of GDM by three diagnostic criteria and the predictive accuracy of commonly used risk factors.

Methods We merged data from four Norwegian cohorts (2002–2013), encompassing 2981 women with complete results from a universally offered OGTT. Prevalences were estimated based on the following diagnostic criteria: $_{1999}$WHO (fasting plasma glucose (FPG) ≥ 7.0 or 2-h glucose ≥ 7.8 mmol/L), $_{2013}$WHO (FPG ≥ 5.1 or 2-h glucose ≥ 8.5 mmol/L), and $_{2017}$Norwegian (FPG ≥ 5.3 or 2-h glucose ≥ 9 mmol/L). Multiple logistic regression models examined associations between GDM and maternal factors. We applied the $_{2013}$WHO and $_{2017}$Norwegian criteria to evaluate the performance of different thresholds of age and BMI.

Results The prevalence of GDM was 10.7%, 16.9% and 10.3%, applying the $_{1999}$WHO, $_{2013}$WHO, and the $_{2017}$Norwegian criteria, respectively, but was higher for women with non-European background when compared to European women (14.5 vs 10.2%, 37.7 vs 13.8% and 27.0 vs 7.8%). While advancing age and elevated BMI increased the risk of GDM, no risk factors, isolated or in combination, could identify more than 80% of women with GDM by the latter two diagnostic criteria, unless at least 70–80% of women were offered an OGTT. Using the $_{2017}$Norwegian criteria, the combination “age ≥ 25 years or BMI ≥ 25 kg/m²” achieved the highest sensitivity (96.5%) with an OGTT required for 93% of European women. The predictive accuracy of risk factors for identifying GDM was even lower for non-European women.

Conclusions The prevalence of GDM was similar using the $_{1999}$WHO and $_{2017}$Norwegian criteria, but substantially higher with the $_{2013}$WHO criteria, in particular for ethnic non-European women. Using clinical risk factors such as age and BMI is a poor pre-diagnostic screening method, as this approach failed to identify a substantial proportion of women with GDM unless at least 70–80% were tested.

Background

Gestational diabetes mellitus (GDM) is glucose intolerance with onset or first diagnosis during pregnancy which is clearly not overt diabetes (1). GDM is associated with higher maternal and neonatal morbidities in the short- and long-term and predisposes both women and their offspring to later development of type 2 diabetes (2). Screening followed by treatment of GDM reduces the risk of several pregnancy complications (3). However, there is no worldwide agreement on the best diagnostic thresholds to define GDM, and a wide variety of clinical guidelines have been employed (4).

In 2013, the World Health Organization (WHO) recommended glycaemic thresholds for the diagnosis of GDM based on findings from the multinational Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study demonstrating a linear dose-response between maternal glycaemia and adverse neonatal outcomes.

These criteria were determined to identify women with an adjusted odds ratio (OR) of 1.75 for adverse events in their offspring relative to the mean (5). Glucose values set to identify women with a higher risk, corresponding to an adjusted OR of 2.0, were also considered but this proposal was rejected. Nonetheless, several countries, among them Canada and Norway, adopted the latter noting the substantial rise in GDM prevalence by $_{2013}$WHO criteria, without clear evidence of clinically important benefits (6). The prior WHO criteria, established in 1999 and used in Norway until 2017, were identical to those for diagnosis of glucose intolerance in a non-pregnant population.

Controversy surrounds not only the thresholds values of glycemia, but also the optimal approach for identifying women with GDM. A high-risk approach has traditionally been recommended based on easily available maternal characteristics such as advanced age and BMI, known to be associated with an increased risk of GDM (7). However, although this approach reduces unnecessary testing in those least likely to test positive, a key issue is their performance as indicators for diagnostic testing and the usefulness of risk factors in a clinical setting today (8). The alternative option, universal screening, has a high detection rate but poses a large immediate burden to healthcare services as well as pregnant women.

In this study that merged data from four existing Norwegian pregnancy and birth cohorts, we aimed to address some of the clinical controversies related to GDM diagnosis and screening. The objectives were: 1) To establish the prevalence of GDM with three diagnostic criteria ($_{1999}$WHO, $_{2013}$WHO, and the $_{2017}$Norwegian criteria), 2) identify cut-off levels for age and BMI that identify at least 80% of women with GDM and 3) assess the predictive accuracy of commonly used risk factors.

Methods

All population-based birth cohort studies in Norway with a special focus on gestational diabetes were eligible. For the present study, the following inclusion criteria were defined: (i) prospective studies comprising women with singleton live-born children recruited early in pregnancy (between week 15–20); (ii) data on maternal pre-pregnancy BMI; (iii) glucose measurements obtained from at least one universally offered 75g 2-hour oral glucose tolerance test (OGTT) performed ≥ 20 weeks' gestation; (iv) at least one offspring measurement (birthweight). Exclusion criteria were studies without the core data and studies that only included specific subgroups (such as obese women only).

Four Norwegian studies (two cohort studies (9, 10) and two randomized controlled trials (RCT)(11, 12)) were identified, and primary investigators were invited to become part of the 4GDM consortium in 2017. Principal investigators from all four studies agreed to participate, providing data from 3315 pregnant women and 2971 live births (Fig. 1).

The original studies collected data between 2002 and 2013. If GDM was diagnosed, women received diabetes care according to local guidelines. Details of the methods and characteristics of participants in each study, including eligibility criteria, methods of recruitment and measurements obtained, have been previously published (9–12). Authors were requested to provide anonymous raw data to be stored and analyzed in The University of Oslo's Service for Sensitive data (TSD) storage platform with access for all the

project partners. Data were further harmonized and assessed for internal consistency and missing items. Investigators were asked for clarification on issues regarding the coding of variables and a final summary of relevant variables was sent for verification. After resolution, all datasets were merged. We excluded from analyses participants for which no OGTT data were available, as well as multi-fetal pregnancies (Fig. 1).

The primary outcome was GDM prevalence. The diagnosis was originally made according to the $_{1999}$WHO criteria which was used during data collection. In addition, we applied the $_{2013}$WHO criteria and the $_{2017}$Norwegian criteria (box 1) for the purposes of this specific study. The $_{2013}$WHO criteria also includes a one-hour plasma glucose which was not measured in the respective studies.

Glucose value	$_{1999}$WHO	$_{2013}$WHO	$_{2017}$Norwegian
Fasting	≥ 7.0 mmol/L	≥ 5.1 mmol/L	≥ 5.3 mmol/L
2-h	≥ 7.8 mmol/L	≥ 8.5 mmol/L	≥ 9.0 mmol/L

Box 1. Based on a 75 g Oral Glucose Load. For the diagnosis, one or more of the glucose values must be met or exceeded.

In each individual study, women were either interviewed or asked to complete a questionnaire including information on current smoking status and their highest educational qualification. Women were further assessed at the study sites with respect to biological and anthropometric data. Height was measured directly while weight prior to becoming pregnant was self-reported in all studies. Categories for age and pre-pregnancy body mass index (BMI) were determined prior to analysis and based on clinical relevance. Furthermore, women were classified as primiparous or parous for the purpose of this study.

STORK Groruddalen (9) was the only study that actively included a multiethnic population (59% ethnic minority women, primarily born outside Europe). Ethnic origin was defined as European (predominantly Scandinavian as well as East and West-European origin) or non-European (mainly Asian, North-African, Middle Eastern or Sub-Sahara African). Family history of diabetes was not measured in the Fit for Delivery study.

Statistical analysis

Distributions of all potential predictors were checked for normality. The characteristics of the women were categorized by GDM-status and the two groups were compared using X^2 statistic for categorical data and the Student's t Test for continuous variables. Data are reported as frequencies and percentages for categorical variables and mean and standard deviation for continuous variables.

Information was available for 95% of the selected covariates. To assign values for the missing data for pre-pregnancy weight (5%), height (0.4%), educational attainment (0.3%) and parity (0.3%) we used Stochastic regression imputation with predictive mean matching as the imputation model to substitute missing items in the observed population (13).

To examine associations between GDM and maternal factors, we modelled GDM as a binary outcome (GDM vs no-GDM) and variables related to GDM in univariate logistic regression models with p-value < 0.2 were considered in separate multivariate analyses. The final model resulted from a backward selection procedure (exclusion if p > 0.15). All models were adjusted for cohort. Results from logistic regression are presented as OR with accompanied 95% confidence intervals (CI), and with Nagelkerke R^2 for model fit.

In the analyses, the two RCT's were treated as cohort studies as the primary outcome (GDM) did not differ between control and intervention group in the original studies (11, 12). The regression analysis was repeated after excluding participants who received the intervention to examine the potential role of the intervention in these RCTs.

Finally, we assessed the diagnostic accuracy across different pre-specified cut-offs for maternal age and BMI with and without the addition of parity, based on previous and current screening guidelines. We calculated sensitivity (proportion of GDM cases correctly identified by the risk factor), specificity (proportion of women without GDM who did not have the risk factor), and the proportion of women with the risk factor (i.e. who would be offered an OGTT). Analyses were performed and presented separately for European and non-European women due to strong effect of ethnicity. For each risk factor, single or in combination, the sensitivity estimates were plotted in Receiver Operating Characteristic (ROC) space against the proportion of women subjected to OGTT. An optimal risk factor combination will have high sensitivity with small numbers needing to be tested (results near the top left of the space). We opted for a sensitivity level of 80% for the risk factors. Statistical analyses were performed using SPSS software, Version 26 (USA).

Results

We excluded more participants from the TRIP study than from the other studies due to missing GDM data (Figure 1). Apart from this, no significant differences were noted between the women who were included in the study and those excluded (not shown). After exclusions, the pooled dataset comprised 2981 women with a mean (SD) age of 30.2 (4.4) years and pre-pregnant BMI of 23.7 kg/m^2 (Table 1). The majority were of European origin (87.0%), had higher education (73.4%) and were in their first pregnancy (61.0%). GDM was diagnosed in 320 (10.7%), 504 (16.9%) and 308 (10.3%) pregnancies with the $_{1999}$WHO, $_{2013}$WHO and $_{2017}$Norwegian criteria, respectively.

The prevalence rates in European women compared to non-European women were 10.2 vs 14.5%, 13.8 vs 37.7% and 7.8 vs 27.0%, applying the $_{1999}$WHO, $_{2013}$WHO and $_{2017}$Norwegian criteria, respectively (Figure 2).

Compared with the non-GDM group, women diagnosed with GDM by either criteria were more likely to be older, heavier, shorter and of non-European origin (Table 2). Moreover, using the $_{2017}$Norwegian criteria, while 25.5% of women without GDM had overweight or obesity (BMI >25kg/m^2), this was observed in 51.3% of women with GDM (P<0.001). There were more primiparas in the non-GDM group (P<0.001), except when applying the $_{1999}$WHO criteria.

In logistic regression analyses, all selected variables except smoking, were significantly associated with GDM with the $_{2017}$Norwegian criteria prior to adjustments (Table 3a). Nevertheless, the associations observed for parity, education and height were strongly attenuated and lost their significance in the multivariate adjusted model 1 (Table 3a). Age, pre-pregnancy BMI and ethnicity remained the only significant predictors in the final multivariate model (model 2). However, compared with women ≤25 years, an increased OR for developing GDM was only found for those above 35 years of age (aOR 1.73; 95% CI: 1.07-2.80; *P*< 0.026).

Applying the $_{2013}$WHO criteria led to similar findings (Table 3b). For the $_{1999}$WHO, however, non-European ethnicity was not significantly associated with GDM, while parity and height remained significant in the final adjusted model (Supporting information table S1, additional file 1). The predictive power of all models was low, with Nagelkerke values ranging from 0.9% to 16.4%, depending on the criteria applied. Sensitivity analysis restricted to individuals without lifestyle intervention in two of the cohorts led to similar findings, although age was no longer significant (not shown).

Table 4 displays estimates of sensitivity and the proportion needed to be screened for selected risk factors combinations, stratified for ethnic origin. In European women, the combination "age≥25 years or BMI≥25 kg/m²" achieved the highest sensitivity of 96.5% (i.e. detected 96.5% of GDM cases), but because these risk factors occurred in 93%, an OGTT would be required in almost all women. By adding parity to the age thresholds (25 years for primipara and 35 years for parous) the number of OGTT needed was reduced to 75%, although a reduction in sensitivity to 85% was observed. Similar trends were observed for women with non-European background, except that family history of diabetes achieved a higher sensitivity (42.6%) than in their European counterparts (11%). Overall, the sensitivity of the risk factors was slightly higher when applying the $_{2017}$Norwegian criteria than the $_{2013}$WHO.

Figure 3 shows the proportion of correctly identified GDM cases for European women, and proportion that would be offered an OGTT for each risk factor or combination of factors by the $_{2017}$Norwegian and $_{2013}$WHO criteria. Irrespective of the risk factor used, the sensitivity increased with the number of women needing a test for both diagnostic criteria, displaying three clusters of four to five factors with poor, moderate and good performance. To identify at least 80% of women with GDM (good performance), at least 75% of all women would need to undergo an OGTT. The risk factor displaying both high sensitivity and the smallest proportion of OGTT's, was the combination "BMI≥25 kg/m² or (primipara+age≥25) or (parous+age≥35)". With 75% requiring a test, this factor combination failed to identify 15% of women with GDM by $_{2017}$Norwegian criteria. The proportion of OGTT required could be reduced to 54% by increasing the threshold for age to ≥30 years for primipara (moderate performance); however, this approach implies that 27% of women with GDM will remain undiagnosed (table 4).

Discussion

In this study of women universally offered an OGTT during the second half of pregnancy, we found a similar overall prevalence of GDM (10.7% vs 10.3%) with the $_{2017}$Norwegian criteria and the previously used

criteria ($_{1999}$WHO), but using lower glucose level thresholds in line with $_{2013}$WHO criteria, identified considerably higher numbers of women with GDM (16.9%). The prevalence more than doubled for non-European women applying the $_{2013}$WHO and $_{2017}$Norwegian criteria, even after adjusting for covariates. Our study further shows that while advancing age and elevated BMI increased the risk of GDM, using these risk factors in pre-diagnostic screening is a poor method for accurately identifying women with GDM, resulting in many missed cases unless 70-80% of European women are tested. The sensitivity of the risk factors was lower for non-European women, indicating an even stronger rationale for universal screening in these women.

Although shifting from the older $_{1999}$WHO criteria to the new $_{2017}$Norwegian criteria resulted in a similar frequency of GDM, the groups identified differ in terms of their metabolic profile. The latter criteria identified more women with a higher pre-pregnancy BMI and non-European ethnicity, presumably attributable to the lower fasting glucose threshold.

Our prevalence rates applying the $_{2013}$WHO criteria are comparable with estimates reported in other studies in the past decade, although differences in screening procedures, demographic characteristics of the subjects as well as the ethnic make-up of the population make direct comparisons complex. Guariguata et al. (14) estimated that the global prevalence of hyperglycaemia using the $_{2013}$WHO criteria was 16.9%. A more recent meta-analysis of high-income countries in Europe found an overall GDM prevalence of 5.4%, regardless of diagnostic criteria used (15). In contrast, a study using $_{2013}$WHO thresholds and only fasting glucose in a Danish pregnancy cohort, found that 40% were classified as having GDM (16). The authors raised important questions about uniform application of diagnostic thresholds across the world, and suggested population-based local recommendations.

Multiple studies have evaluated selective risk factor-based strategies aiming to identify the best diagnostic approach for GDM (17, 18). We demonstrate that the most sensitive and specific cut-offs for maternal age and BMI in European women were age≥25 years and BMI ≥25kg/m² when parity was added. However, used as a screening strategy this would mean inviting the majority of women for an OGTT as at least one of these risk factors applies to most women today. This confirms recent findings from a systematic review and meta-analysis by Farrar et al. (8) concluding that sensitivity increases with the number of women needing a test. This strategy does not vary much from universal screening, and supports the contention that identification of GDM requires testing of almost all pregnant women (19) especially considering the rise in maternal age and overweight/obesity among childbearing over recent years (20).

Selective screening has the potential to spare many pregnant women of diagnostic testing thereby reducing time and resource use. However, consistent with others (21, 22) we found that screening on the basis of risk factors would result in a larger number of missed diagnoses and hence limit the opportunity for immediate and long-term follow up and treatment. This is of concern, as a substantial proportion of women with GDM have no defined risk factors (23, 24). The importance of GDM management is now widely accepted, and evidence supports that treatment of even milder degrees of hyperglycaemia could improve pregnancy outcomes (25, 26). Additionally, universal screening has the unique potential to identify this subset of women who would not otherwise be identified as having GDM, and, therefore, provide clinicians, as well as

the women themselves, an opportunity to plan postpartum lifestyle interventions that could prevent or delay the onset of future type 2 diabetes (27-29).

Our study has several strengths. We merged data from four contemporary birth cohorts, allowing more powerful and flexible analyses. Additionally, although the level of missing was generally low, missing data were adequately handled by multiple imputation to prevent biased results. By including different geographical populations in Norway, we believe that the results may be broadly generalizable in Norway as well as to different antenatal populations in other high-income countries. Moreover, our study included women from various ethnic groups, making our findings relevant to other European countries consisting of ethnic diverse populations. It is of note, however, that almost all non-European women came from one study.

The majority of the European women in our study had a normal BMI and high educational level, which may indicate that our prevalence rates of GDM are less generalizable to more high-risk populations. The rates of overweight and obesity in our cohort were somewhat lower than our background population (8% obesity in our study vs 12% nationally in 2018)(30). A selection bias towards inclusion of individuals with a higher health awareness, as is often seen in clinical studies, may have led to underestimation of the reported prevalence rates and the numbers needed to be screened. A higher proportion of overweight/obesity would require an OGTT of a larger number of women. Second, two of the included studies were RCT's with a lifestyle intervention for half of the women. However, no effect of the intervention on GDM status was reported in these studies and, reassuringly, our findings remained unchanged in sensitivity analyses. Lastly, we present data from four cohorts pooled into one data set where each study differs somewhat in terms of inclusion period, time of OGTT and geography, although by including Norwegian studies only and adjusting for study cohort this source of heterogeneity was limited.

Conclusion

The use of a stricter diagnostic criteria than the $_{2013}$WHO (OR of 2.0 vs. 1.75) limited the prevalence of GDM to approximately the same level as the older $_{1999}$WHO. We found that maternal characteristics are of limited use in identifying women with GDM, requiring testing of almost all women to avoid overlooking a substantial number of cases. The costs and benefits of universal screening, and the use of alternative testing algorithms or biomarkers, require further evaluation.

List Of Abbreviations

BMI

body mass index

GDM

gestational diabetes mellitus

OGTT

oral glucose tolerance test

OR

odds ratio

WHO

World Health Organization

Declarations

Ethics approval and consent to participate

The original studies were based on written informed consent. The Norwegian Regional Ethics committees (REC) approved that each constituent study could contribute to the consortium, and the current study was approved by the REC South East (2017/2533). All methods were performed in accordance with the relevant guidelines and regulations. Privacy and confidentiality were maintained throughout the study.

Consent for publication

Not applicable

Availability of data materials

The datasets generated and/or analyzed during the current study are not publicly available due to the dataset containing clinical data which cannot be shared publicly, and as the study is part of a PhD work. The data are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was funded by South-Eastern Norway Regional Health Authority. The funder was not involved in the design of the study, data collection, analyses or interpretation of data, nor the writing of the manuscript.

Authors' contributors

The original data was collected by AKJ, LS, LRS, SNS and TL. AKJ conceived and designed this study and LS, NCØ and LRS participated in the planning of the project. They also participated in the interpretation of data, the writing process and reviewing the manuscript. ASR analyzed the data and wrote the manuscript

under supervision. AHP assisted in the planning and performing of statistical analyses. All authors have read and approved the final version.

Acknowledgements

Not applicable

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Tables

Table 1. Characteristics of the participating pregnancy and birth cohorts.

Characteristics	Stork Grorudddalen	Stork Rikshospitalet	Fit for Delivery	TRIP	Total
	n=752	n=983	n=545	n=701	n=2981
Study period	2008-2010	2002-2008	2009-2013	2007-2009	
Type of study	cohort	cohort	RCT	RCT	
Gest. age at inclusion (weeks)	15.1 ± 3.4	15.8 ± 1.3	15.1 ± 2.6	20.2 ± 1.6	16.5 ± 3.1
Gest. age at OGTT (weeks)	28.3 ± 1.3	31.2 ± 1.0	29.6 ± 0.8	34.0 ± 2.0	30.8 ± 2.5
European ethnicity	363 (48.3)	983 (100)	541 (99.3)	701 (100)	2588 (86.8)
Current smoker	31 (5.0)	23 (2.3)	20 (3.7)	6 (0.9)	80 (2.8)
Education					
primary or less	124 (16.5)	12 (1.2)	10 (1.8)	3 (0.4)	149 (5.0)
High school education	297 (39.5)	128 (13.0)	158 (29.0)	62 (8.8)	645 (21.6)
Higher education	331 (44.0)	843 (85.8)	377 (69.2)	636 (90.7)	2187 (73.4)
Primipara	345 (45.9)	524 (53.3)	545 (100)	405 (57.8)	1819 (61.0)
Diabetes in family	191 (26.1)	98 (10.5)	NM	61 (9.1)	350 (11.7)
Age (years)					
Total	29.9 ± 4.8	31.3 ± 3.8	28.0 ± 4.3	30.6 ± 4.2	30.2 ± 4.4
Primipara	28.1 ± 4.6	30.0 ± 3.7	28.0 ± 4.3	29.2 ± 3.7	28.9 ± 4.1
Parous	31.4 ± 4.5	32.7 ± 3.6	*	32.4 ± 4.1	32.2 ± 4.0
Prepregnant BMI (kg/m²)	24.6 ± 4.8	23.4 ± 3.7	23.6 ± 3.8	23.1 ± 3.1	23.7 ± 3.9
BMI at inclusion (kg/m²)	25.3 ± 4.8	24.5 ± 3.4	24.5 ± 3.9	24.7 ± 3.1	24.8 ± 4.0
Fasting glucose at OGTT (mmol/L)	4.8 ± 0.6	4.6 ± 0.4	4.6 ± 0.4	4.3 ± 0.4	4.6 ± 0.5
2-h glucose at OGTT (mmol/L)	6.2 ± 1.4	6.2 ± 1.4	6.1 ± 1.3	5.7 ± 1.2	6.1 ± 1.3
GDM, $_{1999}$WHO-criteria	97 (12.9)	124 (12.6)	57 (10.5)	42 (6.0)	320 (10.7)
GDM, $_{2013}$WHO-criteria	236 (31.4)	145 (14.8)	76 (13.9)	47 (6.7)	504 (16.9)
GDM, $_{2017}$Norway-criteria	156 (20.7)	87 (8.9)	38 (7.0)	27 (3.9)	308 (10.3)

Data presented as mean ± SD or n (%). Values are imputed for pre-pregnancy weight, parity and education.

** Only primipara included in the study*

OGTT: oral glucose tolerance test; BMI: body mass index; GDM: gestational diabetes mellitus; WHO: World Health Organization; NM: not measured

Table 2 Characteristics of study participants according to their glucose tolerance status, with three criteria (1999 WHO, 2013 WHO and 2017 Norwegian criteria).

Participant characteristic	2017 Norwegian criteria	
	non-GDM, n=2673 (89.7)	GDM, n=308 (10.3)
Age (years)	30.1 ± 4.3	30.8 ± 5.1
Pre-pregnancy BMI (kg/m²)	23.4 ± 3.6	26.0 ± 5.5
BMI at inclusion (kg/m²)	24.5 ± 3.7	27.2 ± 5.6
Height (cm)	167.6 ± 6.4	165.3 ± 6.8
Primipara, n (%)	1660 (62.1)	159 (51.6)
European ethnicity, n (%)	2386 (89.3)	202 (65.6)
Current smoker, n (%)	68 (2.6)	12 (4.3)
Education, n (%)		
Primary or less	107 (4.0)	42 (13.6)
High school education	549 (20.5)	96 (31.2)
Higher education	2017 (75.5)	170 (55.2)
Fasting glucose at OGTT (mmol)	4.5 ± 0.4	5.5 ± 0.6
2-h glucose at OGTT (mmol/L)	5.9 ± 1.2	7.6 ± 1.7
Gestational age at OGTT (weeks)	29.8 ± 2.2	31.0 ± 2.5
Age groups, (years) n (%)		
≤25	308 (11.5)	39 (12.7)
25-29.9	956 (35.8)	93 (30.2)
30-34.9	1020 (38.2)	106 (34.4)
≥35	389 (14.6)	70 (22.7)
Pre-pregnant BMI groups, (kg/m²) n (%)		
≤25	1992 (74.5)	150 (48.7)
25-26.9	314 (11.7)	44 (14.3)
27-29.9	209 (7.8)	43 (14.0)
≥30	158 (5.9)	71 (23.0)
Age (years)		
Primipara	28.9 ± 4.0	28.9 ± 5.0
Parous	32.1 ± 4.4	32.8 ± 4.4

Data presented as mean ± SD or n (%).

[a]Independent sample T test for continous variables and X² statistic for categorical variables.

WHO: World Health Organization, GDM: gestational diabetes mellitus, BMI: body mass index, OGTT: oral glucose tolerance test, 2-h: 2-hours

Values are imputed for pre-pregnancy weight, parity and education.

Table 3a Associations between maternal risk factors and gestational diabetes mellitus in univariate analysis and multivariate analysis, applying the $_{2017}$Norwegian criteria

	Univariate analysis			Model 1: r²=0.158			Model 2: r²=0.157		
Variables	**Odds ratio**	**95% CI**	*P*-value	**aOR**	**95% CI**	*P*-value	**aOR**	**95% CI**	*P*-value
Age (years)			0.001			0.003			0.003
≤25	1			1			1		
25-29.9	0.76	0.52-1.14	0.191	0.90	0.57-1.41	0.651	0.86	1.20-2.58	0.495
30-34.9	0.82	0.55-0.21	0.319	1.07	0.67-1.71	0.768	1.00	0.64-1.56	0.984
≥35	1.42	0.93-2.16	0.100	1.84	1.10-3.07	0.020	1.73	1.07-2.80	0.026
Pre-pregnancy BMI (kg/m²)			<0.001			<0.001			<0.001
≤25	1			1			1		
25-26.9	1.86	1.30-2.66	0.001	1.76	1.20-2.57	0.004	1.77	1.21-2.58	0.003
27-29.9	2.73	1.89-3.95	<0.001	2.60	1.75-3.87	<0.001	2.64	1.78-3.92	<0.001
≥30	5.97	4.31-8.26	<0.001	4.96	3.43-7.16	<0.001	5.12	3.56-7.35	<0.001
non-European ethnicity	4.36	3.35-5.69	<0.001	2.46	1.53-3.94	<0.001	2.72	1.78-4.13	<0.001
Parous	1.53	1.21-1.94	<0.001	0.99	0.73-1.34	0.955			
Education						0.725			
Higher education	1			1					
high school education	2.07	1.59-2.71	<0.001	1.12	0.79-1.58	0.504			
primary or less	4.60	3.11-6.80	<0.001	1.21	0.69-2.09	0.509			
Height (cm)	0.95	0.93-0.96	<0.001	0.99	0.96-1.01	0.341			
Current smoker	1.66	0.89-3.11	0.112	1.29	0.65-2.56	0.454			
Cohort									
Stork Rikshospitalet	1								
FFF	0.77	0.52-1.15	0.200						
STORK Groruddalen	2.70	2.03-3.57	<0.001						
TRIP	0.41	0.26-0.64	<0.001						
Diabetes in family*	1.88	1.40-2.53	<0.001						

Binary logistic regression was performed,

2017Norway criteria.

Models are adjusted for cohort.

Abbrevations: aOR: adjusted odds ratio, CI: confidens interval, BMI: body mass index.

* Not measured in Fit for Delivery

Table 3b Associations between maternal risk factors and gestational diabetes mellitus in univariate analysis and multivariate analysis, applying the 2013WHO criteria

	Univariate analysis			Model 1: r²=0.164			Model 2: r²=0.163		
Variables	**Odds ratio**	**95% CI**	*P*-value	**aOR**	**95% CI**	*P*-value	**aOR**	**95% CI**	*P*-value
Age (years)			<0.001			<0.001			<0.001
≤25	1			1			1		
25-29.9	0.74	0.53-1.01	0.062	0.91	0.63-1.32	0.622	0.87	0.60-1.25	0.445
30-34.9	0.85	0.62-1.17	0.321	1.24	0.84-1.83	0.267	1.18	0.82-1.70	0.381
≥35	1.50	1.07-2.13	0.020	2.17	1.42-3.33	<0.001	2.07	1.38-3.09	<0.001
Pre-pregnancy BMI (kg/m²)			<0.001			<0.001			<0.001
≤25	1			1			1		
25-26.9	1.84	1.38-2.46	<0.001	1.69	1.24-2.30	0.001	1.70	1.25-2.32	<0.001
27-29.9	3.23	2.40-4.35	<0.001	2.96	2.15-4.09	<0.001	3.02	2.18-4.16	0.001
≥30	4.84	3.60-6.49	<0.001	3.90	2.80-5.43	<0.001	4.06	2.93-5.61	<0.001
non-European ethnicity	3.79	3.00-4.78	<0.001	1.91	1.28-2.86	0.002	2.17	1.51-3.10	<0.001
Parous	1.49	1.23-1.80	<0.001	1.02	0.79-1.31	0.875			
Education						0.340			
Higher education	1			1					
high school education	1.89	1.52-2.36	<0.001	1.43	0.88-2.33	0.148			
primary or less	4.17	2.94-5.92	<0.001	1.11	0.84-1.47	0.474			
Height	0.96	0.94-0.97	<0.001	0.99	0.98-1.00	0.580			
Current smoker	0.65	0.38-1.12	0.119	1.13	0.98-1.01	0.674			
Cohort			<0.001						
Stork Rikshospitalet	1								
FFF	0.94	0.69-1.26	0.668						
STORK G	2.64	2.09-3.34	<0.001						
TRIP	0.41	0.29-0.59	<0.001						

Diabetes in family *	1.85	1.44-2.38	<0.001		

Binary logistic regression was performed, $_{2013}$WHO-criteria.

Models are adjusted for cohort.

Abbrevations: aOR: adjusted odds ratio, CI: confidens interval, BMI: body mass index.

* Not measured in Fit for Delivery

Table 4 Performance of risk factors, alone or in combination, for the identification of GDM, with two criteria (2017 Norwegian and 2013 WHO)

2017 Norwegian criteria

Risk factors	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OGTT's needed (%)	Undetected GDM cases (%)
European background, n=2588						
BMI ≥ 25 kg/m²	53.0	75.6	15.5	95	26.6	47.0
BMI ≥ 27 kg/m²	36.6	87	19.2	94.2	14.9	63.4
BMI ≥ 30 kg/m²	22.8	94.4	24.4	93.9	6.8	77.7
Age ≥ 25 years	91.1	10.1	7.9	93.1	90.0	8.9
Age ≥ 30 years	60.4	45.5	8.6	93.1	54.9	39.6
Age≥25 or BMI≥25	96.5	7.2	8.1	96.1	93.1	3.5
Age≥30 or BMI≥30	71.3	42.7	9.5	94.6	58.4	28.7
Age≥30 or BMI≥27	74.3	39.4	9.4	94.8	61.6	25.7
BMI≥25 or (Primipara + Age≥25) or (parous + age≥35)	85.1	26.0	8.9	95.4	74.9	14.9
BMI≥25 or (Primipara + Age≥25) or (parous + age≥40)	78.7	32.3	9.0	94.7	68.5	21.3
BMI≥25 or (Primipara + Age≥30) or (parous + age ≥35)	72.8	47.9	10.6	95.4	53.7	27.2
BMI≥27 or (Primipara + Age≥30) or (parous + age≥35)	61.9	54.5	10.3	94.4	46.8	38.1
Family history of diabetes*	11.5	89.1	8.7	92.1	10.6	87.3
BMI≥ 25 or Age≥30 or family history of diabetes	87.8	22.8	9.3	95.4	78.1	12.2
Non-European background, n=393						
BMI ≥ 23 kg/m²	64.2	46.0	30.5	77.6	56.7	35.8
BMI ≥ 25 kg/m²	47.2	66.2	34.0	77.2	37.4	52.8
BMI ≥ 27 kg/m²	37.7	80.5	41.7	77.8	24.4	62.3
Age ≥ 25 years	80.2	23.3	27.9	76.1	77.6	19.8
Age ≥ 30 years	50.0	63.4	33.5	77.4	40.2	50.0
Age≥25 or BMI≥25	87.7	17.4	28.2	79.4	84.0	12.3
Age≥30 or BMI≥23	74.5	33.1	29.2	77.9	69.0	25.5
BMI≥25 or (Primipara + Age≥25) or (parous + age≥35)	69.8	42.5	31.0	79.2	60.8	30.2
Family history of diabetes*	42.6	64.3	30.3	75.4	37.6	57.4

2013 WHO criteria

Risk factors	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OGTT's needed (%)	Undetected GDM cases (%)
European background, n=2588						
BMI ≥ 25 kg/m²	48.3	76.8	25.0	90.3	26.6	51.7
BMI ≥ 27 kg/m²	33.2	87.9	29.5	89.7	14.9	66.8
BMI ≥ 30 kg/m²	16.6	94.8	33.7	87.7	6.8	83.4
Age ≥ 25 years	90.4	10.1	13.8	86.9	90.0	9.6
Age ≥ 30 years	62.1	46.2	15.5	88.4	54.9	37.9
Age≥25 or BMI≥25	95.2	7.2	14.1	90.4	93.1	4.8
Age≥30 or BMI≥30	69.7	43.4	16.4	90.0	58.4	30.3
Age≥30 or BMI≥27	75.0	40.5	16.7	91.0	61.6	25.0
BMI≥25 or (Primipara + Age≥25) or (parous	83.1	26.4	15.3	90.8	74.9	16.9

+ age≥35)						
BMI≥25 or (Primipara + Age≥25) or (parous + age≥40)	76.4	32.7	15.3	89.7	68.5	23.6
BMI≥25 or (Primipara + Age≥30) or (parous + age ≥35)	71.1	49.1	18.2	91.4	53.7	28.9
BMI≥27 or (Primipara + Age≥30) or (parous + age≥35)	62.9	55.8	18.5	90.4	46.8	37.1
Family history of diabetes*	13.2	89.5	17.3	86.6	10.6	86.8
BMI≥ 25 or Age≥30 or family history of diabetes	87.5	23.5	16.2	91.8	78.1	12.5
Non-European background, n=393						
BMI ≥ 23 kg/m²	66.2	49.0	43.9	70.6	56.7	33.8
BMI ≥ 25 kg/m²	47.3	68.6	47.6	68.3	37.4	52.7
BMI ≥ 27 kg/m²	36.5	89.2	56.3	68.4	24.4	63.5
Age ≥ 25 years	80.4	24.1	39.0	67.0	77.6	19.6
Age ≥ 30 years	48.0	64.5	44.9	67.2	40.2	52.0
Age≥25 or BMI≥25	87.8	18.4	39.4	71.4	84.0	12.2
Age≥30 or BMI≥23	76.4	35.5	41.7	71.3	69.0	23.6
BMI≥25 or (Primipara + Age≥25) or (parous + age≥35)	69.6	44.5	43.1	70.8	60.8	30.4
Family history of diabetes*	40.1	64.0	40.1	64.0	37.6	59.9

Abbrevations: BMI: body mass index; WHO: World Health Organization; PPV: positive predictive value; NPV: negative predictive value, OGTT: oral glucose tolerance test, GDM: gestational diabetes

*Family history of diabetes not measured in Fit for Delivery

Figures

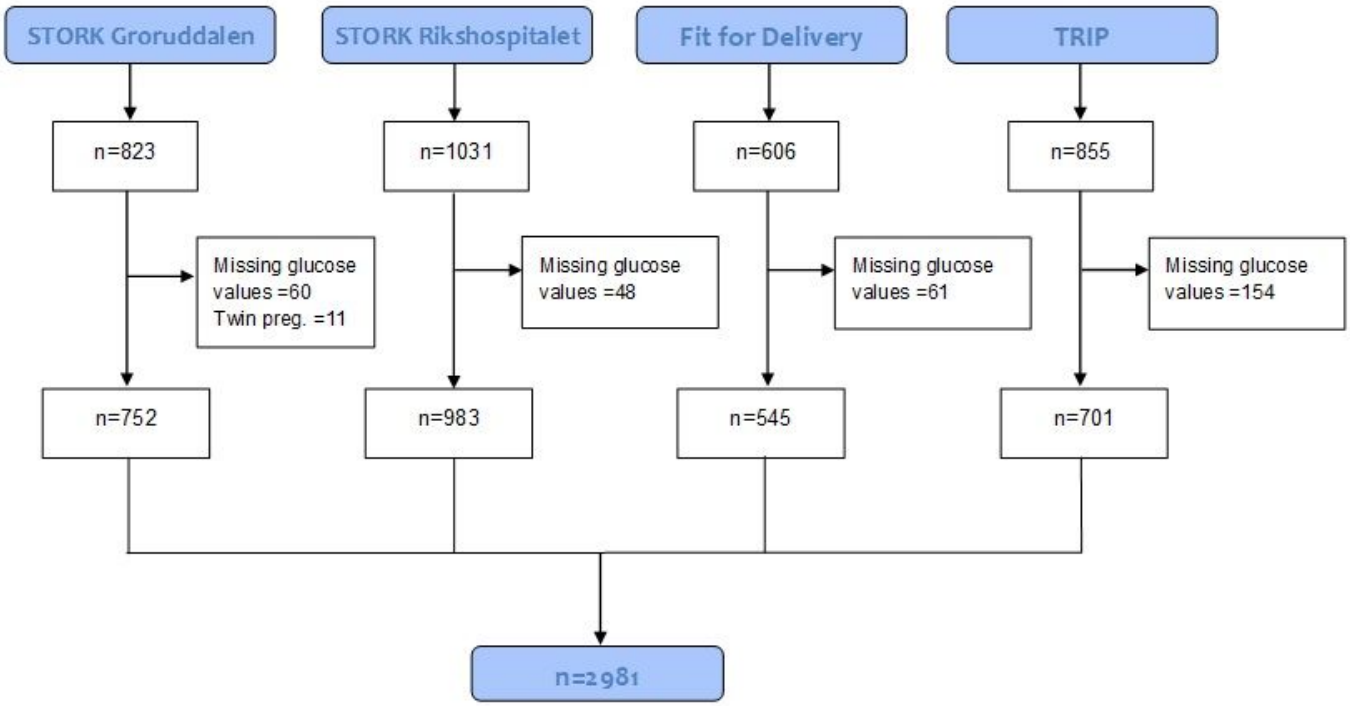


Figure 1

Flowchart of included studies and excluded participants from each study.

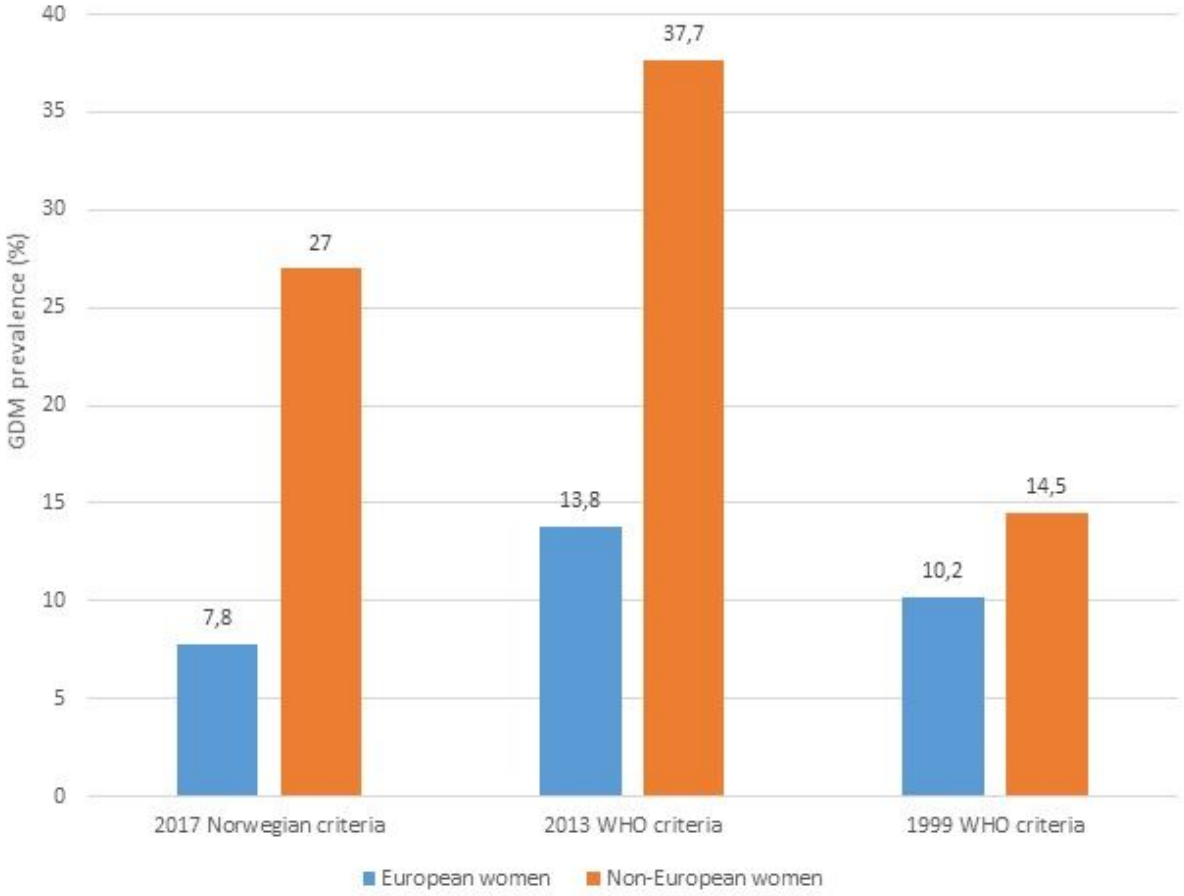
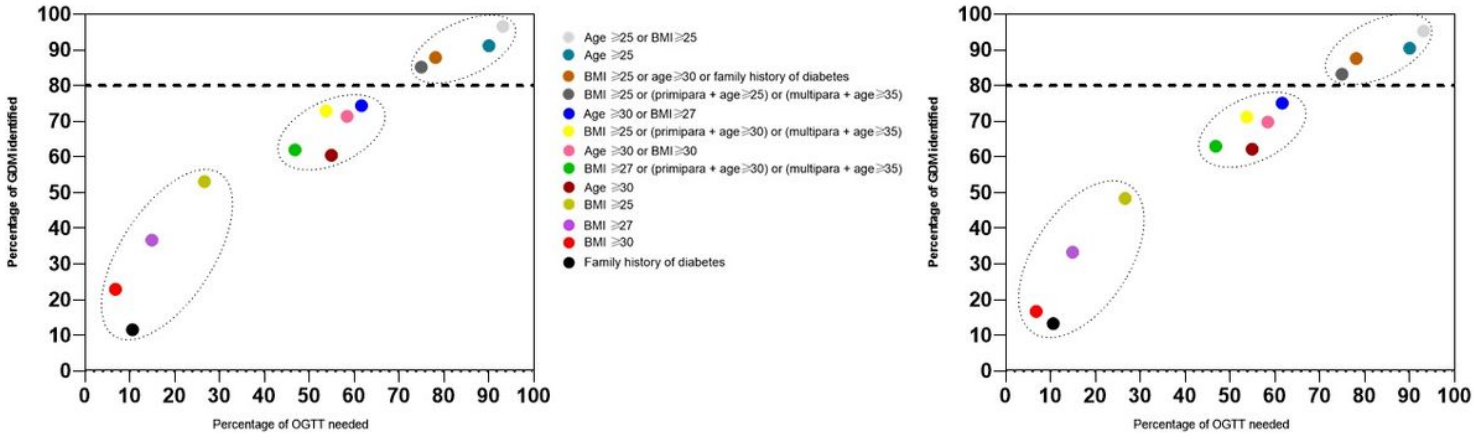


Figure 2

GDM prevalence based on three diagnostic criteria (2017Norwegian, 2013WHO, 1999WHO) for European and non-European women



a) Based on 2017Norway criteria

b) Based on 2013WHO criteria

Figure 3

Screening performance (sensitivity and percentage offered an OGTT) of risk factors (single or in combinations) for European women with the 2017Norwegian criteria (a) and 2013WHO criteria (b). The color of the points indicates the risk factors used, and the line indicates 80% sensitivity. The clusters indicate poor (bottom left corner), moderate and good performance (top right corner).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables14.xlsx
- Additionalfile1.xlsx