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ABSTRACT

Aims. – In addition to screening for hyperglycaemia during pregnancy after 24 weeks of gestation (WG), the current guidelines also suggest screening in early pregnancy and referring women with early gestational diabetes mellitus (eGDM) or overt diabetes (OD) for immediate care. Our aim was to evaluate this strategy.

Methods. – This study evaluated, at our hospital (2012–2016), whether the incidence of a predefined composite outcome (preeclampsia, large-for-gestational-age infant, shoulder dystocia) and secondary outcomes was different when women were screened only after 22 WG ('late screening only') or before 22 WG and treated for eGDM or OD if present, with repeat screening after 22 WG if absent ('early ± late screening').

Results. – Early ± late screening (n = 4605, 47.0%) increased between 2012 and 2016 ($P < 0.0001$) and was associated with more risk factors for GDM than late screening only. Glycaemic status differed in both groups (early ± late screening: eGDM 10.3%, GDM 12.1%, OD 0.9% *vs* late screening only: GDM 16.8%, OD 1.2%; $P < 0.001$), with a higher rate of insulin therapy (8.9% *vs* 6.0%; $P < 0.001$) and less gestational weight gain (11.1 ± 5.4 kg *vs* 11.4 ± 5.5 kg; $P = 0.013$) in the early ± late screening group. Rates of those meeting the composite criterion were similar in both groups [11.6% *vs* 12.0%, respectively; odds ratio (OR): 1.040, 95% confidence interval (CI): 0.920–1.176; $P = 0.53$] and remained comparable after adjusting for propensity scores (OR: 1.046, 95% CI: 0.924–1.185; $P = 0.4790$). Rates for secondary outcomes were also similar in both groups.

Conclusion. – While a strategy including early measurement of fasting plasma glucose during pregnancy increases the incidence and care of hyperglycaemia during pregnancy, it may not significantly improve pregnancy outcomes.

Key words: Diabetes in pregnancy; Early gestational diabetes mellitus; International Association of Diabetes and Pregnancy Study Groups; Guidelines; Prognosis

Abbreviations:

1h-PG: plasma glucose value 1 hour after 75-g oral glucose tolerance test

2h-PG: plasma glucose value 2 hours after 75-g oral glucose tolerance test

eGDM: early gestational diabetes mellitus

FPG: fasting plasma glucose

GDM: gestational diabetes mellitus

IADPSG: International Association of Diabetes and Pregnancy Study Groups

OGTT: oral glucose tolerance test

SD: standard deviation

WG: weeks of gestation

Disclosure statement:

The authors report no conflict of interest. In particular, apart from funding, Lilly France did not participate in any part of this study.

Introduction

Hyperglycaemia in pregnancy includes both gestational diabetes mellitus (GDM) and overt diabetes (OD) [1], also called ‘diabetes in pregnancy’ [2]. The OD category was introduced in the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations [1] to capture unknown but preexistent type 2 diabetes (T2D) in pregnancy [1], and is now widely used [2,3].

Hyperglycaemia in pregnancy typically appears in the second half of pregnancy when insulin resistance increases [4]. However, waiting for 24 weeks of gestation (WG) to diagnose OD leads to a delay in diabetes care that could result in severe obstetric outcomes [5–8]. Therefore, screening at the first prenatal visit was advised in IADPSG recommendations as well as in other guidelines [1–3,9–12]. Early hyperglycaemia during pregnancy, also called ‘early GDM’ (eGDM) [13,14], is diagnosed when glucose levels in early pregnancy are between normal and OD glucose values; the higher the fasting plasma glucose (FPG) value during early pregnancy, the greater the incidence of adverse pregnancy outcomes [15,16]. Therefore, it was recommended that women with eGDM—including those with OD—be referred for immediate care [1,3,9–12]. As the condition has become more common, it has led to ‘medicalized’ pregnancies previously categorized as normal [8,14].

However, at present, no randomized controlled trial has tested the benefit–cost ratio for screening and treatment in early pregnancy of various degrees of hyperglycaemia that may be less severe than OD, although some studies are currently ongoing [8,14,17]. Just as our team determined in a previous study [18], experts from the IADPSG also recently concluded that normative data regarding glycaemia in early pregnancy, and the consequences of its detection and treatment, are urgently required and should be a priority for future research [19]. Thus, the present study was designed to partly address this issue by exploring, in a large series of women, whether screening for hyperglycaemia during early pregnancy with eGDM/OD

treatment, or planning for repeat screening at 22 WG if normal, is indeed associated with better pregnancy outcomes compared with late screening only.

Materials and methods

Participants

This single-centre observational study was conducted at our university hospital in a suburban area of Paris, France, based on the electronic medical records of women delivering at our hospital, as obstetric data at birth are routinely entered into the database by the midwife assisting with the delivery. These data were checked and collected during hospitalization in the obstetric department by a midwife (I.P.) qualified in data management and collection [20]. In addition, from November 2014 to late October 2016, data on screening for hyperglycaemia during pregnancy were prospectively collected and retrospectively analyzed for the January 2012 to October 2014 period.

As per French law, all patients in hospital waiting rooms and hospital bedrooms were informed that their medical data could be used for research purposes unless they opposed such use. Also, it should be noted that, for observational studies, neither consent nor approval of the ethics committee is required (articles L.1121-1 paragraph 1 and R1121-2 of the Public Health Code). However, all data were analyzed anonymously, and our database was declared to the French Committee for Computerized Data [Commission Nationale de l'Informatique et des Libertés (CNIL), number 1704392v0].

Study inclusion and non-inclusion criteria are presented in Fig. 1 (flow chart): women had to be aged 18–50 years, have a singleton pregnancy, and no personal history of either diabetes or bariatric surgery. In addition, in the absence of either eGDM or OD, women were included only if they had been screened after 22 WG. Finally, the presence or absence of screening

before 22 WG had to be known in order to allocate women to ‘early ± late screening’ or ‘late screening only’ groups, respectively.

Glycaemic status during pregnancy and care of dysglycaemia

Our study defined hyperglycaemia during pregnancy according to IADPSG criteria [1], as those guidelines have been endorsed in France [10]. The prevalence of risk factors in our population was particularly high [20], and our policy was to universally screen women both at the beginning of pregnancy and after 24 WG if prior screening was normal or not done. However, this decision was taken at the discretion of healthcare providers, as the most recent national guidelines have suggested a selected screening strategy for women at high risk of pathological events [10]. Early screening was limited to FPG testing, while late screening included a 75-g oral glucose tolerance test (OGTT), with measurement of FPG and plasma glucose levels at 1 and 2 h after glucose intake (1h-PG and 2h-PG, respectively) [10]. In addition, a final screening by OGTT could have been prescribed if either macrosomia or hydramnios was present and no previous hyperglycaemia had been diagnosed [10].

eGDM was defined as FPG between 5.1 and 6.9 mmol/L (92 and 125 mg/dL) before a threshold time of 22 WG, rather than 24 WG, to avoid considering women screened only by OGTT a few weeks before 24 WG as having had early screening only. OD was defined as FPG $\geq$ 7.0 mmol/L (126 mg/dL) and/or 2h-PG $\geq$ 11.1 mmol/L (200 mg/dL) at any time. Typical GDM was defined as FPG 5.1–6.9 mmol/L (92–125 mg/dL) and/or 1h-PG $\geq$ 10.0 mmol/L (180 mg/dL) and/or 2h-PG 8.4–11.0 mmol/L (153–199 mg/dL) during OGTT performed after 22 WG [21].

Women with hyperglycaemia during pregnancy were immediately referred to a multidisciplinary team comprising a diabetologist, obstetrician, midwife, dietitian and nurse educator [10]. All received individualized dietary advice and self-monitoring of blood glucose

education, with recommendations for six tests per day, and were followed-up every 2 to 4 weeks and started on insulin therapy if fasting and/or 2-h postprandial glucose levels were > 5.3 mmol/L and/or 6.6 mmol/L (95 mg/dL and/or 120 mg/dL), respectively, according to French guidelines [10]. Oral hypoglycaemic agents are never used in France during pregnancy. Obstetric care was managed according to French recommendations [10], and was similar in women with hyperglycaemia, whereas those with OD were further examined for the presence of retinopathy and also underwent resting electrocardiography (ECG).

Endpoints

The main predefined study endpoint was the occurrence of a GDM-related event. The composite outcome included at least one of the following events: (*i*) preeclampsia (blood pressure ≥ 140/90 mmHg on two recordings 4 h apart and proteinuria ≥ 300 mg/24 h or 3+ or more on dipstick testing of a random urine sample); (*ii*) large-for-gestational-age (LGA) newborn (birth weight > 90th percentile for the standard French population) [22]; and (*iii*) shoulder dystocia, defined as requiring the use of obstetric manoeuvres (McRoberts episiotomy after delivery of the fetal head, suprapubic pressure, posterior arm rotation to an oblique angle, rotation of the infant by 180 degrees, delivery of the posterior arm) [23]. Also considered was a secondary composite endpoint which further included neonatal hypoglycaemia, defined as at least one blood glucose value < 2.0 mmol/L (36 mg/dL) during the first two days of life [24].

Each of the above-mentioned events were then considered separately, as were also: caesarean sections; small-for-gestational-age (SGA) newborns (birth weight < 10^{th} percentile for the standard French population) [22]; preterm (before 37 completed weeks) delivery; offspring hospitalization (admission to neonatal intensive care unit); respiratory distress syndrome (based on the clinical course, chest X-ray findings, blood-gas and acid-base values);

intrauterine fetal or neonatal (within the first 24 h of life) death; any malformation; and hyperbilirubinaemia, defined as the need for neonatal phototherapy. Finally, gestational weight gain during pregnancy (difference between weight at time of delivery and self-reported weight before pregnancy) and the need for insulin at the time of delivery were also considered.

Statistical analyses

Our study hypothesis was that early ± late screening would be associated with a reduction in GDM-related events compared with late screening only. Sample size calculations for this hypothesis included: (*i*) around 50% of women would be screened before 22 GW; (*ii*) the rate of events would be 11% in the 70% of women with normal glycaemic status [20], 20% in the 16% of women with typical GDM [20], 25% in the 12% of women diagnosed and treated for eGDM, but 40% if left untreated (the late screening only group) [15,16]; and (*iii*) 30% in women diagnosed and treated early for OD, but 60% in women diagnosed later with OD [5,6]. Thus, it was estimated that 14.5% of women in the early ± late screening group would experience a GDM-related event compared with 17.1% of women in the late screening only group. In the end, it was decided to include 7160 women (3080 in each group) to allow a power of 80% to detect a 2.6% absolute reduction in the incidence of GDM-related events.

Baseline continuous variables were expressed as means ± standard deviation (SD), and categorical variables as frequencies (percentages). The two groups (early ± late screening *vs* late screening only) were compared using Student's *t* test and Mann–Whitney test for Gaussian and non-Gaussian continuous variables, respectively, and chi-squared (χ^2) and Fisher's exact tests for categorical variables. In addition, the rate of GDM-related events was compared using an inverse probability propensity-score weighting method [25] to reduce or eliminate the effects of confounders associated to eGDM when using observational data

(model 1). Also used was a more recent approach, known as 'doubly robust estimation', which combines a form of outcome regression with a propensity-score model to estimate the causal effect of exposure on an outcome [26]. This latter approach (model 2) also considered the *a priori* risk factors for outcomes during pregnancy [age, body mass index (BMI), personal history of hypertension, parity, personal history of hypertensive disorders and fetal death during pregnancy, ethnicity, year of delivery, smoking during pregnancy].

All tests were two-sided and used a significance level of P values < 0.05. All analyses were carried out using SAS 9.4 software (SAS Institute, Cary, NC, USA) and R Project 2.8 software (www.r-project.org).

Results

Characteristics of the study population

Our study included 9795 of the 11,718 women who delivered between January 2012 and October 2016 at our hospital (Fig. 1). A total of 4605 women (47.0%) comprised the early ± late screening group (Fig. 2) and, compared with those in the late screening only group (n = 5190), they were older, had higher BMIs and were more likely to be working [odds ratio (OR): 1.0910, 95% confidence interval (CI): 1.0060–1.1836] (Table I). Those in the early ± late screening group were also more likely to have at least one risk factor for GDM according to French guidelines [10] (OR: 1.16, 95% CI: 1.06–1.26), to be obese (OR: 1.21, 95% CI: 1.09–1.35) or overweight (OR: 1.12, 95% CI: 1.03–1.21), to have a family history of diabetes (OR: 1.14, 95% CI: 1.04–1.25) and a previous pregnancy with GDM or a macrosomic newborn (Table I), as well as a history of hypertensive disorder or fetal death during pregnancy, but were less likely to smoke during pregnancy (OR: 0.84, 95% CI: 0.71–0.98). Furthermore, the two groups differed significantly by ethnicity (P < 0.001). Moreover, the proportion of women with early ± late screening increased with time, rising from 35.6% of

women delivering in 2012 to 44.5% of those delivering in 2013, 49.0% in 2014, 51.4% in 2015 and 53.7% in 2016 ($P < 0.0001$).

Glycaemic status and care during pregnancy

FPG and 1h-PG values after 22 WG were higher in the late screening only group than in the early ± late screening group. Glycaemic status differed in both groups, with a lower prevalence of hyperglycaemia during pregnancy in the late screening only group (18.0%) *vs* the early ± late screening group (23.3%; $P < 0.001$; Table II, Fig. 2). The latter group was also more likely to have been treated with insulin during pregnancy (OR: 1.52, 95% CI: 1.31–1.77) and to have less gestational weight gain (Table II).

Outcomes

The rate of those fulfilling the composite endpoint was similar in the early ± late screening *vs* late screening only groups (12.0% *vs* 11.6%, respectively; OR: 1.04, 95% CI: 0.92–1.18; $P = 0.53$; Table III). A similar result was observed with model 1 (OR: 1.03, 95% CI: 0.91–1.17; $P = 0.60$), in which the propensity score included the following variables, associated or not with early screening (Table I): age; BMI; occupational status; history of GDM, macrosomia, hypertensive disorder and/or fetal death during pregnancy; ethnicity; year of delivery; and smoking status during pregnancy. Similar results were seen with model 2 (OR: 1.05, 95% CI: 0.92–1.18; $P = 0.48$), as well as for rates of other outcomes (Table III).

In addition, sensitivity analysis considering only the 6656 women who had at least one risk factor of GDM, according to French recommendations, was performed. Before propensity-score modelling, the rate of those meeting the composite endpoint was similar in the early ± late screening *vs* late screening only groups (14.3% *vs* 13.7%, respectively; OR: 1.05, 95% CI: 0.91–1.21; $P = 0.48$; Table IV). The result was similar for model 1 (OR: 1.08, 95% CI:

0.94–1.25; *P* = 0.26), in which the propensity score included (or not) variables associated with early screening (Table S1; see supplementary material associated with this article online): history of GDM, macrosomia and/or fetal death during pregnancy; ethnicity; year of delivery; and smoking status during pregnancy. Likewise, the results were also similar for model 2 (OR: 1.06, 95% CI: 0.92–1.22; *P* = 0.43).

Discussion

Screening for hyperglycaemia during early pregnancy is supposed to allow earlier treatment of diagnosed hyperglycaemia and, therefore, improve pregnancy outcomes. The present observational study has shown that a strategy including early measurement of FPG during pregnancy increases the number of hyperglycaemia cases from 18.0% to 23.3%. The strategy is also associated with increased patients' care and education, with more insulin therapy and less gestational weight gain in women screened early in pregnancy compared with those who were not. Yet, despite this, and even after propensity-score modelling because early screening was associated with risk factors for GDM and GDM-related outcomes, the prognoses were similar whether women had early ± late screening or late screening only. Thus, when not only women with hyperglycaemia but all women who delivered are considered, our results suggest that such a universal strategy may not be useful for improving pregnancy outcomes.

High FPG values have been reported in 7.2–11.9% of women during the first trimester of pregnancy in various studies [15,27,28], which is in line with our present results (10.3%). Our study also reported a 30% increase in hyperglycaemia during pregnancy when early screening was performed. Similarly, in Belgium [29] and in the US [30], implementing early screening was reported to nearly double the number of detected hyperglycaemias compared with the previous standard two-step approach (Carpenter–Coustan criteria) [30].

Diagnosing eGDM and early OD leads to earlier initiation of treatment and, indeed, our study found that the use of insulin was more frequent in women who had been screened early (8.9%) compared with those who had not (6.0%), with rates of 42.3% and 30.3%, respectively, among women with hyperglycemia in both groups. This is consistent with the increased need for insulin in cases of eGDM compared with typical GDM [30–36], probably because the women who experience eGDM are characterized by a metabolic syndrome profile [14], greater insulin resistance [37,38] and more lifelong glycaemic exposure [39] than women with typical GDM. It is also possible that the lower gestational weight gain observed was the result of lifestyle education [40]. As in other studies [31–33,36], our study found that gestational weight gain was less in the early ± late screening than in the late screening only group, driven by a reduction of gestational weight gain in women with hyperglycaemia (data not shown).

Our initial hypothesis was that earlier diagnosis of hyperglycaemia during pregnancy would improve pregnancy outcomes through earlier intervention with diet/physical activity, and insulin therapy when needed, in women with eGDM and OD. However, one observational study comparing treated women with eGDM and those with typical GDM showed a similar prognosis for both groups [32]. Nevertheless, several other studies have shown a poorer prognosis for women with eGDM compared with typical GDM [8,31,33,36,41,42].

Our present study compared women who had been screened early with those who were not, irrespective of their glycaemic status. Therefore, our study also included women with normal glycaemic status. This point appears to be crucial, as eGDM is not persistent throughout pregnancy. In fact, fewer than half the patients with FPG in the 5.1–6.9 mmol/L (92–125 mg/dL) range in early pregnancy present thereafter with GDM, according to IADPSG criteria, even with no intervention between the two evaluations [27,28]. This was also illustrated by our present results: if eGDM were consistent throughout pregnancy, then the prevalence of abnormal glucose metabolism would have been similar whether or not an initial screening was

performed early in pregnancy. Indeed, women in the late screening only group with unknown eGDM would have been diagnosed with typical GDM after 22 WG if eGDM was persistent, although this may have been different if OGTT and not only FPG had been measured in early pregnancy. Thus, women with typical GDM are not comparable to women with eGDM, as 50% of the latter eventually show normal OGTT results after 24 WG.

In an attempt to avoid this limitation, Hong *et al.* [34] analyzed a retrospective cohort of women with singleton pregnancies diagnosed with GDM who had indications for early screening, including the presence of obesity and/or a history of GDM or macrosomia during a previous pregnancy. Among the women who were screened early (< 20 WG), 24% had normal early screening results, yet developed the usual GDM. As in our present study, early screening was not associated with significant reductions in the risk of caesarean deliveries, preeclampsia, macrosomia or birth injury, although a greater prevalence of preterm delivery was observed [34]. However, those results were not adjusted for potential confounders whereas, in our study, women who underwent early screening had more risk factors for GDM and GDM-related outcomes.

A very recent study has explored the prognosis for at-risk women with hyperglycaemia during pregnancy according to the period of time they were screened [13]. Women screened after the implementation of a protocol encouraging early screening compared with those screened according to the previous routine screening protocol had a twofold greater proportion of eGDM, with care beginning 22 days earlier, but with a similar need for pharmacological treatment [13]. Their risk of the primary composite outcome (emergency caesarean section, neonatal hypoglycaemia, macrosomia) was reduced significantly by 38% during the early screening protocol, suggesting that it had provided a greater window of opportunity for lifestyle intervention [13]. However, no confounding factors and, particularly, no other

possible changes in the management of these women during both periods of time, were considered.

Although our present study was unique, it nevertheless had some limitations and strengths. Our recruitment at a public hospital included women living in Europe, which has lower rates of obesity compared with other regions, such as the US [30,34,36]. However, a greater proportion of our patients had precarious lifestyles and/or had multiple ethnicities, thereby precluding generalization of our results to other populations. Our study was observational, and women in the early ± late screening group had more risk factors than those in the late screening only group, and were at higher risk of GDM and more likely to experience a GDM-related event, which may have counterbalanced the potential benefits of early diagnosis and care of hyperglycaemia during pregnancy. However, our cohort was large enough to use propensity-score models, which can take into account a number of potential confounders, and was sufficiently powered to assess differences in events. Nevertheless, despite our efforts, unmeasured differences between groups may have influenced the results. For example, it may be that women screened early are followed-up by a different type of physician (those who prescribe early screening). However, this is highly unlikely as women are followed-up with uniform procedures by both obstetric and diabetes teams, and usually not by any one specific physician. Also, socioeconomic status was not available in our study, and neither were whether targeted glucose levels were achieved nor compliance with frequency of self-monitoring of blood glucose [43]. Finally, it may be argued that our study should have focused on women with risk factors for GDM, as recommended by some guidelines [1,3,9–11]. However, sensitivity analyses showed that our results were similar in this population.

Conclusion

Our present results confirm that universal early screening for GDM leads to an increase in the proportion of women diagnosed with hyperglycaemia during pregnancy. However, despite earlier education and care in our total cohort, no reduction in GDM-related events was detected, not even with the use of propensity-score models and sensitivity analysis in women with at least one risk factor. All our analyses were global (involving the whole population) and were therefore independent of glycaemic status. To add to this real-world evidence, randomized controlled studies are still necessary before any definite conclusions can be drawn on the usefulness of early screening for hyperglycaemia and early treatment of eGDM and OD [8,14]. At present, only a secondary analysis of data from Denmark's Lifestyle in Pregnancy (LiP) study, a randomized controlled trial of 360 obese pregnant women, shows that the obstetric outcome prognosis for women with early FPG $\geq$ 5.1 mmol/L (but not treated for GDM according to local Danish GDM criteria) was similar whether they had been randomized to the intervention (n = 36) or control (n = 54) group, although the study was not powered to address the issue [44]. Also, the possible prognostic improvement with treatment could perhaps differ according to FPG levels in early pregnancy (for example, between women with eGDM and those with OD). In fact, diagnosing women with unknown diabetes/OD late in pregnancy might even be deleterious, given the poor prognoses for these women compared with those with GDM [6,45,46]. Nevertheless, the fact that early screening is not associated with better pregnancy outcomes does not preclude long-lasting effects beyond those of pregnancy, such as favourable effects for T2D prevention.

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Appendix supplementary material

Supplementary materials (Table S1) associated with this article can be found at http://www.scincedirect.com at doi . . .

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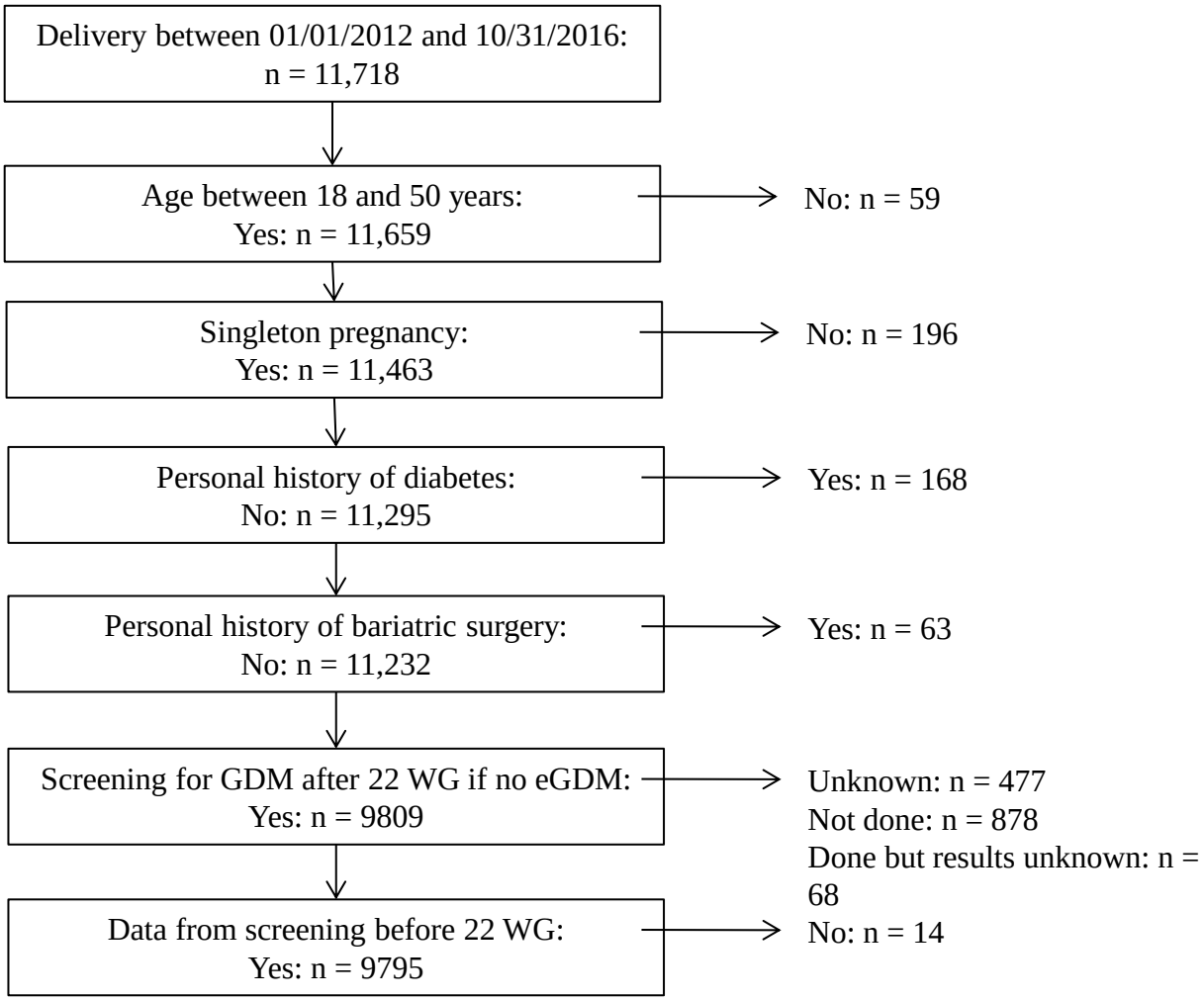
Figure legends

Fig. 1. Flow chart of study inclusion/exclusion criteria. eGDM: early gestational diabetes mellitus; GDM: gestational diabetes mellitus; WG: weeks of gestation.

Fig. 2. Main study results. eGDM: early gestational diabetes mellitus; GDM: gestational diabetes mellitus; WG: weeks of gestation; LGA: large for gestational age.


Delivery between 01/01/2012 and 10/31/2016:
n = 11,718
Age between 18 and 50 years:
Yes: n = 11,659
No: n = 59
Singleton pregnancy:
Yes: n = 11,463
No: n = 196
Personal history of diabetes:
No: n = 11,295
Yes: n = 168
Personal history of bariatric surgery:
No: n = 11,232
Yes: n = 63
Screening for GDM after 22 WG if no eGDM:
Yes: n = 9809
Unknown: n = 477
Not done: n = 878
Done but results unknown: n = 68
Data from screening before 22 WG:
Yes: n = 9795
No: n = 14

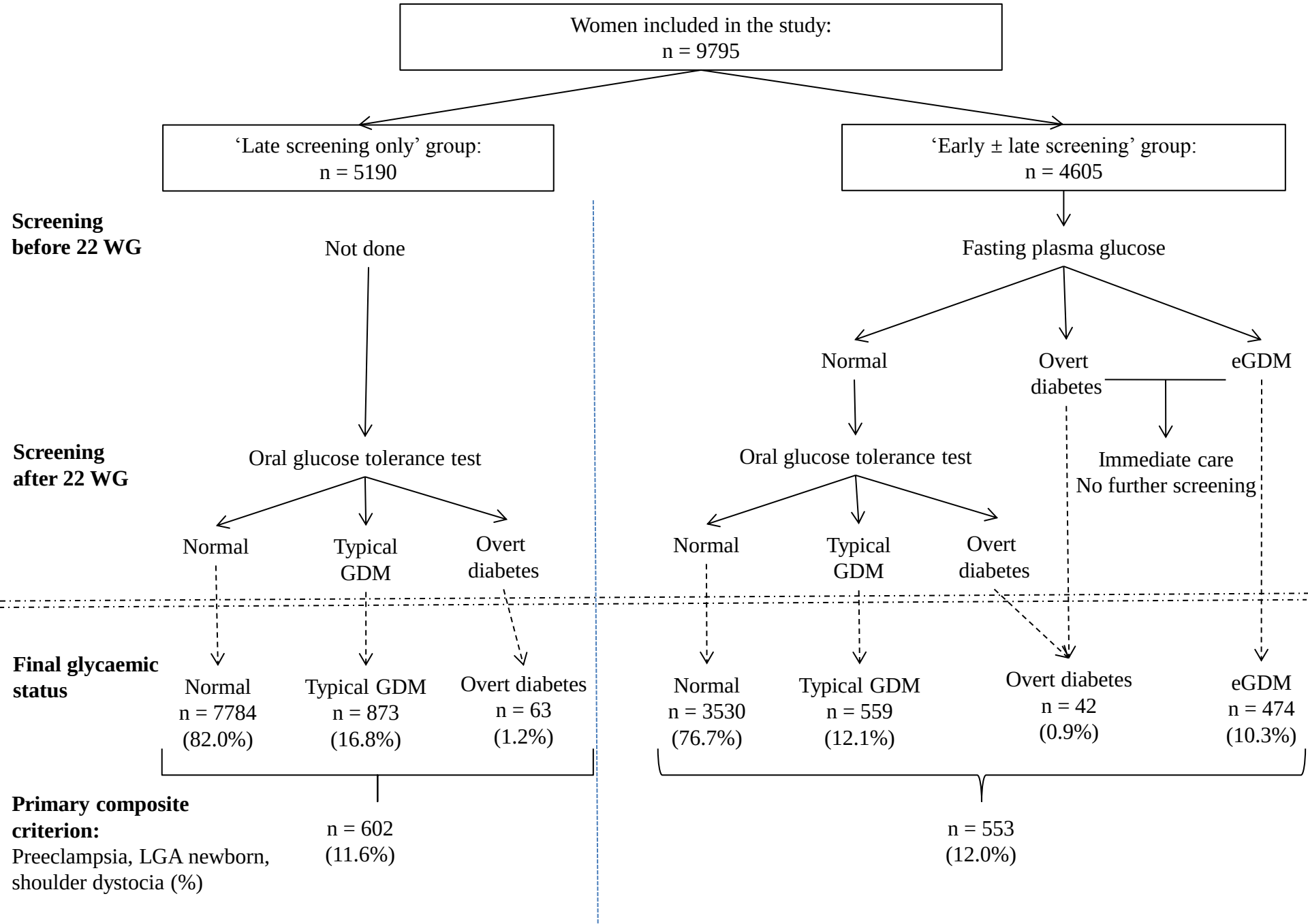

Women included in the study:
n = 9795
'Late screening only' group:
n = 5190
'Early ± late screening' group:
n = 4605
Screening before 22 WG
Not done
Fasting plasma glucose
Normal
Overt diabetes
eGDM
Screening after 22 WG
Oral glucose tolerance test
Immediate care
No further screening
Oral glucose tolerance test
Normal
Typical GDM
Overt diabetes
Normal
Typical GDM
Overt diabetes
Final glycaemic status
Normal
n = 7784
(82.0%)
Typical GDM
n = 873
(16.8%)
Overt diabetes
n = 63
(1.2%)
Normal
n = 3530
(76.7%)
Typical GDM
n = 559
(12.1%)
Overt diabetes
n = 42
(0.9%)
eGDM
n = 474
(10.3%)
Primary composite criterion:
Preeclampsia, LGA newborn, shoulder dystocia (%)
n = 602
(11.6%)
n = 553
(12.0%)

Table I
Characteristics of women screened early, or not, for gestational diabetes mellitus (GDM)

	Total	**Late screening only**	**Early ± late screening**	***P***
Characteristics	**n = 9795**	**n = 5190**	**n = 4605**	
Age (years)	30.4 ± 5.5	30.2 ± 5.6	30.5 ± 5.5	< 0.01
Body mass index before pregnancy (kg/m^2)	25.0 ± 5.1	24.7 ± 5.0	25.2 ± 5.1	< 0.01
Hypertension before pregnancy (%)	72 (0.7)	39 (0.8)	33 (0.7)	0.840
Parity	2.1 ± 1.2	2.1 ± 1.2	2.1 ± 1.2	0.107
Smoking before pregnancy (%)	1050 (10.7)	585 (11.3)	465 (10.1)	0.061
Obesity (%)	1599 (16.9)	780 (15.6)	819 (18.3)	< 0.001
Currently working (%)	3796 (38.8)	1961 (37.9)	1835 (39.9)	0.036
French risk-factor criteria:				
At least one risk factor (%)	6656 (69.5)	3449 (68.1)	3207 (71.2)	< 0.01
Body mass index ≥ 25 kg/m² (%)	4467 (47.2)	2293 (45.9)	2174 (48.7)	< 0.01
Age ≥ 35 years (%)	2321 (23.7)	1198 (23.1))	1123 (24.4)	0.130
Family history of diabetes (%)	2596 (26.5)	1312 (25.3)	1284 (27.9)	< 0.01
Previous pregnancy with GDM:				< 0.001
First pregnancy (%)	3766 (38.4)	1948 (37.5)	1818 (39.5)	
No (%)	5523 (56.4)	3020 (58.2)	2503 (54.3)	
Yes (%)	506 (5.2)	222 (4.3)	284 (6.2)	
Previous pregnancy with macrosomia:				< 0.01
First pregnancy (%)	3766 (38.4)	1948 (37.5)	1818 (39.5)	
No (%)	5734 (58.5)	3104 (59.8)	2630 (57.1)	
Yes (%)	295 (3.0)	138 (2.7)	157 (3.4)	
History of hypertensive disorder during pregnancy:				0.021
First pregnancy (%)	2631 (26.9)	1354 (26.1)	1277 (27.7)	
No (%)	6959 (71.0)	3741 (72.1)	3218 (69.9)	
Yes (%)	205 (2.1)	95 (1.8)	110 (2.4)	
History of fetal death during pregnancy:				0.018
First pregnancy (%)	2631 (26.9)	1354 (26.1)	1277 (27.7)	
No (%)	6945 (70.9)	3703 (71.3)	3242 (70.4)	
Yes (%)	219 (2.2)	133 (2.6)	86 (1.9)	
Ethnicity:				< 0.001
North African (%)	2869 (29.3)	1500 (28.9)	1369 (29.8)	
European (%)	2711 (27.7)	1437 (27.7)	1274 (27.7)	
Sub-Saharan African (%)	1888 (19.3)	1050 (20.3)	838 (18.2)	
Indian, Pakistani or Sri Lankan (%)	976 (10.0)	459 (8.9)	517 (11.2)	
Caribbean (%)	568 (5.8)	307 (5.9)	261 (5.7)	
Other (%)	766 (7.8)	429 (8.3)	337 (7.3)	
Year of delivery:				< 0.0001
2012 (%)	1842 (18.8)	1187 (22.9)	655 (14.2)	
2013 (%)	1914 (19.5)	1062 (20.5)	852 (18.5)	
2014 (%)	2052 (21.0)	1047 (20.2)	1005 (21.8)	
2015 (%)	2109 (21.5)	1025 (19.7)	1084 (23.5)	
2016 (%)	1878 (19.2)	869 (16.7)	1009 (21.9)	
Maternal smoking during pregnancy (%)	678 (6.9)	387 (7.5)	291 (6.3)	0.027

Table II
Glycaemic status of women screened early, or not, for gestational diabetes mellitus (GDM)

	Total	**Late screening only**	**Early ± late screening**	***P***
	n = 9795	**n = 5190**	**n = 4605**	
SCREENING				
Before 22 WG:				
Gestational age (WG)	12.3 ± 4.2	NA	12.3 ± 4.2	–
Fasting plasma glucose (mg/dL)	82.8 ± 9.2	NA	82.8 ± 9.2	–
Screening after 22 WG:				
Gestational age (WG)	27.7 ± 3.7	28.0 ± 3.8	27.4 ± 3.6	< 0.001
Fasting plasma glucose (mg/dL)	79.8 ± 9.5	80.5 ± 10.4	79.0 ± 8.2	< 0.001
1-h plasma glucose (mg/dL)	126.6 ± 33.3	127.4 ± 34.2	125.6 ± 32.1	0.0104
2-h plasma glucose (mg/dL)	110.5 ± 28.1	110.9 ± 29.3	110.0 ± 26.5	0.157
Screening for macrosomia or hydramnios:*				
Fasting plasma glucose (mg/dL)	78.8 ± 10.0	79.1 ± 9.0	78.6 ± 10.8	0.695
1-h plasma glucose (mg/dL)	141.0 ± 30.5	139.0 ± 31.4	142.9 ± 29.7	0.288
2-h plasma glucose (mg/dL)	120.2 ± 30.2	120.2 ± 30.2	120.2 ± 30.3	0.992
GLYCAEMIC STATUS				< 0.001
No GDM	7784 (79.5)	4254 (82.0)	3530 (76.7)	
Early GDM	474 (4.8)	0	474 (10.3)	
Typical GDM	1432 (14.6)	873 (16.8)	559 (12.1)	
Overt diabetes	105 (1.1)	63 (1.2)	42 (0.9)	
EVENTS DURING PREGNANCY				
Gestational weight gain (kg)	11.3 ± 5.5	11.4 ± 5.5	11.1 ± 5.4	0.0129
Insulin therapy (%)	723 (7.4)	313 (6.0)	410 (8.9)	< 0.0001

* In 130 women in late screening only group, in 155 women in early ± late screening group;
WG: weeks of gestation; NA: not applicable

Table III
Pregnancy-related outcomes in women screened early, or not, for gestational diabetes mellitus (GDM)

	Total	**Late screening only**	**Early ± late screening**	***P***
	n = 9795	**n = 5190**	**n = 4605**	
Primary composite criterion				
Preeclampsia, LGA newborn, shoulder dystocia (%)	1155 (11.8)	602 (11.6)	553 (12.0)	0.53
Secondary composite criterion				
Preeclampsia, LGA newborn, shoulder dystocia, neonatal hypoglycaemia (%)	1210 (12.4)	638 (12.3)	572 (12.4)	0.85
Maternal events				
Preeclampsia (%)	182 (1.9)	107 (2.1)	75 (1.6)	0.11
Caesarean section (%)	2046 (20.9)	1055 (20.3)	991 (21.5)	0.15
Neonatal events				
LGA (%)	974 (9.9)	498 (9.6)	476 (10.3)	0.22
SGA (%)	967 (9.9)	520 (10.0)	447 (9.7)	0.60
Birth weight (g)	3295 ± 507	3291 ± 503	3300 ± 511	0.38
Shoulder dystocia (%)	15 (0.2)	6 (0.1)	9 (0.2)	0.31
Term at delivery (WG)	36.89 ± 3.08	36.67 ± 3.13	37.20 ± 3.00	0.25
Preterm delivery (%)	520 (5.3)	281 (5.4)	239 (5.2)	0.62
Offspring hospitalization (%)	1796 (18.4)	940 (18.1)	856 (18.6)	0.55
Respiratory distress syndrome (%)	437 (4.5)	223 (4.3)	214 (4.6)	0.41
Intrauterine fetal or neonatal death (%)	23 (0.2)	13 (0.3)	10 (0.2)	0.73
Any malformation (%)	97 (1.0)	50 (1.0)	47 (1.0)	0.78
Neonatal hypoglycaemia (%)	71 (0.9%)	41 (1.0%)	30 (0.8%)	0.47
Neonatal hyperbilirubinaemia (%)	193 (2.0)	106 (2.0)	87 (1.9)	0.59

LGA/SGA: large/small for gestational age; WG: weeks of gestation

Table IV
Pregnancy-related outcomes in women at risk* and screened early, or not, for gestational diabetes mellitus (GDM)

	Total	**Late screening only**	**Early ± late screening**	***P***
	n = 6656	**n = 3449**	**n = 3207**	
Primary composite criteria				
Preeclampsia, LGA infant, shoulder dystocia (%)	932 (14.0)	473 (13.7)	459 (14.3)	0.482
Secondary composite criteria				
Preeclampsia, LGA infant, shoulder dystocia, neonatal hypoglycaemia (%)	969 (14.6)	495 (14.4)	474 (14.8)	0.85
Maternal events				
Preeclampsia (%)	137 (2.1)	80 (2.3)	57 (1.8)	0.120
Caesarean section (%)	1545 (23.2)	791 (22.9)	754 (23.5)	0.577
Neonatal events				
LGA (%)	797 (12.0)	397 (11.5)	400 (12.5)	0.227
SGA (%)	600 (9.0)	323 (9.4)	277 (8.6)	0.300
Weight at delivery (g)	3330 ± 518	3320 ± 515	3340 ± 521	0.110
Shoulder dystocia (%)	12 (0.2)	4 (0.1)	8 (0.2)	0.200
Term at delivery (WG)	39.67 ± 1.58	39.64 ± 1.60	39.71 ± 1.57	0.063
Preterm delivery (%)	364 (5.5)	196 (5.7)	168 (5.2)	0.426
Offspring hospitalization (%)	1233 (18.5)	618 (17.9)	615 (19.2)	0.188
Respiratory distress syndrome (%)	290 (4.4)	150 (4.3)	140 (4.4)	0.974
Intrauterine fetal or neonatal death (%)	15 (0.2)	7 (0.2)	8 (0.2)	0.6902
Any malformation (%)	67 (1.0)	30 (0.9)	37 (1.2)	0.246
Neonatal hypoglycaemia (%)	50 (0.9)	26 (0.9)	24 (0.9)	0.472
Neonatal hyperbilirubinaemia (%)	121 (1.8)	66 (1.9)	55 (1.7)	0.544

* Defined by French recommendations as at least one of the following risk factors: body mass index ≥ 25 kg/m², age ≥ 35 years, family history of diabetes, or previous pregnancy with either GDM or macrosomia;
LGA/SGA: large/small for gestational age; WG: weeks of gestation