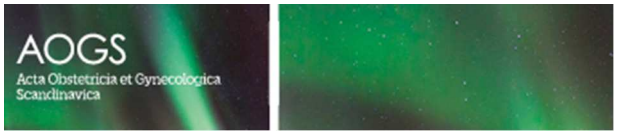

Towards national comprehensive gestational diabetes screening -Consequences for neonatal outcome and care

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Towards national comprehensive gestational diabetes screening – Consequences for neonatal outcome and care

Short title: Neonatal care after comprehensive GDM screening

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Abstract

Introduction: The change from risk-factor based to nearly comprehensive screening of gestational diabetes (GDM) identifies more but milder cases of the disease. The main aim of this study was to evaluate the effect of this screening policy change on neonatal outcomes and care.

Material and methods: A population-based register study in Finland. GDM cases during risk factor–based (year 2006, n=5179) and comprehensive (2010, n=6679) screenings were identified through Medical Birth Register. All singletons without maternal GDM or pre-pregnancy diabetes served as controls (n=51 746 and 52 386, respectively). The main outcomes were macrosomia, neonatal hypoglycemia and the need of care in a neonatal ward.

Results: In the GDM group, the mean birth weight decreased between the study years from 3660 g to 3595 g and the prevalence of macrosomia from 5.6% to 4.1% even after adjustment for maternal age, parity and pre-pregnancy body mass index (BMI). The adjusted mean difference in birth weight between GDM and control newborns decreased from 70 g to 22 g between the study years. The prevalence of neonatal hypoglycemia increased from 18.0% to 22.1% in the GDM group. However, neonatal hypoglycemia was more often treated without care in a neonatal ward. The proportion of infants treated at a neonatal ward decreased in both the GDM and control groups between the study years.

Conclusions: In newborns, comprehensive GDM screening led to decreased mean birth weight and macrosomia rates, but the prevalence of neonatal hypoglycemia increased. This places substantial demands for delivery hospitals and healthcare resources.

Keywords: Gestational diabetes mellitus, diagnosis, screening, neonatal outcome, neonatal care

Comment [VS1]: Since not all women were screened, you might want to use: "nearly comprehensive" or "broad". The same applies for the title.

Comment [EK2]: Please see also our response to comment 1 of Reviewer 1.

Comment [SK3]: The aim was change the screening method as comprehensive. This and our previous studies tells how this implementation went.

Abbreviations

BMI	Body mass index
CI	Confidence interval
GDM	Gestational diabetes mellitus
GW	Gestational weeks
HAPO	Hyperglycemia and Adverse Pregnancy Outcome study
IADPSG	International Association of the Diabetes and Pregnancy Study Group
ICD 10	International Statistical Classification of Diseases and Related Health Problems
LGA	Large for gestational age
MBR	Finnish medical Birth Register
OGTT	Oral glucose tolerance test
OR	Odds ratio
SD	Standard deviation

Key message: Comprehensive screening of GDM led to decreased mean birth weight and macrosomia rates, but the prevalence of neonatal hypoglycemia increased.

Introduction

Gestational diabetes mellitus (GDM), defined as an abnormal glucose metabolism with onset or first recognition during pregnancy, is associated with an increased risk of perinatal complications and neonatal morbidities such as hypoxia, hypoglycemia, hyperbilirubinemia and birth trauma due to macrosomia (1-6). In the long term, prenatal exposure to maternal GDM increases the risk of overweight and metabolic syndrome in the offspring during childhood and adolescence (7-13).

GDM is common. Using the uniform diagnostic criteria of the International Association of the Diabetes and Pregnancy Study Group (IADPSG) based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, its prevalence varies from 9.3 to 25.5% in different populations (14). The reason for this large variation in frequency is unclear, but it may partly depend on genetic susceptibility and obesity. It is important to diagnose GDM because its effective treatment reduces perinatal complications and may also improve the offspring's long-term outcomes (7, 15-18).

In Finland, new national screening and diagnostic guidelines for GDM were launched in 2008. The previously used risk factor–based screening was replaced with nearly comprehensive screening, excluding only the estimated approximately 20% of women at very low risk of GDM. The shift to wide-scale screening led to a significant increase in women with mainly diet-treated GDM, who were more often primiparous and had a lower body mass index (BMI) (19). Our aim was to evaluate how this change of policy affected the perinatal outcome and the need for care at a neonatal ward.

Material and methods

Medical Birth Register

Our data are based on the Finnish Medical Birth Register (MBR), which was initiated in 1987 and reformed in 2004 to improve its reliability. The MBR contains data on all mothers with live births or stillbirths with a gestational age ≥ 22 weeks or a birth weight ≥ 500 g. For each delivery in Finland, a structured form for the MBR is completed by the delivery hospital within 7 days of delivery, including data regarding the course and complications of the pregnancy and the delivery, as well as information related to the perinatal health of the newborn, such as birth weight and length, Apgar score, cord blood pH, treatments and diagnosis with ICD-10 codes until the 7th day after birth. The register is completed using data compiled by the Population Register Centre on live births and by Statistics Finland regarding stillbirths and infant deaths. The data quality of the MBR has been shown to be high for most of the applicable variables (20, 21).

Definition of GDM

Since 2004, the MBR has also included information on whether the oral glucose tolerance test (OGTT) was performed to diagnose GDM, whether the result was abnormal and whether insulin treatment was initiated. For the present study, mothers were identified through the MBR using these OGTT data.

A diagnosis of GDM was applied if a woman had an abnormal OGTT result or insulin therapy was initiated during pregnancy according to the MBR. After the exclusion of multiple births, mothers with pre-pregnancy type 1 or type 2 diabetes (ICD-10 codes O24.0 or O24.1) and preterm delivery (<37 gestational weeks [gw]) of neonates with abnormally high birth weight standard deviation (>3SD) scores (birth weight standardised for the length of gestation), which are likely to reflect erroneous recordings, 5179 (9.1%) women in 2006 and 6679 (11.3%) women in 2010 fulfilled the GDM criteria. Women who did not fulfil the GDM criteria served as controls, numbering 51,746 for 2006 and 52,386 for 2010 (Figure S1).

Screening for GDM

In 2008, new national guidelines to screen and diagnose GDM were launched in Finland. Risk factor–based screening was replaced by nearly comprehensive screening (Table I). According to both screening policies, both the screening and diagnosis of GDM were carried out via a standard 2 h 75 g OGTT, which was mainly performed between the 24th and 28th gw. For both years, the OGTT was recommended between the 12th and 16th gw for high-risk groups (before 2008, prior

GDM; from 2008 onwards, prior GDM, BMI 35 or more or polycystic ovary syndrome with insulin resistance), and if the result was normal, the OGTT would be repeated between the 24th and 28th gw. In the OGTT, blood glucose concentrations are measured after an overnight fast. Venous plasma glucose equal to or higher than 5.3, 10.0, and 8.6 mmol/l at fasting and 1 and 2 h after the glucose dose, respectively, was diagnostic during both years. In both periods, a diagnosis of GDM was applied when at least one abnormal value was present in the OGTT. After the diagnosis of GDM, the patients received dietary and lifestyle counselling and began the self-monitoring of plasma glucose concentrations. According to the treatment guidelines at the time, insulin therapy was initiated if blood glucose concentrations exceeded the target levels repeatedly (5.3 mmol/l fasting and 6.7 mmol/l 1.5 h postprandial before 2008 and 5.5 mmol/l fasting and 7.8 mmol/l 1 h postprandial thereafter). In 2006, 1126 (21.7%) women with GDM were treated with insulin; the corresponding proportion in 2010 was 884 (13.2%).

Outcome

Gestational age was based on the best estimate of the duration of pregnancy at delivery. During these years, systematic ultrasound examination to determine gestational age was offered to all pregnant women between 10+0 and 13+6 gw, and detailed examination of foetal anatomy was offered between 19+0 and 22+0 gw. The MBR data include the weight of the newborn in grams and the length in full centimetres. The ponderal index, representing the body constitution of the newborn, was calculated using weight/length^3 (kg/m^3). Macrosomia was defined as being large for gestational age (LGA), as indicated by a birth weight that was +2 SD from a reference value (22).

Regarding neonatal outcomes, umbilical cord artery pH, asphyxia, Apgar score and the need and indication for treatment at a neonatal ward were reported. The six most frequent neonatal diagnoses, according to the ICD-10 codes set by a pediatrician, were used to evaluate neonatal morbidity. Those diagnoses were hypoglycemia (P70.0–70.9), hyperbilirubinemia (P59.0–59.9), neonatal respiratory distress syndrome (P22.0), transient tachypnea of the newborn (P22.1), fracture of the clavicle (P13.4) and Erb's and Klumpke's palsy (P14.0; P14.1). The Current Care Guidelines recommend repeated plasma glucose measurements for all newborns of GDM mothers; for non-symptomatic infants usually 6 measurements during the first 48 hours and for symptomatic infants more frequently. Intravenous glucose is recommended a) if a single measurement 1.4 mmol/l or less or; b) if a single measurement is 1.5 to 2.5 mmol/l and a repeated measurement after supplementary feeding is 2.5 mmol/l or less. There is no clear definition of neonatal hypoglycemia; in our experience these diagnostic codes where set when the neonate received intravenous glucose (23).

Comment [SK4]: We prefer the previous version of this sentence, but this one is ok also.

Perinatal mortality was defined as the combined rate of stillbirth and early neonatal mortality within the first 7 days of life. The time for hospital treatment in days and the location of the newborn at the seventh day after birth (at home, in a neonatal ward, in a maternal ward with mother or in another hospital) was recorded.

Comment [VS5]: Please, specify this sentence

This study was approved by the regional Ethics Committee in the Northern Ostrobothnia Hospital District, Number 2008/43, date of approval 2008-6-19.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics Versions 21 and 22. The differences between the study groups were compared by using Pearson's χ^2 test or an independent sample t-test. P-values <0.05 are regarded as statistically significant. Logistic regression analyses were performed to estimate the odds ratios and 95% confidence intervals (CIs) for the risk of outcomes consequent upon GDM in different study periods. Mean differences with 95% CI were calculated using linear regression. We present unadjusted regression analyses and those adjusted for maternal age, parity and pre-pregnancy BMI. We also report the results after further adjusting for maternal occupational status and smoking during pregnancy. Interactions were tested by adding the product term between the two variables of interest into the regression model.

Results

During the risk factor–based screening in 2006, 15 682 women (27.5% of all parturients) underwent OGTT and 5179 (9.1%) were diagnosed GDM. The corresponding rates in 2010 were 30 365 (51.4%) and 6679 (11.3%), respectively (Figure SI, Table II). Unexpectedly, both the absolute number and the proportion of insulin-treated GDM mothers decreased significantly (Table III).

Newborn body size and gestational age at birth

Both the mean birth weight and the rate of LGA decreased among newborns of GDM mothers after the implementation of comprehensive screening (65 g from 3660 [SD 542] to 3595 g [SD 561] and from 5.6% to 4.1% [adjusted ORs 1.81 and 1.46, respectively, Table SI]). In the GDM group, both the ponderal index and the absolute number of LGA cases decreased between the study years (Table II). In the control group, there was a smaller decrease in birth weight and birth weight SD score (Table II). The birth weight difference between the GDM and control groups decreased from 70 g to 22 g between the study years when adjusted for maternal age, pre-pregnancy BMI, and parity (SD scores of 0.20 and 0.11, respectively; Table SI).

Newborns in the GDM group were born earlier than those in the control group during both study years. The difference in gestational age increased between the GDM and control groups from 0.18 to 0.25 weeks between the study years (Table II).

Neonatal care

Newborns of GDM mothers were 1.7-fold more likely to require care in a neonatal ward than controls during both study years (Table SI). The need for care at a neonatal ward decreased similarly between the study years in both the GDM and control groups (II). Although the proportion of GDM group newborns treated at a neonatal ward decreased, their absolute number did not change substantially.

Neonatal complications and conditions

Table II shows the incidence of neonatal conditions, while Table SI shows the adjusted and unadjusted odds ratios for these outcomes. The incidence of neonatal hypoglycemia clearly increased in the GDM group (18.0% vs. 22.1%) after the new screening policy was introduced (Tables II, III and Table SI). However, it was the most common indication for care at a neonatal ward during both study years (Tables II and III) but was less often treated at a neonatal ward during

comprehensive screening (Table SII). Transient tachypnea was more common in infants of GDM mothers, but the rates of respiratory distress syndrome did not differ between the study groups. These odds ratios were similar during both study periods, and they were attenuated after adjustment. The higher incidence of fractures of the clavicle seen in GDM group disappeared after comprehensive screening, but Erb's palsy was more common in infants of GDM mothers during both study years. Perinatal mortality rates did not differ in the GDM and control groups between the study years. (Table II).

In addition to the adjustment for maternal age, parity and pre-pregnancy BMI shown in Table SI, we further adjusted for maternal occupational status and smoking during pregnancy for most of the neonatal outcomes. This adjustment did not alter the results.

Comparison of infants of GDM mothers treated with diet or insulin

The body size and LGA rate of infants of diet-treated mothers decreased significantly from the risk factor–based to the comprehensive screening period. This change was not seen among infants of insulin-treated mothers – the ponderal index of their offspring was higher during comprehensive screening. They were also more likely to be admitted to a neonatal ward, but the difference to offspring of diet-treated mothers narrowed between the study periods. The most common indication for care at a neonatal ward with both diet- and insulin-treated mothers was neonatal hypoglycemia (Table III, SII).

Discussion

We showed previously that the introduction of a large scale screening policy for gestational diabetes led to a significant increase in the proportion of GDM women, who mainly had a mild form of the disease (19). In the present study, we further found that in newborns, screening policy change led to decreased mean birth weight and macrosomia rates, but the prevalence of neonatal hypoglycemia increased in both diet- and insulin-treated mothers. However, this was not accompanied by an increase in care at a neonatal ward.

The need for care at a neonatal ward did not grow to the same degree as the prevalence of GDM, which may be due to the increased proportion of mild forms of disease. The amount of insulin treated GDM mothers decreased significantly, when the new uniform guidelines standardized both screening policy and cut-off levels to insulin treatment (19). However, the effect of this change to the increased incidence of neonatal hypoglycemia is unclear. Detailed new guidelines may also have encouraged a more intensive neonatal hypoglycemia screening policy in which all newborns of GDM mothers were monitored regardless of the symptoms, leading to increased hypoglycemia rates. However, the proportion of hypoglycemia as a primary indication for care at a neonatal ward did not increase, which indicates that low blood glucose concentration was mainly treated at a maternity ward with intensified oral feedings; administration of intravenous glucose generally requires treatment at a neonatal ward. The monitoring of neonatal hypoglycemia, however, places substantial demands on nursing staff and it might be worth considering whether systematic monitoring to this extent is necessary. Therefore, we agree with the conclusion of the Atlantic Diabetes in Pregnancy study arguing that the new comprehensive screening requires a great deal of manpower and resources, although it provides an opportunity to reduce the morbidity of the mother and infant (24).

Infants of GDM mothers are known to require care at a neonatal ward more often than infants of non-GDM mothers (5, 24), which was also seen in the present study. To some extent, the threshold for follow-up at a neonatal ward may be lower in GDM cases than in controls; it may also vary between hospitals. In the present study, in-ward treatment decreased to the same degree in both the GDM and control groups, which may reflect a common trend of supporting rooming-in instead of separating the mother from her newborn. In addition, optimal GDM treatment is known to decrease the risk of severe neonatal morbidity (15). Although the proportion of infants treated in a neonatal ward decreased, their absolute number remained nearly the same because of an increased number of GDM pregnancies.

During comprehensive screening, infants born to GDM mothers had lower birth weight and birth weight SD and were less likely to be macrosomic compared to risk factor–based screening. The decrease was accompanied by a lower rate of clavicle fracture. However, the decrease of macrosomia was limited to the diet-treated group, also after adjustment for maternal age, parity and pre-pregnancy BMI..There are two possible explanations for this decrease. First, comprehensive screening possibly identifies milder cases, and therefore, macrosomia is less probable. Another explanation is that the reduction is a result of uniform counselling and follow-up based on the new Current Guidelines. Indeed, treatment of mild GDM has been shown to reduce the risk of macrosomia (15, 17).

The strength of our study is that it included a large, unselected study population based on comprehensive national register data. In Finland, virtually all pregnant women receive maternal health care free of charge and give birth in a public hospital. Therefore, systematic and unselected data acquisition is possible. The coverage of the Finnish MBR is practically complete, and most variables are of high quality. Because of the study design, however, we did not have data on woman's previous pregnancies; therefore, we were unable to estimate the exact proportion of very low risk women for whom the new guidelines do not recommend OGTT or to evaluate the significance of specific GDM risk factors during different study periods.

In conclusion, comprehensive GDM screening detects more cases of GDM, but these are less severe. This is also reflected in the neonatal outcomes: During comprehensive screening, infants of GDM mothers were smaller, less often macrosomic and required care in a neonatal ward less often. Although the proportion of infants treated at a neonatal ward did not increase in the same relation with the total GDM cases, the increased prevalence of GDM and neonatal hypoglycemia placed substantial demands on the nursing staff and the delivery hospitals.

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Legends of figures and tables

Table I. The GDM screening indications and proportion of GDM diagnoses in the study years.

Table II. Clinical characteristics and outcome in GDM and control mothers and their offspring during risk factor–based (year 2006) and comprehensive (2010) GDM screening.

Table III. Clinical characteristics and outcome of mothers and their offspring divided according to diet and insulin treatment during risk factor–based (year 2006) and comprehensive (2010) screening.

Supplementary Table I (Table SI). Odds ratios (for dichotomous outcomes) and mean differences (for continuous outcomes) comparing mothers with GDM and their offspring to control mothers and their offspring during risk factor–based (year 2006) and comprehensive (2010) screening. P-values for interaction indicate whether the association of GDM with the outcome is different during comprehensive as compared to risk factor–based screening.

Supplementary Table II (Table SII). Diagnoses of infants admitted to the neonatal ward.

Supplementary Figure I (Figure SI). Flow chart of the study.

Table I: The GDM screening indications and proportion of GDM diagnoses in the study years

OGTT screening population*		OGTT performed, n (% of all included mothers)	Gestational diabetes diagnosed, n (% of all included mothers)
Risk factor–based screening (2006)	Screening based on risk factors • Prior GDM • Overweight (BMI† > 25 kg/m^2) • Glucosuria • Age > 40 years • Previous macrosomic newborn (> 4500 g) • Suspected macrosomia in the current pregnancy	15 682 (27.5%‡)	5179 (9.1%‡)
Comprehensive screening (2010)	All women, excluding those with very low GDM risk: Primiparous: • Age <25 years • BMI† < 25 kg/m^2 • No family history of diabetes Parous: • Age < 40 years • BMI† < 25 kg/m2 • No prior GDM • No previous macrosomic newborn	30 365 (51.4%‡)	6679 (11.3%‡)

* OGTT= oral glucose tolerance test: cut-off levels of glucose concentrations in venous plasma ≥ 5.3, 10.0 and 8.6 mmol/l at fasting and 1 and 2 h after the 75 g glucose load

†Body mass index (kg/m^2)

‡ The proportion of all included mothers that year, N = 56 925 in 2006 and N = 59 065 in 2010.

Table II. Clinical characteristics and outcome in GDM and control mothers and their offspring during risk factor–based (year 2006) and comprehensive (2010) GDM screening.

Characteristic	GDM 2006	GDM 2010	P-value	Control 2006	Control 2010	P-value
N (%)	5179 (9.1)	6679 (11.3)		51 746 (90.9)	52 386 (88.7)	
Maternal age, years (SD)	31.09 (5.65)	31.02 (5.45)	0.526	29.30 (5.37)	29.39 (5.27)	0.007
Primiparous, n (%)	1787 (34.5)	2634 (39.4)	<0.001	22 226 (43.1)	22 290 (42.6)	0.084
BMI before pregnancy, kg/m^{2} * (SD)	28.6 (5.82)	28.2 (6.11)	<0.001	23.7 (4.26)	23.8 (4.36)	<0.001
Neonatal characteristics						
Gestational age, weeks (SD)	39.65 (1.61)	39.62 (1.66)	1.000	39.83 (1.79)	39.87 (1.75)	0.001
Preterm births, < 37 wk, n (%)	246 (4.7)	348 (5.2)	0.254	2286 (4.4)	2174 (4.1)	0.033
Birth weight, grams (SD)	3660 (542)	3595 (561)	<0.001	3515 (545)	3505 (539)	0.003
Length at birth, cm (SD)	50.5 (2.25)	50.3 (2.40)	<0.001	50.1 (2.47)	50.1 (3.18)	0.672
Ponderal index, kg/m^{3} (SD)	28.3 (2.70)	28.1 (3.22)	<0.001	27.9 (3.41)	27.8 (4.02)	0.015
LGA †, n (%)	289 (5.6)	276 (4.1)	<0.001	1011 (2.0)	966 (1.8)	0.153
Neonatal outcomes						
5 min Apgar score < 7, n (%)	109 (2.1)	136 (2.0)	0.795	974 (1.9)	1049 (2.0)	0.160
Cord arterial pH < 7.15, n (%)	333 (6.4)	505 (7.6)	0.017	3305 (6.4)	3755 (7.2)	<0.001
Asphyxia, n (%)	206 (4.0)	371 (5.6)	<0.001	2167 (4.2)	2712 (5.2)	<0.001
Neonatal care						
~~Location of the newborn at 7 days of age, n (%)~~			~~<0.001~~			~~<0.001~~
~~Home~~	~~4871 (94.1)~~	~~6144 (92.0)~~		~~48 694 (94.1)~~	~~48 723 (93.0)~~	
~~Maternity ward~~	~~70 (1.4)~~				~~2024 (3.9)~~	
~~Other ward~~	~~180 (3.5)~~			~~1511 (2.9)~~		
Admitted to neonatal ward, n (%)	834 (16.1)	861 (12.9)	<0.001	5075 (9.8)	4119 (7.9)	<0.001
Transferred to other hospital, n (%)	38 (0.7)	112 (1.7)	<0.001	311 (0.6)	649 (1.2)	<0.001
Perinatal mortality, n (%)	16 (0.3)	22 (0.3)	0.919	237 (0.5)	187 (0.4)	0.012
Neonatal diagnoses						
Hypoglycemia, n (%)	932 (18.0)	1478 (22.1)	<0.001	1371 (2.6)	1407 (2.7)	0.716
Neonatal RDS‡, n (%)	18 (0.3)	15 (0.2)	0.207	202 (0.4)	139 (0.3)	<0.001
Transient tachypnea, n (%)	85 (1.6)	120 (1.8)	0.520	656 (1.3)	670 (1.3)	0.872
Hyperbilirubinemia, n (%)	303 (5.9)	324 (4.9)	0.016	2160 (4.2)	1776 (3.4)	<0.001
Fracture of the clavicle, n (%)	87 (1.7)	53 (0.8)	<0.001	533 (1.0)	378 (0.7)	<0.001
Erb's or Klumpke's palsy, n (%)	26 (0.5)	22 (0.3)	0.142	120 (0.2)	72 (0.1)	0.0004

The numbers are n (%) or mean (SD)
*Body mass index (kg/m^{2}); †Large for gestational age (>+2 SD); ‡ Respiratory distress syndrome.

Table III. Clinical characteristics and outcome of mothers and their offspring divided according to diet and insulin treatment during risk factor–based (year 2006) and comprehensive (2010) screening.

Characteristic	Diet 2006	Diet 2010	P-value	Insulin 2006	Insulin 2010	P-value
N (%)	4053 (78.3)	5795 (86.8)	<0.001	1126 (21.7)	884 (13.2)	<0.001
Maternal age, years (SD)	30.9 (5.7)	30.0 (5.4)	0.504	31.7 (5.6)	32.1 (5.4)	0.071
Primiparous, n (%)	1403 (34.6)	2325 (40.1)	<0.001	384 (34.0)	310 (35.0)	0.665
BMI* before pregnancy, kg/m^2 (SD)	28.6 (5.7)	27.9 (5.9)	<0.001	28.8 (6.3)	30.2 (6.9)	<0.001
Neonatal characteristics						
Gestational age, weeks (SD)	39.77 (1.56)	39.67 (1.70)	0.020	39.23 (1.71)	39.27 (1.38)	1.000
Preterm births, < 37 wk, n (%)	172 (4.2)	304 (5.2)	0.022	74 (6.6)	44 (5.0)	0.131
Birth weight, grams (SD)	3674 (540)	3587 (564)	<0.001	3613 (546)	3644 (540)	0.202
Length at birth, cm (SD)	50.52 (2.24)	50.31 (2.42)	<0.001	50.36 (2.26)	50.25 (2.25)	0.258
Ponderal index, kg/m3 (SD)	28.38 (2.68)	28.04 (3.21)	<0.001	28.12 (2.75)	28.68 (3.25)	<0.001
LGA†, n (%)	216 (5.3)	213 (3.7)	<0.001	73 (6.5)	63 (7.1)	0.564
Neonatal outcomes						
5 min Apgar score < 7, n (%)	80 (2.8)	118 (2.0)	0.824	31 (2.7)	19 (2.1)	0.385
Cord arterial pH <7.15, n (%)	253 (6.2)	448 (7.7)	0.005	80 (7.1)	57 (6.4)	0.562
Asphyxia, n (%)	161 (4.0)	321 (5.5)	<0.001	45 (4.0)	50 (5.7)	0.082
Neonatal care						
Location of the newborn at 7-days of age, n (%)			<0.001			<0.001
Home	3834 (94.6)	5333 (92.0)		1037 (92.1)	811 (91.7)	
Maternity ward	55 (1.4)	234 (4.0)		15 (1.3)	39 (4.4)	
Other ward	123 (3.0)	191 (3.3)		57 (5.1)	30 (3.4)	
Other hospital	21 (0.5)	20 (0.3)		4 (0.4)	4 (0.5)	
Deceased	12 (0.3)	15 (0.3)		1 (0.1)	0 (0.0)	
Admitted to neonatal ward, n (%)	531 (13.1)	710 (12.3)	0.211	303 (26.9)	151 (17.1)	<0.001
Child transferred to other hospital, n (%)	31 (0.8)	97 (1.7)	<0.001	7 (0.6)	15 (1.7)	0.021
Perinatal mortality, n (%)	15 (0.4)	22 (0.4)	0.875	1 (0.09)	0 (0.0)	0.375
Neonatal diagnoses						
Hypoglycemia, n (%)	619 (15.3)	1184 (20.4)	<0.001	313 (27.8)	294 (33.3)	0.008
Neonatal RDS‡, n (%)	10 (0.2)	12 (0.2)	0.682	8 (0.7)	3 (0.3)	0.263
Transient tachypnea, n (%)	65 (1.6)	107 (1.8)	0.366	20 (1.8)	13 (1.5)	0.593
Hyperbilirubinemia, n (%)	199 (4.9)	256 (4.4)	0.252	104 (9.2)	68 (7.7)	0.219
Fracture of the clavicle, n (%)	74 (1.8)	51 (0.9)	<0.001	14 (1.2)	3 (0.3)	0.028
Erb's or Klumpke's palsy, n (%)	16 (0.4)	19 (0.3)	0.653	10 (0.9)	3 (0.3)	0.127

The numbers are n (%) or mean (SD).
* Body mass index (kg/m^2); †Large for gestational age (>+ 2 SD); ‡ Respiratory distress syndrome

Supplementary Table I~~V~~. Odds ratios (for dichotomous outcomes) and mean differences (for continuous outcomes) comparing mothers with GDM and their offspring to control mothers and their offspring during risk factor–based (year 2006) and comprehensive (2010) screening. P-values for interaction indicate whether the association of GDM with the outcome is different during comprehensive as compared to risk factor–based screening.

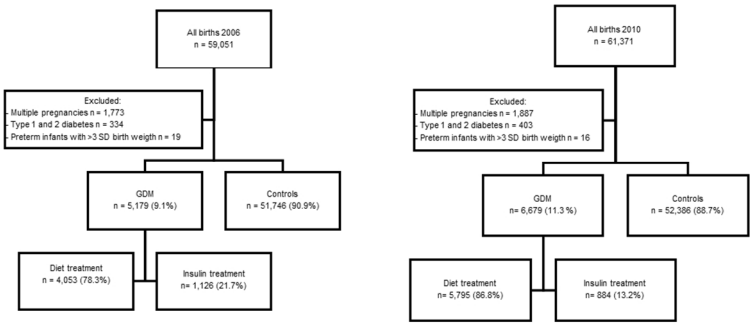
	2006 Unadjusted		2006 Adjusted §		2010 Unadjusted		2010 Adjusted §		Un-/ Adjusted §
	Mean difference/ OR*	95% CI	Mean difference/ OR	95% CI	Mean difference/ OR	95% CI	Mean difference/ OR	95% CI	p-value for interaction
Gestational age, wk	-0.18	-0.23, -0.13	-0.19	-0.24, -0.14	-0.26	-0.30,-0.21	-0.29	-0.34 -0.24	0.026/0.026
Preterm births	1.08	0.94-1.23	1.02	0.88-1.18	1.27	1.13-1.43	1.26	1.11-1.42	0.07/0.06
Birth weight (g)	145	129-160	70	54-87	89	76-103	22	8-37	<0.001/<0.001
Birth weight SD score	0.37	0.34-0.40	0.20	0.17-0.22	0.26	0.25-0.29	0.11	0.09-0.14	<0.001/<0.001
Ponderal index, kg/m3	0.47	0.37-0.56	0.20	0.09-0.30	0.33	0.23-0.43	0.14	0.04-0.25	0.054/0.054
LGA†	2.95	2.58-3.37	1.81	1.56-2.10	2.29	2.00-2.63	1.46	1.26-1.69	0.010/0.051
Care in neonatal ward	1.77	1.63-1.91	1.50	1.38-1.64	1.73	1.60-1.88	1.48	1.36-1.61	0.756/0.837
Hypoglycemia	8.06	7.38-8.81	6.20	5.61-6.86	10.3	9.52-11.14	8.40	7.71-9.15	<0.001/<0.0001

*OR, odds ratio; †Large for gestational age (+ 2 SD); ‡ Respiratory distress syndrome; § Adjusted for maternal age, parity and pre-pregnancy BMI

Supplementary Table II. Diagnoses of infants admitted to the neonatal ward.

	GDM			Controls		
Characteristic	**2006**	**2010**	**P-value**	**2006**	**2010**	**P-value**
N (%*)	834 (16.1*)	861 (12.9*)		5075 (9.8*)	4119 (7.9*)	
LGA†, n (%)	72 (8.6)	53 (6.2)	0.051	147 (2.9)	134 (3.3)	0.323
Diagnoses ~~among them~~						
Hypoglycemia, n (%)	410 (49.2)	385 (44.7)	0.067	928 (18.3)	722 (17.5)	0.347
Asphyxia, n (%)	71 (8.5)	50 (5.8)	0.017	504 (9.9)	444 (10.8)	0.183
RDS‡, n (%)	16 (1.9)	15 (1.7)	0.787	197 (3.9)	133 (3.2)	0.094
Transient tachypnea, n (%)	69 (8.3)	84 (9.8)	0.287	528 (10.4)	497 (12.1)	0.012
Hyperbilirubinemia, n (%)	120 (14.4)	106 (12.3)	0.208	708 (14.0)	534 (13.0)	0.169
Fracture of the clavicle, n (%)	16 (1.9)	7 (0.8)	0.049	63 (1.2)	37 (0.9)	0.115
Erb's or Klumpke's palsy, n (%)	5 (0.6)	4 (0.5)	0.702	26 (0.5)	14 (0.3)	0.212
~~Asphyxia, n (%)~~	~~71 (8.5)~~	~~50 (5.8)~~	~~0.017~~	~~504 (9.9)~~	~~444 (10.8)~~	~~0.183~~

* % of all infants in that group and that year; † Large for gestational age (>+2 SD); ‡ Respiratory distress syndrome.



Flow chart of the study.
Figure SI
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