In the name of God

The Importance of Early Hyperglycemia in Pregnancy

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1402/08/15

Gestational diabetes mellitus, a common pregnancy complication, is associated with increased risks of preeclampsia, surgical intervention, large-for gestational- age neonates, shoulder dystocia, birth trauma, and neonatal hypoglycemia.

This dramatic rise in the GDM prevalence will have a major impact on health care systems

For over 50 years and Now , Screening and treatment for gestational diabetes at 24 to 28 weeks' gestation are recommended.

This is the time during pregnancy when insulin resistance is increasing and hyperglycemia develops among those with insufficient insulin secretory capacity to maintain euglycemia

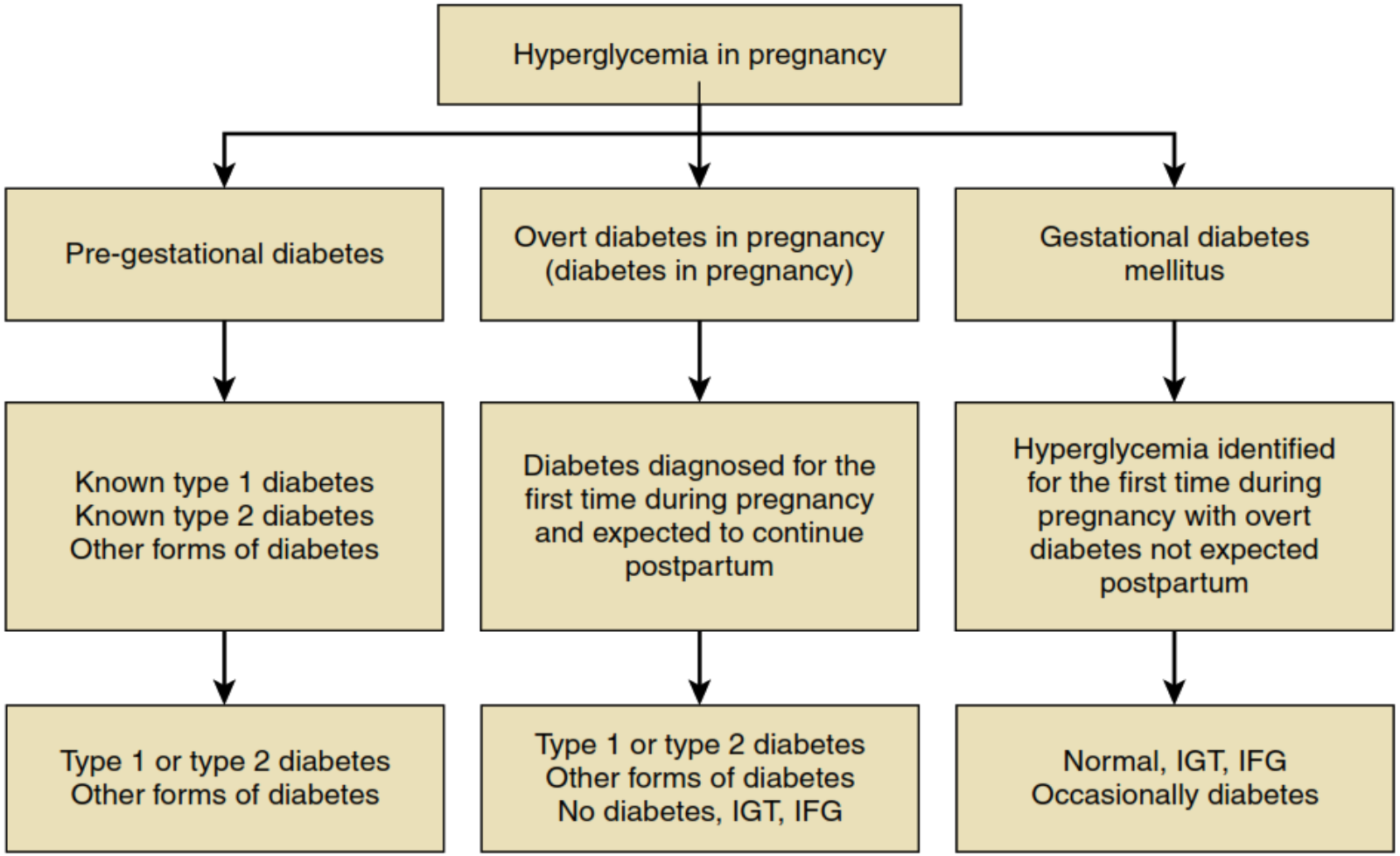

Fig. 34.1 Current classification of hyperglycemia in pregnancy and postpartum state. *IFG,* Impaired fasting glucose; *IGT,* impaired glucose tolerance.

WHO AND IADPSG diagnostic criteria

Table 1. Diagnostic criteria for gestational diabetes mellitus

	Carpenter and Coustan (100g OGTT)	WHO* (75g OGTT)	IADPSG^ (75g OGTT)
Number of abnormal values required for GDM diagnosis	≥ 2	≥ 2	≥ 1
Fasting glucose (mg/dL)	95	95	92
1st hour (mg/dL)	180	180	180
2nd hour (mg/dL)	155	155	153
3rd hour (mg/dL)	140	--	--

**World Health Organization*

^International Association of Diabetes and Pregnancy Study Group

Criteria	Diagnosis
IADPSG (75 gram OGTT) [6]	**At least one value meeting the threshold:** Fasting plasma glucose $\geq$ 5.11 mmol/l 1-h plasma glucose $\geq$ 10 mmol/l 2-h plasma glucose $\geq$ 8.5 mmol/l
Old ADA (100 g OGTT) [11]	**At least two values meeting the thresholds:** Fasting plasma glucose $\geq$ 5.28 mmol/l 1-h plasma glucose $\geq$ 10 mmol/l 2-h plasma glucose $\geq$ 8.61 mmol/l 3-h plasma glucose $\geq$ 7.78 mmol/l
WHO (75 g OGTT) [12]	**At least one value meeting the threshold:** Fasting plasma glucose $\geq$ 7 mmol/l 2-h plasma glucose $\geq$ 7.78 mmol/l

IADPSG, International Association of Diabetes and Pregnancy Study Groups; ADA, American Diabetes Association; WHO, World Health Organisation.

Diabetes and Pregnancy: An Endocrine Society Clinical Practice Guideline

Table 2. Diagnostic Criteria for Overt Diabetes and Gestational Diabetes Using a 2-Hour 75-g OGTT at 24 to 28 Weeks Gestation[a]

Diagnosis	Fasting Plasma Glucose,[b] mg/dL (mmol/L)	1-h Value, mg/dL (mmol/L)	2-h Value, mg/dL (mmol/L)
Overt diabetes (type 1, type 2, or other)	≥126 (≥7.0)	NA	≥200 (≥11.1)
Gestational diabetes	92–125 (5.1–6.9)	≥180 (≥10.0)	153–199 (8.5–11.0)

ADA (41)	Universal	One-step: 75-g 2-h OGTT Two-step: 50-g GCT	≥7.2 to 7.8[a]	75-g 2-hour OGTT 100-g 3-hour OGTT	Fasting ≥ 5.1 1-h ≥ 10.0 2-h ≥ 8.5 One abnormal value needed for diagnosis Carpenter and Coustan[b] (17) or NDDG (13) Fasting ≥ 5.3 Fasting ≥ 5.8 1-hour ≥ 10.0 1-hour ≥ 10.6 2-hour ≥ 8.6 2-hour ≥ 9.2 3-hour ≥ 7.8 3-hour ≥ 8.0 Two abnormal values needed for diagnosis
ACOG[c] (19)	Universal	Two-step: 50-g GCT	≥7.2 to 7.8*	100-g OGTT	Carpenter and Coustan[b] (17) or NDDG (13) Fasting ≥ 5.3 Fasting ≥ 5.8 1-hour ≥ 10.0 1-hour ≥ 10.6 2-hour ≥ 8.6 2-hour ≥ 9.2 3-hour ≥ 7.8 3-hour ≥ 8.0 Two abnormal values needed for diagnosis[d]
CDA (42)	Universal	Two-step: 50-g GCT (preferred) One-step: 75-g 2-h OGTT (alternative)	≥7.8	50-g GCT 75-g 2-hour OGTT	≥11.1 mmol/L[e] Fasting ≥ 5.3 1-hour ≥ 10.6 2-hour ≥ 9.0 One abnormal value needed for diagnosis
NICE (38)	Selective	Risk factors[f]		75-g 2-hour OGTT	Fasting ≥ 7.0 2-hour ≥ 7.8 One abnormal value needed for diagnosis
CNGOF (39)	Selective[g]			First trimester fasting glucose 75-g OGTT[h]	≥5.1 Fasting ≥ 5.1 1-hour ≥ 10.0 2-hour ≥ 8.5 One abnormal value needed for diagnosis
DDG/DGGG (43)	Universal	Two-step: 50-g GCT One-step: 75-g OGTT (preferred)	≥7.5	50-g GCT 75-g OGTT	≥11.1 mmol/L[e] Fasting ≥ 5.1 1-hour ≥ 10.0 2-hour ≥ 8.5 One abnormal value needed for diagnosis
DIPSI (44)	Universal	One-step: 75-g OGTT		75-g OGTT	2-hour ≥ 7.8[i]

The GDM is associated with adverse maternal and neonatal sequelae. In a Hyperglycemia and Adverse Pregnancy Outcomes Study (HAPO), a large-scale (25,000 pregnant women) multinational epidemiologic study found significant associations between adverse pregnancy outcomes, and higher levels of maternal glucose with no defined levels, after which the risk increases.

The frequency of GDM when the IADPSG criteria in the HAPO study it ranged from 9 to 26%

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Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group*

Table 3. Adjusted Odds Ratios for Associations between Maternal Glycemia as a Continuous Variable and Primary and Secondary Perinatal Outcomes.*

Outcome	Plasma Glucose Level		
	Fasting	At 1 Hr	At 2 Hr
	odds ratio (95% CI)		
Primary outcome			
Birth weight >90th percentile	1.38 (1.32–1.44)	1.46 (1.39–1.53)	1.38 (1.32–1.44)
Primary cesarean section†	1.11 (1.06–1.15)	1.10 (1.06–1.15)	1.08 (1.03–1.12)
Clinical neonatal hypoglycemia	1.08 (0.98–1.19)‡	1.13 (1.03–1.26)	1.10 (1.00–1.12)
Cord-blood serum C peptide >90th percentile	1.55 (1.47–1.64)	1.46 (1.38–1.54)	1.37 (1.30–1.44)
Secondary outcome			
Premature delivery (before 37 wk)	1.05 (0.99–1.11)	1.18 (1.12–1.25)	1.16 (1.10–1.23)
Shoulder dystocia or birth injury	1.18 (1.04–1.33)	1.23 (1.09–1.38)	1.22 (1.09–1.37)
Intensive neonatal care	0.99 (0.94–1.05)	1.07 (1.02–1.13)	1.09 (1.03–1.14)
Hyperbilirubinemia	1.00 (0.95–1.05)	1.11 (1.05–1.17)	1.08 (1.02–1.13)
Preeclampsia	1.21 (1.13–1.29)	1.28 (1.20–1.37)	1.28 (1.20–1.37)

Table 1—*Threshold values for diagnosis of GDM or overt diabetes in pregnancy*

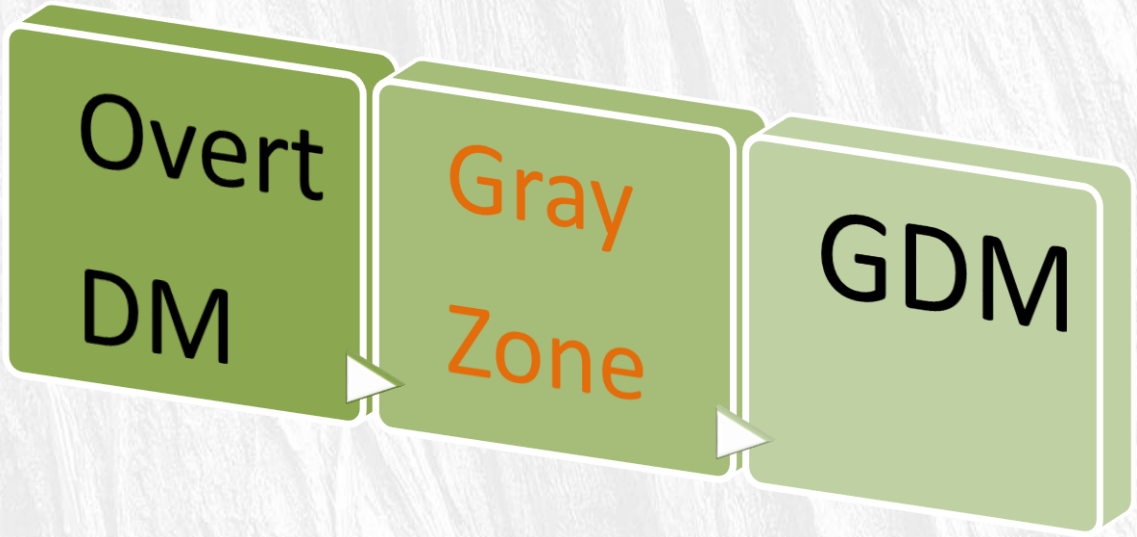
To diagnose GDM and cumulative proportion of HAPO cohort equaling or exceeding those thresholds

	Glucose concentration threshold*		Above threshold (%)
Glucose measure	mmol/l	mg/dl	Cumulative
FPG	5.1	92	8.3
1-h plasma glucose	10.0	180	14.0
2-h plasma glucose	8.5	153	16.1†

To diagnose overt diabetes in pregnancy

Measure of glycemia	Consensus threshold
FPG‡	≥7.0 mmol/l (126 mg/dl)
A1C‡	≥6.5% (DCCT/UKPDS standardized)
Random plasma glucose	≥11.1 mmol/l (200 mg/dl) + confirmation§

*One or more of these values from a 75-g OGTT must be equaled or exceeded for the diagnosis of GDM. †In addition, 1.7% of participants in the initial cohort were unblinded because of FPG >5.8 mmol/l (105 mg/dl) or 2-h OGTT values >11.1 mmol/l (200 mg/dl), bringing the total to 17.8%. ‡One of these must be met to identify the patient as having overt diabetes in pregnancy. §If a random plasma glucose is the initial measure, the tentative diagnosis of overt diabetes in pregnancy should be confirmed by FPG or A1C using a DCCT/UKPDS-standardized assay.



- **Pregnant womens in first Half of pregnancy that have fasting blood glucose less than overt diabetis 93-125**

Most international guidelines now recommend early antenatal testing for women at high risk to identify women with DIP.

Studies in women with GDM have reported that between 27% and 66% of GDM (at 24 – 28 week) can be detected in early pregnancy

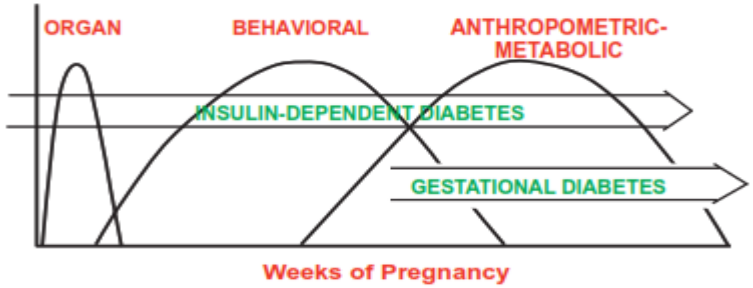


Figure 1—Freinkel's iconic schematic from the Banting Lecture in 1980 (5) of how hyperglycemia affects fetal development and the stage during pregnancy when the hyperglycemia commenced.

In cohort studies, women with pregnancies complicated by early (<20 weeks' gestation) hyperglycemia showed accelerated fetal growth by 24 to 28 weeks' gestation and had greater perinatal mortality than women who received a diagnosis of gestational diabetes later in pregnancy

A linear relationship has been shown between fasting glucose levels in early pregnancy and adverse pregnancy outcomes.

It is assumed that the early detection of GDM may lead to an earlier metabolic control that improves perinatal outcomes

Blumer I, Hadar E, Hadden DR, Jovanovič L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab 2013; 98: 4227-424*

Currently, there is no consensus for the preferred testing approach or diagnostic glycemic thresholds for early GDM.

The IADPSG recommends diagnosing early GDM based on a fasting glucose of 5.1 mmol/L to 6.9 mmol/L (92-125 mg/dL) consistent with the diagnostic fasting glucose threshold for standard GDM.

Metzger BE, Gabbe SG, Persson B, *et al; International Association* of Diabetes and Pregnancy Study Groups Consensus Panel. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia
in pregnancy. *Diabetes Care*. 2010;33(3):676-682

Problems :

- **Data from randomized, controlled trials that show a benefit from such treatment are lacking…**

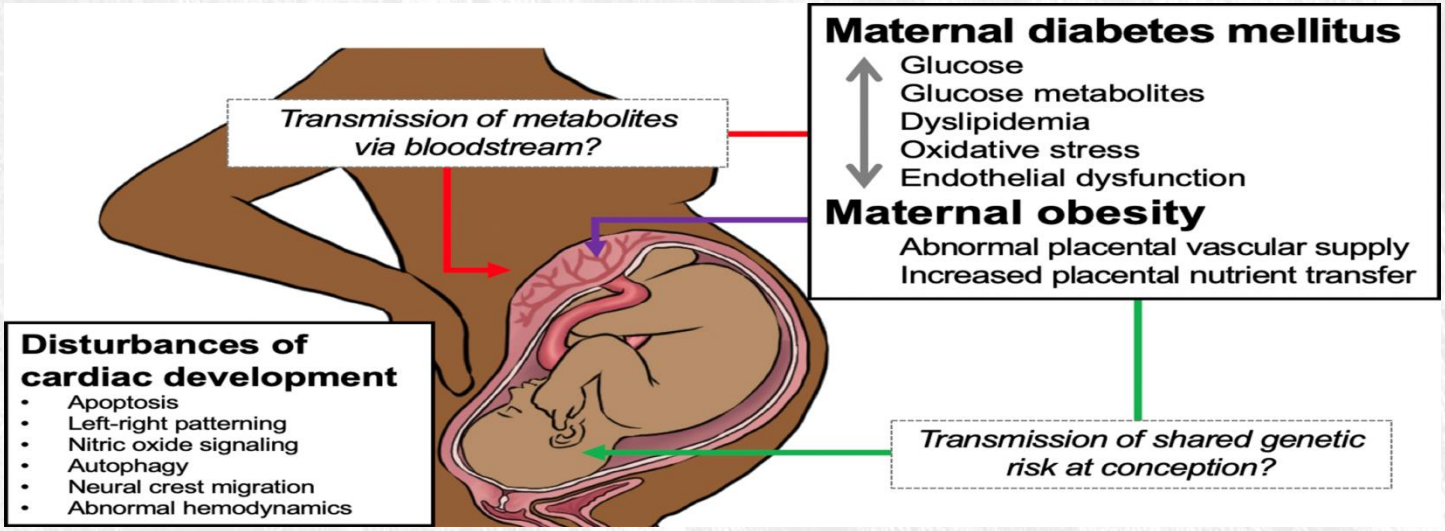
- **Confliction in maternal and neonatal outcomes in pervious study ….**

- **Whether criteria that had been established for OGTT at 24 to 28 weeks' gestation , can be applied to testing early in pregnancy….**

- **Early GDM is a potential harm or no….**

early or “booking” GDM

Booking GDM may be divided into mild hyperglycemia already present at the beginning of pregnancy (“prevalent GDM”) and that arising de novo during pregnancy (“incident GDM”)



If there are benefits from identifying and treating early GDM, then the "test characteristics" of using risk factor screening for DIP need to be considered.

Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and metaanalysis. ***Curr Diab Rep. 2017;17(11):115.***

Paradigm Shifts in the Management of Diabetes in Pregnancy: The Importance of Type 2 Diabetes and Early Hyperglycemia in Pregnancy

The 2020 Norbert Freinkel Award Lecture

Diabetes Care 2021;44:1075–1081 | https://doi.org/10.2337/dci20-0055

Recent studies evaluating the relationship between maternal glycemia and fetal growth trajectories confirm the early impact of maternal glycemia on excess fetal growth and adiposity prior to the diagnosis of standard GDM from 24 weeks' gestation.

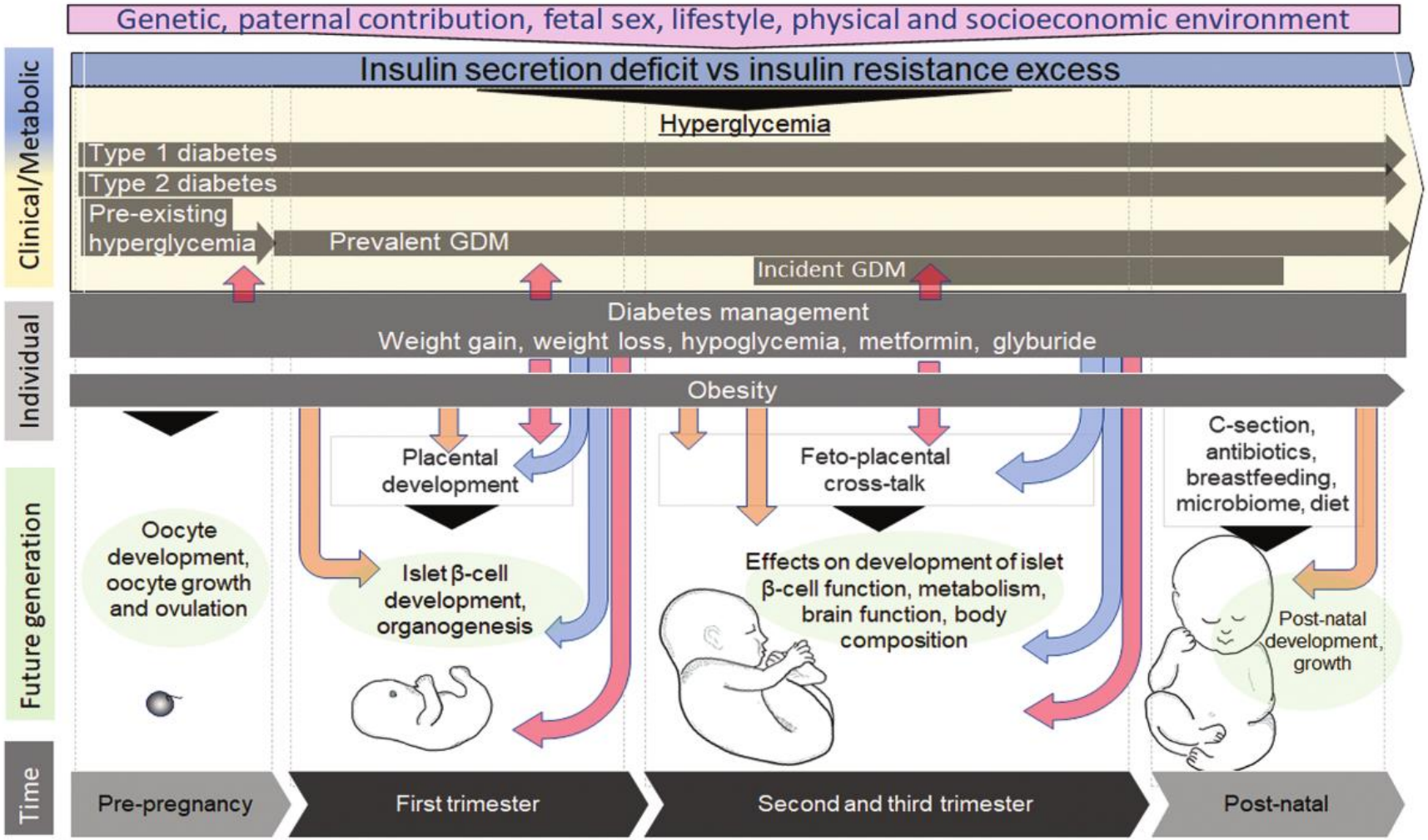


Figure 2—2021 adaptation of Freinkel model to include effects on the fetus beyond hyperglycemia. Blue = effects of maternal hyperglycemia; orange = effects of maternal obesity; dark pink = effects of maternal diabetes management including effects of weight change and pharmacotherapy. Light pink summarizes the wider effects of maternal genetics, any paternal contributions, fetal sex, maternal lifestyle, the physical (e.g., climate) and socioeconomic environment.

Glycaemic status during pregnancy and longitudinal measures of fetal growth in a multi-racial US population: a prospective cohort study

In this study , women's glucose concentrations at weeks 10–14 were significantly associated with a larger Fetal Weight from week 27 through term.

GDM-related fetal over growth may start before 28 gestational weeks

Li M, Hinkle SN, Grantz KL, Kim S, Grewal J, Grobman WA, Skupski DW, Newman RB, Chien EK, Sciscione A, Zork N, Wing DA, Nageotte M, Tekola-Ayele F, Louis GMB, Albert PS, Zhang C. Glycaemic status during pregnancy and longitudinal measures of fetal growth in a multi-racial US population: a prospective cohort study. Lancet Diabetes Endocrinol. 2020 Apr;8(4):292-300. doi: 10.1016/S2213-8587(20)30024-3. Epub 2020 Mar 2. PMID: 32135135; PMCID: PMC7676113.

Early diagnosis of gestational diabetes mellitus and prevention of diabetes-related complications

Jose L. Bartha*, Pilar Martinez-Del-Fresno, Rafael Comino-Delgado

Department of Obstetrics and Gynaecology, University Hospital of Puerto Real, Carretera Nacional IV, KM 665, 11150 Puerto Real, Cádiz, Spain

Received 30 January 2002; received in revised form 18 June 2002; accepted 14 November 2002

This study evaluated pregnancy complications commonly related to diabetes between :

(later screening group)

and (earlier screening group) women with GDM

In conclusion, early glucose intolerance screening could avoid some diabetes-related complications such as hydramnios, fetal anomalies and preterm births in women diagnosed as having gestational diabetes.

Bartha JL, Martinez-Del-Fresno P, Comino-Delgado R. Early diagnosis of gestational diabetes mellitus and prevention of diabetes-related complications. Eur J Obstet Gynecol Reprod Biol. 2003 Jul 1;109(1):41-4. doi: 10.1016/s0301-2115(02)00480-3. PMID: 12818441.

Table II. Pregnancy complications

	Early-onset gestational diabetes (n = 65)		*Late-onset gestational diabetes (n = 170)*		
	No.	*%*	*No.*	*%*	*Statistical significance*
Hypertension (total)	12	18.5	10	5.9	*P* = .006
Chronic hypertension	7	10.8	4	2.4	*P* = .01
Preeclampsia	2	3.1	0	0	*P* = .07
Superimposed preeclampsia	2	3.1	1	0.6	NS
Total preeclampsia (preeclampsia plus superimposed preeclampsia)	4	6.2	1	0.6	*P* = .02
Gestational hypertension	1	1.5	5	2.9	NS
Hydramnios	2	3.1	7	4.1	NS
Preterm labor	2	3.1	6	3.5	NS
Fetal anomalies	0	0	0	0	NS
Oligohydramnios	0	0	11	6.47	*P* = .02

NS, Not significant.

Table III. Glycemic control and insulin therapy

	Early-onset gestational diabetes (n = 65)	*Late-onset gestational diabetes (n = 170)*	*Statistical significance*
Fasting glucose level (mg/ dL, mean ± SD)	91.4 ± 16.1	79.8 ± 14.2	*P* < .00001
Glucose level after breakfast (mg/ dL, mean ± SD)	104.6 ± 29.3	95.9 ± 20.6	*P* = .03
Glucose level after lunch (mg/ dL, mean ± SD)	102.6 ± 19.4	91.57 ± 16.2	*P* = .00009
Glucose level before dinner (mg/ dL, mean ± SD)	82.1 ± 17.3	77.1 ± 14.6	*P* = .039
Glucose level after dinner (mg/ dL, mean ± SD)	102.8 ± 26.0	93.7 ± 17.3	*P* = .01
Mean glycemic profile (mg/ dL, mean ± SD)	96.7 ± 15.0	87.6 ± 10.4	*P* = .00002
Glycosylated hemoglobin (%, median and interquartile range)	4.5 (4.2-5.2)	4.6 (4.3-4.9)	NS
Insulin therapy (No.)	22/ 65 (33.9%)	12/ 170 (7.1%)	*P* < .00001

NS, Not significant.

Short communication

Normal fasting plasma glucose levels during pregnancy: a hospital-based study

an Israeli cohort study of women who underwent a fasting glucose test at a median of 9.5 weeks' gestation demonstrated a positive association between first trimester fasting glucose up to 5.8 mmol/L (104.5 mg/dL) and increased risk for subsequent diagnosis of GDM, LGA, macrosomia, and cesarean section.

Similar to the HAPO study, a clear glucose threshold was lacking, with pregnancy complications evident at fasting glucose levels <92

Riskin-Mashiah S, Damti A, Younes G, *et al. Normal fasting* plasma glucose levels during pregnancy: a hospital-based study. *J Perinat Med. 2011;39(2):209-211*

First-Trimester Fasting Hyperglycemia and Adverse Pregnancy Outcomes

The aim of this study was to evaluate the associations between first-trimester fasting plasma glucose level and adverse pregnancy outcomes.

Higher first-trimester fasting glucose levels, within what is currently considered a nondiabetic range, increase the risk of adverse pregnancy outcomes.

Early detection and treatment of women at high risk for these complications might improve pregnancy outcome

Diabetes Care 32:1639–1643, 2009

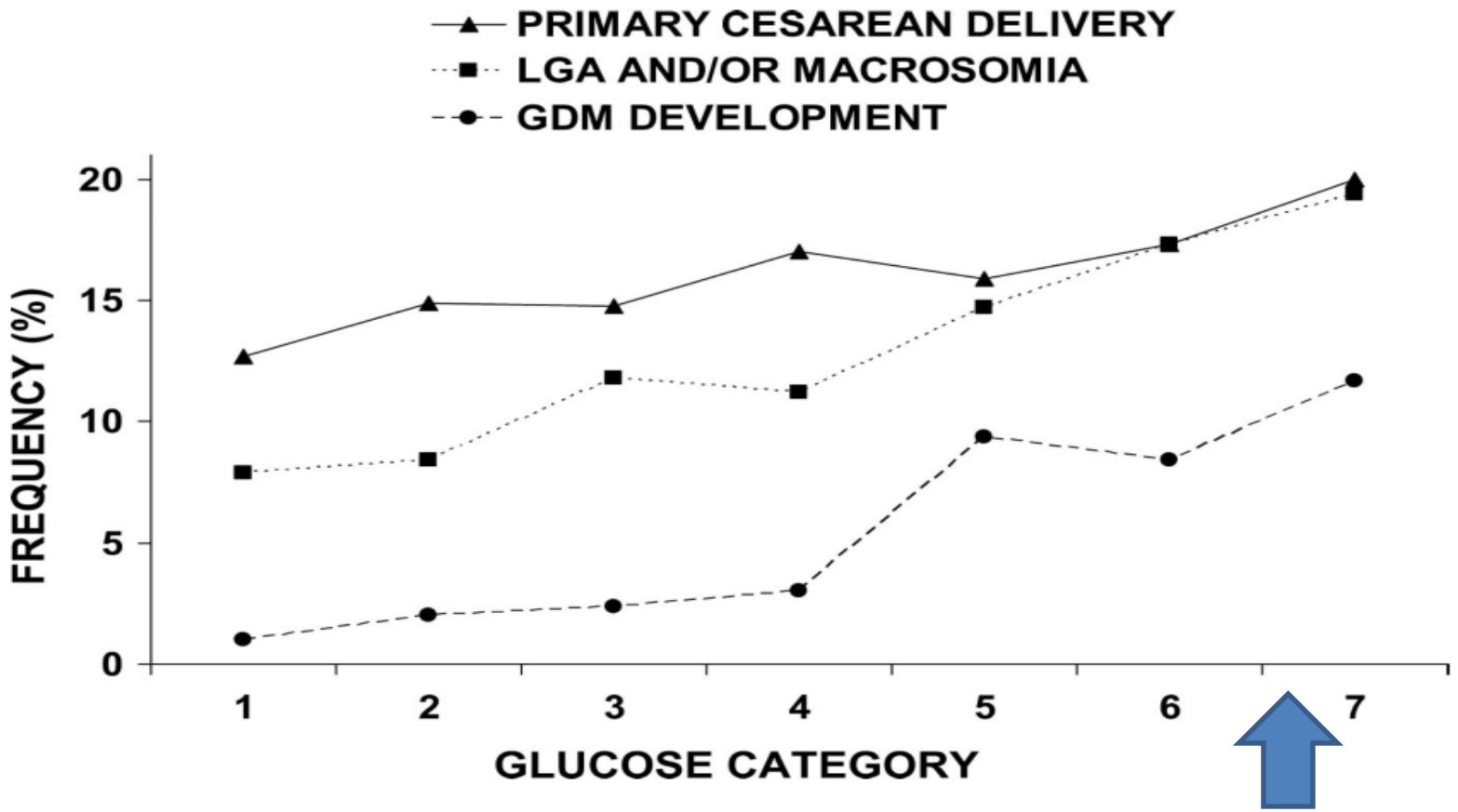


Figure 1—*The relationship between maternal first-trimester fasting glucose level and frequency of primary outcomes. Fasting glucose categories are defined as follows: category 1, <75 mg/dl; category 2, 75–79 mg/dl; category 3, 80–84 mg/dl; category 4, 85–89 mg/dl; category 5, 90–94 mg/dl; category 6, 95–99 mg/dl; and category 7, 100–105 mg/dl.*

Gestational Diabetes Mellitus in Early Pregnancy: Evidence for Poor Pregnancy Outcomes Despite Treatment

Diabetes Care 2016;39:75–81 | DOI: 10.2337/dc15-0433

RESULTS

Hypertensive disorders in pregnancy including pre-eclampsia, preterm delivery, cesarean section, and neonatal jaundice (all $P < 0.001$) were more prevalent in women with pre-existing diabetes and early GDM. Macrosomia (21.8% vs. 20.3%, $P = 0.8$), large for gestational age (39.6% vs. 32.8%, $P = 0.4$), and neonatal intensive care admission (38.5% vs. 39.7%, $P = 0.9$) in women in whom GDM was diagnosed at <12 weeks of gestation were comparable to rates seen in women with pre-existing diabetes.

Sweeting AN, Ross GP, Hyett J, *et al. Gestational diabetes mellitus* in early pregnancy: evidence for poor pregnancy outcomes despite treatment. *Diabetes Care. 2016;39(1):75-81*

Table 3—Maternal outcomes for type 2 diabetes and GDM stratified by timing of diagnosis

Maternal outcomes	T2DM (n = 65)	GDM <12 weeks (n = 68)	GDM 12–23 weeks (n = 1,247)	GDM ≥24 weeks (n = 3,493)	P value
Gestation at delivery (weeks)	37.4 ± 1.9*	37.5 ± 3.2*	38.3 ± 2.4*	38.8 ± 1.7	<0.0001
Preterm delivery (%)	25.9*	16.7*	11.2*	6.4	<0.0001
Cesarean section (%)	57.9*	30.7	36.2*	28.1	<0.0001
Hypertensive disorders in pregnancy (%)	34.6*	26.3*	13.8*	11.2	<0.0002
Postpartum OGTT (%)#		(N = 28)	(N = 702)	(N = 1,877)	<0.0001
Normal		79*	71*	85	
IGT		11	24	14	
T2DM		11	5	1	

Data are presented as mean ± SD, unless otherwise indicated. Hypertensive disorders in pregnancy, either pre-eclampsia or systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a previously normotensive pregnant woman whose pregnancy is at ≥20 weeks of gestation and has no proteinuria or new signs of end-organ dysfunction; preterm delivery, <37 weeks of gestation. IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus. *Different from GDM diagnosed after 24 weeks of gestation (comparator group). #Performed 3 months postpartum, IGT was defined as either a fasting BGL of 6.1–6.9 mmol/L and/or a 2-h BGL of 7.8–11.0 mmol/L, and T2DM was defined as a fasting BGL of ≥7.0 mmol/L and/or a 2-h BGL of ≥11.1 mmol/L.

Sweeting AN, Ross GP, Hyett J, *et al. Gestational diabetes mellitus* in early pregnancy: evidence for poor pregnancy outcomes despite treatment. *Diabetes Care. 2016;39(1):75-81*

Another study :

an increased risk of peri-natal mortality and congenital abnormalities has also been reported in the offspring of women with early GDM and in some study No clear connection was seen

Bartha JL, Martinez-Del-Fresno P, Comino-Delgado R. Gestational diabetes mellitus diagnosed during early pregnancy. *Am J Obstet Gynecol. 2000;182(2):346-350*

Hawkins JS, Lo JY, Casey BM, *et al. Diet-treated gestational diabetes* mellitus: comparison of early vs routine diagnosis. *Am J Obstet Gynecol. 2008;198(3):287 e1-287 e6*

Most OL, Kim JH, Arslan AA, *et al. Maternal and neonatal* outcomes in early glucose tolerance testing in an obstetric population in New York city. *J Perinat Med. 2009;37(2):114-117.*

BMJ Open Diabetes Research & Care

High probability of false-positive gestational diabetes mellitus diagnosis during early pregnancy

Review

Screening for Gestational Diabetes Mellitus in Early Pregnancy: What Is the Evidence?

Lore Raets [1], Kaat Beunen [1] and Katrien Benhalima [2,*]

Early diagnosis of gestational diabetes mellitus during the first trimester of pregnancy based on the one-step approach of the International Association of Diabetes and Pregnancy Study Groups

Melekoglu Rauf [1] · Eraslan Sevil [1] · Celik Ebru [1] · Colak Cemil [2]

Screening and Treatment for Early-Onset Gestational Diabetes Mellitus: a Systematic Review and Meta-analysis

Jincy Immanuel[1] · David Simmons[1]

A recent meta-analysis of 13 cohort studies showed greater perinatal mortality among women with early GDM compared to women with a later diagnosis of GDM despite treatment.

This meta-analysis shows that Early hyperglycemia is

associated with significantly increased risk for perinatal mortality, neonatal hypoglycemia, and insulin therapy.

These women also are at increased risk of neonatal ICU admission in developed countries

Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and metaanalysis. *Curr Diab Rep. 2017;17(11):115.*

Table 2 Summary of evidence: comparison of pregnancy outcomes between treated early- and late-onset GDM women

Outcomes	No. of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with late GDM treated	Risk difference with early GDM treated
Large for gestational age	9622 (7 observational studies)	⊕⊕◯◯ LOW	RR 1.07 (0.86 to 1.35)	187 per 1000	*13 more per 1000* (26 fewer to 66 more)
Perinatal mortality	9130 (7 observational studies)	⊕⊕◯◯ LOW	RR 3.58 (1.91 to 6.71)	2 per 1000	*6 more per 1000* (2 more to 14 more)
Neonatal hypoglycemia	6818 (7 observational studies)	⊕⊕◯◯ LOW	RR 1.61 (1.02 to 2.55)	134 per 1000	*82 more per 1000* (3 more to 207 more)
Neonatal intensive care unit admission	7992 (5 observational studies)	⊕⊕◯◯ LOW	RR 1.16 (0.90 to 1.49)	209 per 1000	*33 more per 1000* (21 fewer to 102 more)
Insulin use	8103 (11 observational studies)	⊕◯◯◯ VERY LOW[a]	RR 1.71 (1.45 to 2.03)	365 per 1000	*259 more per 1000* (164 more to 376 more)
Macrosomia	9966 (10 observational studies)	⊕⊕◯◯ LOW	RR 1.05 (0.77 to 1.41)	108 per 1000	*5 more per 1000* (25 fewer to 44 more)
Small for gestational age	5900 (5 observational studies)	⊕⊕◯◯ LOW	RR 1.27 (0.92 to 1.75)	73 per 1000	*20 more per 1000* (6 fewer to 55 more)
Hypertensive disorders in pregnancy	10,091 (10 observational studies)	⊕◯◯◯ VERY LOW[b]	RR 1.34 (0.98 to 1.82)	93 per 1000	*32 more per 1000* (2 fewer to 76 more)
Preterm delivery	7039 (7 observational studies)	⊕⊕◯◯ LOW	RR 1.16 (0.84 to 1.61)	80 per 1000	*13 more per 1000* (13 fewer to 49 more)
Cesarean delivery	9685 (9 observational studies)	⊕◯◯◯ VERY LOW[c]	RR 1.09 (0.94 to 1.26)	313 per 1000	*28 more per 1000* (19 fewer to 81 more)
Shoulder dystocia	2936 (2 observational studies)	⊕◯◯◯ VERY LOW[d]	RR 1.76 (0.96 to 3.24)	16 per 1000	*12 more per 1000* (1 fewer to 36 more)
Hyperbilirubinemia	9231 (7 observational studies)	⊕⊕◯◯ LOW	RR 1.16 (0.91 to 1.48)	130 per 1000	*21 more per 1000* (12 fewer to 62 more)
Respiratory distress syndrome	6351 (5 observational studies)	⊕◯◯◯ VERY LOW[d]	RR 1.00 (0.76 to 1.32)	38 per 1000	*0 fewer per 1000* (9 fewer to 12 more)

A key issue is the current lack of high-quality evidence that :

diagnosing and treating early GDM improves pregnancy outcomes.

“Early GDM is a potentially harm”

Author, Year/Country (Ref.)	Subjects (*N*)	Study Population	Timeframe Testing (Weeks)	GDM Criteria	Comparison	Main Results
Simmons, 2018 (ToBOGM study protocol)/ International [40]	4000	Hi risk women with singleton pregnancy	<20.0 weeks (4–19.6 weeks)	2 h 75 g OGTT/2014 Australasian Diabetes-in-Pregnancy Society criteria for pregnant women with GA 24–28 weeks	Intervention (immediate treatment) vs. control (no treatment) vs. decoys (NGT but undergo all procedures) vs. non-active (NGT and records reviewed postnatally)	First results expected mid-2021
Vinter, 2018 (LiP study)/ Denmark [41]	90	Obese pregnant women (BMI 30–45 kg/m^2) with singleton pregnancy	12–15 weeks	2 h 75 g OGTT/ IADPSG Criteria	Lifestyle intervention vs. SoC	Lifestyle intervention was not effective in improving obstetric or metabolic outcomes
Roeder, 2019 (RCT)/ US [42]	157	Women with hyperglycemia and singleton pregnancy without ODIP	≤15.0 weeks	HbA1c and/or FPG, respectively, 5.7–6.4% and/or 5.1–6.9 mmol/L	Early pregnancy vs. 3rd trimester treatment of hyperglycemia	Treatment in early pregnancy did not improve maternal or neonatal outcomes significantly
Harper, 2020 (EGGO study)/ US [43]	922	Obese women (BMI ≥30 kg/m^2) without ODIP and history of bariatric surgery	14–20 weeks	2-step method: 1 h 50 g GCT followed by a 3 h 100 g OGTT/C&C criteria	Early GDM screening (14–20 weeks) vs. routine screening (24–28 weeks)	Early GDM screening in obese women did not reduce the composite perinatal outcomes, such as macrosomia, C-section and shoulder dystocia
Hung-Yuan Li (TESGO study)/ Taiwan (NCT03523143)	2068	Singleton pregnancy without ODIP	18–20 weeks	75 g 2 h OGTT/ IADPSG criteria	Early screening group (18–20 weeks) vs. standard screening group (24–28 weeks)	Results expected beginning of 2021

Author, Year/Country (Ref.)	Subjects (N)	Study Population	Timeframe Testing (Weeks)	GDM Criteria	Comparison	Main Results
Osmundson, 2016/US [37]	83	Women with singleton pregnancy and without ODIP	<14.0 weeks	HbA1c/between 5.7 and 6.4%	Usual care vs. early treatment for GDM with diet, BG monitoring, and insulin as needed	Early treatment did not significantly reduce the risk of GDM except in non-obese women
Hughes, 2018 (PINTO feasibility study)/New Zealand [38]	47	Women with singleton pregnancy and without ODIP	<14.0 weeks	HbA1c/between ≥5.9 and 6.4%/2 h 75 h OGTT New Zealand criteria	Standard care vs. early intervention in pregnancies complicated by prediabetes	First results expected in 2021
Simmons, 2018 (ToBOGM pilot study)/ Australia [39]	79	Hi risk women with singleton pregnancy	<20.0 weeks (4–19.6 weeks)	2 h 75 g OGTT/ IADPSG criteria	Women with booking GDM receiving immediate (clinical referral or ongoing treatment) vs. deferred (no) treatment vs. women without booking GDM ("decoys")	More NICU admission in the early GDM group with a tendency for more SGA but less LGA

Early Gestational Diabetes Screening in Obese Women: A Randomized Controlled Trial

A recent major RCT in the United States evaluating

early testing for GDM in ≈ 900 women with obesity included a subgroup analysis of women diagnosed and treated for GDM based on the 2-step testing approach (50-g GCT followed by 100-g 3- h OGTT)

Harper LM, Jauk V, Longo S, *et al. Early gestational diabetes* screening in obese women: a randomized controlled trial. *Am J Obstet Gynecol. 2020;222(5):495 e1-495 e8*

OBSTETRICS

Early gestational diabetes screening in obese women: a randomized controlled trial

Lorie M. Harper, MD, MSCI; Victoria Jauk, MPH; Sherri Longo, MD; Joseph R. Biggio, MD, MS; Jeff M. Szychowski, PhD; Alan T. Tita, MD, PhD

There was no difference in pregnancy outcomes, although the primary composite perinatal outcome was non significantly higher in the early-screen group.

Requirement for insulin therapy was almost 4-fold higher, while gestational age at delivery was lower in women with early GDM

TABLE 3

Outcomes among women diagnosed with gestational diabetes, by screening group

Outcome	Early screen (n = 69)	Routine screen (n = 56)	*P*	Relative risk (95% CI)
Primary composite outcome[a]	51 (73.9%)	37 (66.1%)	.34	1.12 (0.89–1.41)
Secondary outcomes				
Macrosomia	4 (5.9%)	5 (8.9%)	.73	0.66 (0.19–2.34)
Primary cesarean delivery	16 (23.2%)	13 (23.2%)	>.99	1.0 (0.53–1.90)
Gestational hypertension	14 (20.3%)	8 (14.3%)	.38	1.42 (0.64–3.14)
Preeclampsia	15 (21.7%)	9 (16.1%)	.42	1.35 (0.64–2.86)
Without severe features	9 (13.0%)	7 (12.5%)	.93	1.04 (0.41–2.63)
With severe features	6 (8.7%)	2 (3.6%)	.30	2.43 (0.51–11.60)
Hyperbilirubinemia	18 (26.1%)	13 (23.2%)	.71	1.12 (0.60–2.09)
Shoulder dystocia	4 (5.8%)	5 (8.9%)	.51	0.65 (0.18–2.30)
Neonatal hypoglycemia	7 (10.1%)	8 (14.3%)	.48	0.71 (0.27–1.84)
Gestational age at delivery, wk	36.7 (4.5)	38.7 (1.7)	.001	—
Any diabetic medication	30 (43.5%)	18 (32.1%)	.20	1.35 (0.85–2.16)
Insulin medication	11 (15.9%)	3 (5.4%)	.06	2.98 (0.87–10.15)
Large for gestational age	6 (8.7%)	7 (12.5%)	.49	0.70 (0.25–1.95)

CI, confidence interval.

[a] Primary composite outcome is composed of macrosomia, primary cesarean delivery, gestational hypertension, preeclampsia, hyperbilirubinemia, shoulder dystocia, and neonatal hypoglycemia.

Harper et al. Early GDM screening. Am J Obstet Gynecol 2020.

AJOG at a Glance:

A. **Why was the study conducted?** The American College of Obstetricians and Gynecologists recommends early screening for preexisting diabetes or early gestational diabetes in a high-risk population, based on expert opinion. The National Institute of Diabetes and Digestive and Kidney Disease Consensus workshop on research gaps in gestational diabetes called for a randomized controlled trial examining the risks and benefits of early screening. The study was performed to compare perinatal outcomes in obese women undergoing early screening (14–20 weeks) for gestational diabetes compared to routine screening (24–28 weeks).

B. **What are the key findings?** Early screening did not reduce the incidence of the primary composite outcome (macrosomia (>4000g), primary cesarean, hypertensive disease of pregnancy, shoulder dystocia, neonatal hyperbilirubinemia, and neonatal hypoglycemia): 56.9% in early screen vs 50.8% in routine screen, p=0.07, RR 1.12, 95% CI 0.99–1.26).

C. **What does this study add to what is already known?** This randomized controlled trial did not demonstrate benefit of early screening for gestational diabetes in obese women. To our knowledge, this is the first US-based trial to compare early versus routine screening for gestational diabetes in a randomized fashion, although other trials are ongoing (NCT02377531, ACTRN12616000924459).

RESEARCH ARTICLE Open Access

The treatment of booking gestational diabetes mellitus (TOBOGM) pilot randomised controlled trial

This study show that early GDM treatment could be associated with a play off between a reduced LGA rate but an increased NICU admission rate and Managing GDM is not without risk

Early treatment may have both benefits and harms.

A full RCT is urgently required!

Simmons D, Nema J, Parton C, et al. The treatment of booking gestational diabetes mellitus (TOBOGM) pilot randomised controlled trial. BMC Pregnancy Childbirth 2018;18:151
47. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy

ORIGINAL ARTICLE

Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy

In this randomized trial involving women who had a risk factor for hyperglycemia in pregnancy and had received a diagnosis of gestational diabetes before 20 weeks' gestation on the basis of WHO criteria, those who received immediate treatment had a significantly, albeit modestly, lower incidence of a composite of adverse neonatal events (the first primary outcome) than those who received deferred or no treatment.

Glucose measurement	Plasma glucose concentration	
	[mg/dL]	[mmol/L]
Fasting	92–125	5.1–6.9
60 minutes	≥ 180	≥ 10
120 minutes	153–199	8.5–11.0

the results were compatible with anywhere from a 1.2 to a 10.1 percentage point reduction in the risk of an adverse neonatal outcome event.

No significant difference was shown with respect to the two other prespecified primary outcomes (pregnancy-related hypertension and neonatal lean body mass)

Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, Flack JR, McLean M, Wong V, Hibbert E, Kautzky-Willer A, Harreiter J, Backman H, Gianatti E, Sweeting A, Mohan V, Enticott J, Cheung NW; TOBOGM Research Group. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. N Engl J Med. 2023 Jun 8;388(23):2132-2144. doi: 10.1056/NEJMoa2214956. Epub 2023 May 5. PMID: 37144983.

Table 2. Primary and Secondary Pregnancy Outcomes.*

Outcome	Immediate Treatment (N=400)	Control (N=393)	Adjusted Treatment Effect†	
			Difference in Value (95% CI)	Relative Risk (95% CI)
Primary Pregnancy Outcomes				
Adverse neonatal outcomes — no./total no. (%)‡	94/378 (24.9)	113/370 (30.5)	−5.6 (−10.1 to −1.2)	0.82 (0.68 to 0.98)
Pregnancy-related hypertension — no./total no. (%)§	40/378 (10.6)	37/372 (9.9)	0.7 (−1.6 to 2.9)	1.08 (0.85 to 1.38)
Maternal Secondary Pregnancy Outcomes¶				
Median maternal gestational weight gain from first to final predelivery visit (IQR) — kg	6.0 (2.0 to 9.5)	6.9 (3.4 to 10.0)	−1.2 (−3.2 to 0.8)	NA
Cesarean delivery — no./total no. (%)	144/377 (38.2)	146/368 (39.7)	0.2 (−4.2 to 4.6)	1.00 (0.90 to 1.13)
Induction of labor — no./total no. (%)	187/377 (49.6)	177/372 (47.6)	1.0 (−8.3 to 10.3)	1.02 (0.84 to 1.23)
Perineal injury — no./total no. (%)	3/375 (0.8)	13/365 (3.6)	−2.8 (−4.1 to −1.5)	0.23 (0.10 to 0.51)
Median EQ-5D score at 24 to 28 wk of gestation (IQR)‖	0.83 (0.76 to 1.00)	0.81 (0.73 to 1.00)	0.02 (0.01 to 0.04)	1.03 (1.01 to 1.04)
Neonatal Secondary Pregnancy Outcomes**				
Neonatal lean body mass — kg	2.86±0.34	2.91±0.33	−0.04 (−0.09 to 0.02)	NA
Birth weight — g	3258±563	3343±588	−72.1 (−127.6 to −16.6)	NA
Large-for-gestational-age status — no./total no. (%)††	63/375 (16.8)	72/368 (19.6)	−4.6 (−11.8 to 2.5)	0.77 (0.51 to 1.17)
Small-for-gestational-age status — no./total no. (%)††	45/375 (12.0)	34/368 (9.2)	3.0 (−0.8 to 6.8)	1.32 (0.93 to 1.85)
Upper arm circumference — cm	10.8±1.4	10.9±1.3	−0.1 (−0.2 to 0.1)	NA
Sum of neonatal caliper measurements — mm	20.0±4.6	21.5±5.4	−1.4 (−2.2 to −0.5)	NA
Neonatal fat mass — kg	0.45±0.17	0.48±0.19	−0.03 (−0.05 to −0.01)	NA
Heel-prick blood glucose <29 mg/dl within 72 hr after birth	22/355 (6.2)	14/303 (4.6)	1.5 (−2.2 to 5.3)	1.31 (0.65 to 2.66)
Heel-prick blood glucose ≤40 mg/dl at 1 to 2 hr after birth	61/323 (18.9)	57/251 (22.7)	−4.2 (−13.4 to 5.0)	0.81 (0.55 to 1.19)
Median no. of bed days in neonatal special care nursery or neonatal ICU‡‡	2.0 (0.3 to 4.8)	2.0 (1.0 to 6.0)	−0.8 (−1.3 to −0.3)	0.60 (0.41 to 0.89)

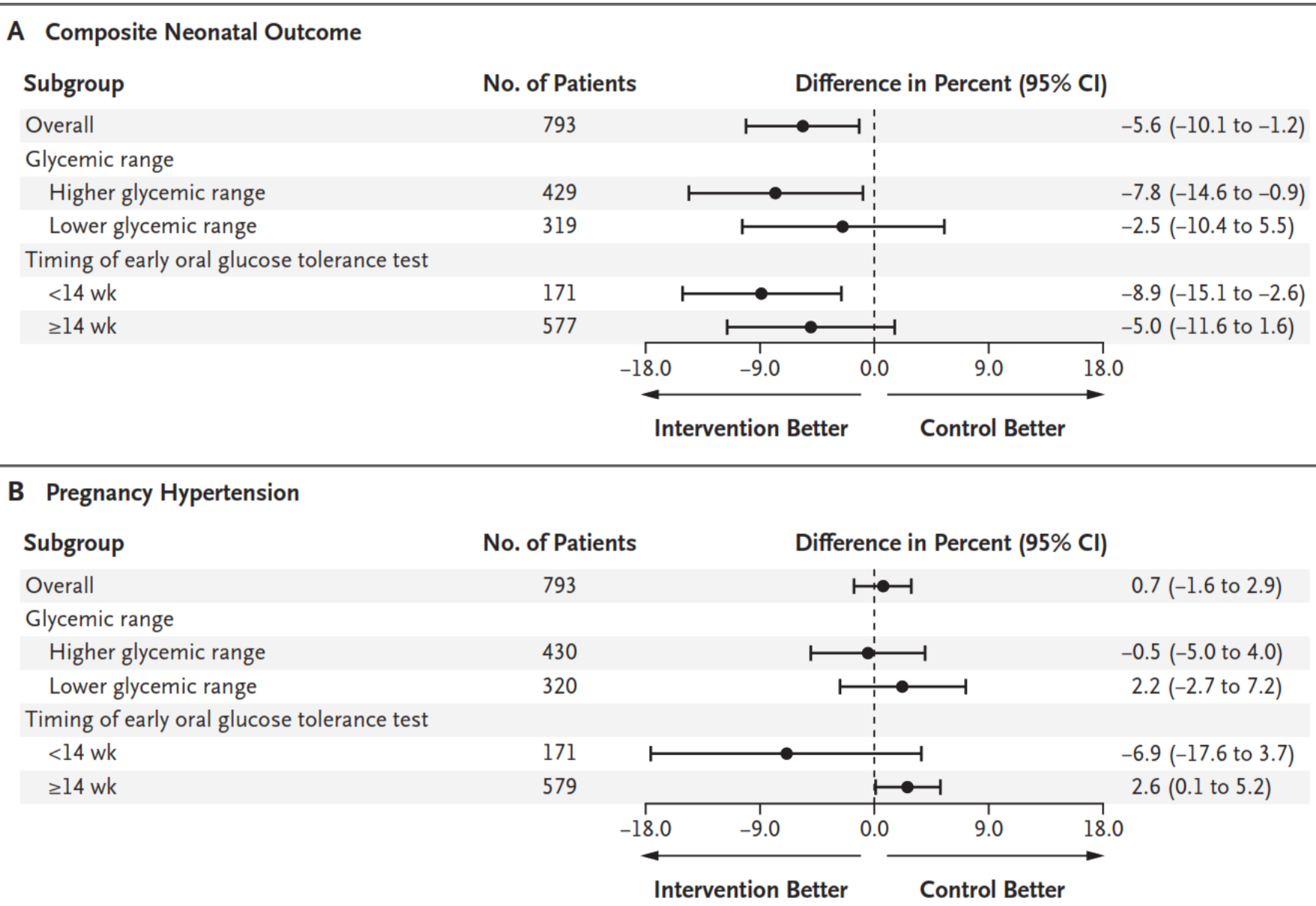


Figure 2. Primary Outcomes Overall and within Prespecified Subgroups.

This paper showed that a third of the women who had received a diagnosis of early gestational diabetes according to the WHO criteria did not have gestational diabetes on repeat OGTT at 24 to 28 weeks' gestation.

A finding that was consistent with previous observations.

This finding raises questions about whether criteria that had been established for OGTT at 24 to 28 weeks' gestation can be applied to testing early in pregnancy, particularly if there is a potential for harm, such as an increase in the number of small-for-gestational-age births among women who had received early treatment

HbA1c for Diagnosis in Early Pregnancy

three observational studies that investigated the association of higher first trimester HbA1c (5.9–6.4%) and adverse pregnancy Outcomes :

The study found a 3-fold increased risk of macrosomia and preeclampsia associated with an early HbA1c of 5.9–6.4%

Mañé L, Flores-Le Roux JA, Benaiges D, Rodríguez M,Marcelo I, Chillarón JJ, et al. Role of first-trimester HbA1c as a predictor of adverse obstetric outcomes in a multiethnic cohort. J Clin Endocrinol Metab. 2017;102(2):390–7. A prospective study showing the utility of HbA1c in ealry pregnancy

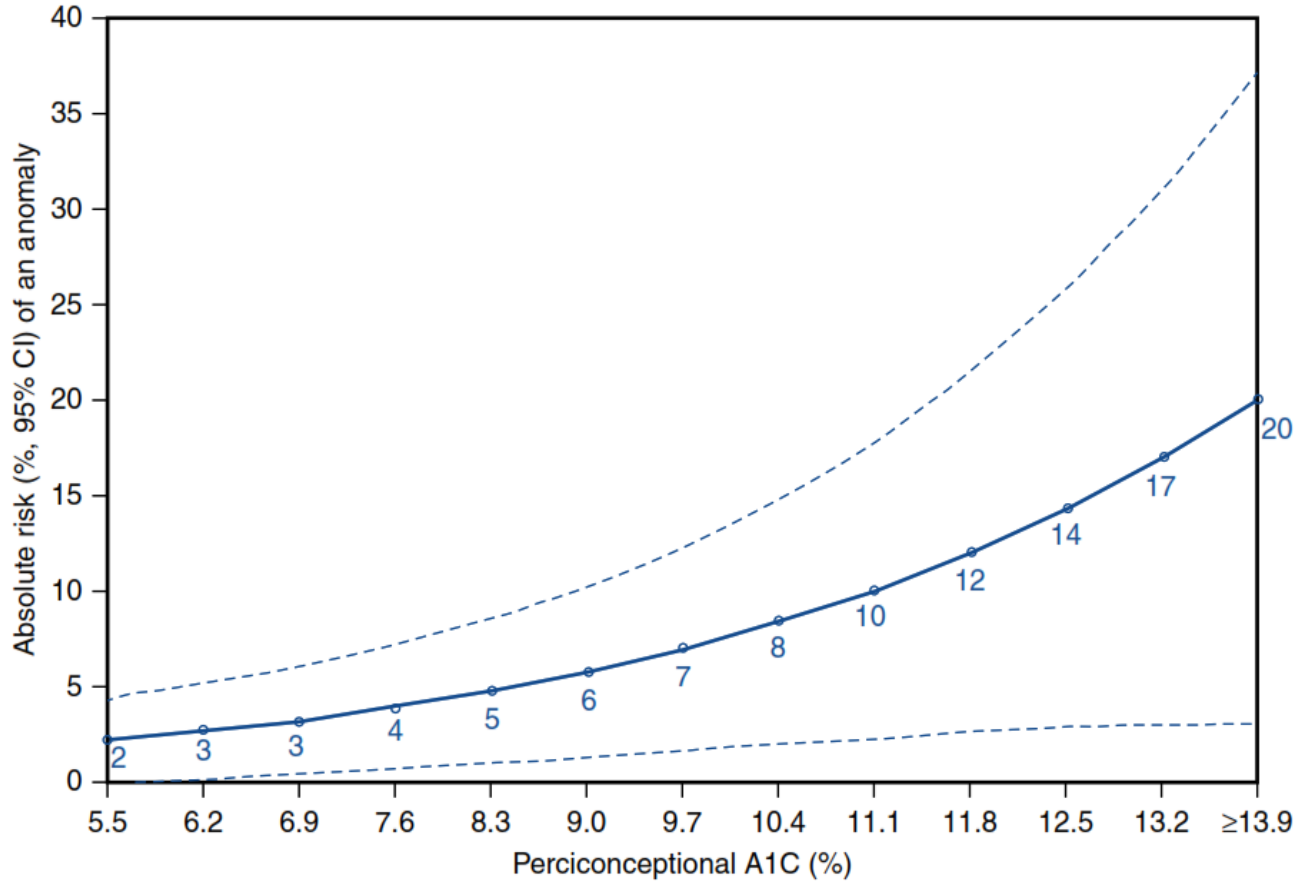


Fig. 34.2 Relationship between glycated hemoglobin in percent and absolute risk of a fetal anomaly. *A1C,* Glycated hemoglobin test; *CI,* confidence interval.

The another study reported significantly increased risk of adverse pregnancy outcomes such as macrosomia, hypertensive disorders, and cesarean section among women with HbA1c of 5.9–6.4%

The higher HbA1c did not adequately capture all the risks associated with early-onset GDM such as LGA, SGA, and neonatal hypoglycemia.

Hughes RC, Moore MP, Gullam JE, Mohamed K, Rowan J. An early pregnancy HbA1c >/=5.9% (41 mmol/mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. Diabetes Care. 2014;37(11):2953–9. A large cohort study demonstrating the potential utility of HbA1c in early pregnancy

A Cluster Randomized Noninferiority Field Trial of Gestational Diabetes Mellitus Screening

Fahimeh Ramezani Tehrani,[1] Samira Behboudi-Gandevani,[2] Farshad Farzadfar,[3,4] Farhad Hosseinpanah,[5] Farzad Hadaegh,[6] Davood Khalili,[6] Masoud Soleymani-Dodaran,[7] Majid Valizadeh,[5] Mehrandokht Abedini,[8] Maryam Rahmati,[1] Razieh Bidhendi Yarandi,[9] Farahnaz Torkestani,[10] Zahra Abdollahi,[11] Marzieh Bakhshandeh,[12] Mehdi Zokaee,[13] Mina Amiri,[1] Farzam Bidarpour,[14] Mehdi Javanbakht,[15] Iraj Nabipour,[16] Ensieh Nasli Esfahani,[17] Afshin Ostovar,[18,4] and Fereidoun Azizi[19]

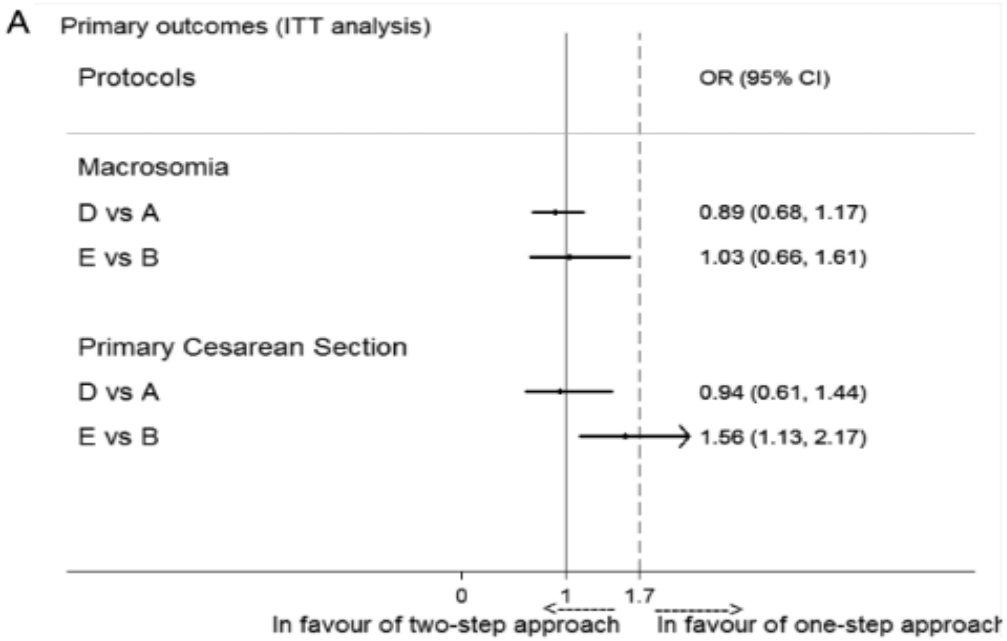
The IADPSG GDM definition significantly increased the prevalence of GDM diagnosis. However, the less strict approaches were not inferior to other criteria in terms of adverse maternal and neonatal outcomes. There were no statistically significant differences in the adjusted odds of adverse pregnancy outcomes in the 2-step compared

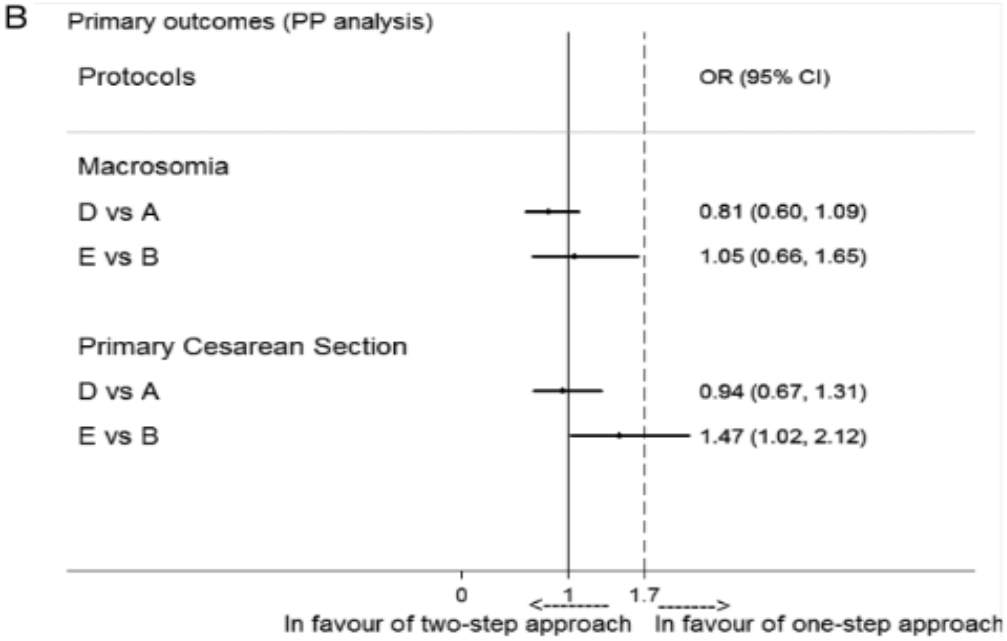
with the 1-step screening approaches, considering multiplicity adjustmen

Table 1. Definitions of various protocols for screening of gestational diabetes mellitus

		Protocol A	Protocol B	Protocol C	Protocol D	Protocol E
First trimester	Diagnostic criteria for GDM	GDM is defined as: 5.1 mmol/L (92 mg/dL) < FPG < 7 mmol/L (126 mg/dL)	GDM is defined as: 5.6 mmol/L (100 mg/dL) < FPG < 7 mmol/L (126 mg/dL)	GDM is defined as: 5.6 mmol/L (100 mg/dL) < FPG < 7 mmol/L (126 mg/dL)	GDM is defined as: 5.1 mmol/L (92 mg/dL) < FPG < 7 mmol/L (126 mg/dL)	GDM is defined as: 5.6 mmol/L (100 mg/dL) < FPG < 7 mmol/L (126 mg/dL)
Second trimester	Method for GDM screening	One step with 2-h 75-g OGTT	One step with 2-h 75-g OGTT	One step with 2-h 75-g OGTT	Two steps with 50-g GCT-1 h following 3-h 100-g OGTT	Two steps with 50-g GCT-1 h following 3-h 100-g OGTT
	Diagnostic threshold of test	Fasting ≥ 5.1 mmol/L (92 mg/dL) 1 h ≥ 10 mmol/L (180 mg/dL) 2 h ≥ 8.5 mmol/L (153 mg/dL)	Fasting ≥ 5.1 mmol/L (92 mg/dL) 1 h ≥ 10 mmol/L (180 mg/dL) 2 h ≥ 8.5 mmol/L (153 mg/dL)	Fasting ≥ 5.1 mmol/L (92 mg/dL) 1 h ≥ 10 mmol/L (180 mg/dL) 2 h ≥ 8.5 mmol/L (153 mg/dL)	50-g GCT: BS-1 h: ≥ 7.8 mmol/L (140 mg/dL) 100-g OGTT: Fasting ≥ 5.3 mmol/L 1 h ≥ 10 mmol/L (180 mg/dL) 2 h ≥ 8.6 mmol/L (155 mg/dL) 3 h ≥ 7.8 mmol/L (140 mg/dL)	50-g GCT: BS-1 h: ≥7.8 mmol/L (140 mg/dL) 100-g OGTT: Fasting ≥ 5.3 mmol/L 1 h ≥ 10 mmol/L (180 mg/dL) 2 h ≥ 8.6 mmol/L (155 mg/dL) 3 h ≥ 7.8 mmol/L (140 mg/dL)
	Diagnostic criteria for GDM	GDM defined as any of the given plasma glucose values are met or exceeded	GDM defined as 2 or more of the given plasma glucose values are met or exceeded	GDM defined as any of the given plasma glucose values are met or exceeded	GDM defined as 2 or more of the given plasma glucose are met or exceeded	GDM defined as 2 or more of the given plasma glucose values are met or exceeded

Abbreviations: BS, blood sugar; FPG, fasting plasma glucose; GCT, glucose challenge test; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.


A
Primary outcomes (ITT analysis)
Protocols
OR (95% CI)
Macrosomia
D vs A
0.89 (0.68, 1.17)
E vs B
1.03 (0.66, 1.61)
Primary Cesarean Section
D vs A
0.94 (0.61, 1.44)
E vs B
1.56 (1.13, 2.17)
0
1
1.7
In favour of two-step approach
In favour of one-step approach


B
Primary outcomes (PP analysis)
Protocols
OR (95% CI)
Macrosomia
D vs A
0.81 (0.60, 1.09)
E vs B
1.05 (0.66, 1.65)
Primary Cesarean Section
D vs A
0.94 (0.67, 1.31)
E vs B
1.47 (1.02, 2.12)
0
1
1.7
In favour of two-step approach
In favour of one-step approach

Does fasting plasma glucose values 5.1-5.6 mmol/l in the first trimester of gestation a matter?

This study was secondary analysis of a randomized community non-inferiority trial involving pregnant women with FBS level between 5.1-5.6 mmol/l (92-124 mg/dl) in the first trimester of pregnancy assessing Adverse maternal and neonatal outcoms.

This study indicated that GDM treatment at the first trimester of pregnancy was not associated with a reduced risk of adverse maternal and neonatal outcomes, including macrosomia, LBW, primary C-S, preterm birth, neonatal hypoglycemia, neonatal hypocalcemia, hyperbilirubinemia, preeclampsia, NICU admission, and birth trauma.

Ramezani Tehrani F, Farzadfar F, Hosseinpanah F, Rahmati M, Firouzi F, Abedini M, Hadaegh F, Valizadeh M, Torkestani F, Khalili D, Solaymani-Dodaran M, Bidhendi-Yarandi R, Bakhshandeh M, Ostovar A, Dovom MR, Amiri M, Azizi F, Behboudi-Gandevani S. Does fasting plasma glucose values 5.1-5.6 mmol/l in the first trimester of gestation a matter? Front Endocrinol (Lausanne). 2023 Jun 2;14:1155007. doi: 10.3389/fendo.2023.1155007. PMID: 37334302; PMCID: PMC10273274.

TABLE 2 Prevalence and Risk ratio and 95% confidence interval of adverse pregnancy outcomes in participants based on study groups[ʃ].

	Prevalence		P-value *	Unadjusted Model		Adjusted Model [§]	
	GDM (n = 1198)	Non-GDM (n = 2099)		RR (95% CI)	P-value *	RR (95% CI)	P-value **
Macrosomia	89 (7.8)	124 (6.4)	0.1	1.23 (0.74-2.01)	0.4	1.41 (0.83-2.40)	0.2
Primary cesarean-section [¥]	175 (19.8)	294 (21.0)	0.5	0.94 (0.74-1.19)	0.6	0.97 (0.81-1.17)	0.8
Preterm birth [§]	79 (6.9)	131 (6.7)	0.8	1.03 (0.64-1.66)	0.9	1.02 (0.61-1.71)	0.9
Neonatal Hypoglycemia	30 (2.6)	29 (1.5)	0.03	1.77 (1.11-2.80)	**0.015**	1.35 (0.80-2.27)	0.2
Neonatal Hypocalcemia	19 (1.6)	22 (1.0)	0.2	1.51 (0.77-3.00)	0.2	0.92 (0.39-2.19)	0.9
Neonatal Hyperbilirubinemia	96 (8.5)	130 (6.8)	0.08	1.26 (0.58-2.74)	0.5	1.05 (0.57-1.92)	0.8
Preeclampsia	124 (10.3)	218 (10.4)	0.9	1.00 (0.60-1.65)	0.9	0.99 (0.65-1.52)	0.9
NICU admission	82 (6.8)	112 (5.3)	0.08	1.29 (0.82-2.01)	0.3	1.08 (0.69-1.68)	0.7
Birth trauma	9 (0.7)	14 (0.7)	0.8	1.13 (0.37-3.48)	0.8	1.03 (0.45-2.33)	0.9
Low Birth Weight [€]	94 (8.4)	162 (8.5)	0.9	0.99 (0.77-1.27)	0.9	0.99 (0.85-1.15)	0.9

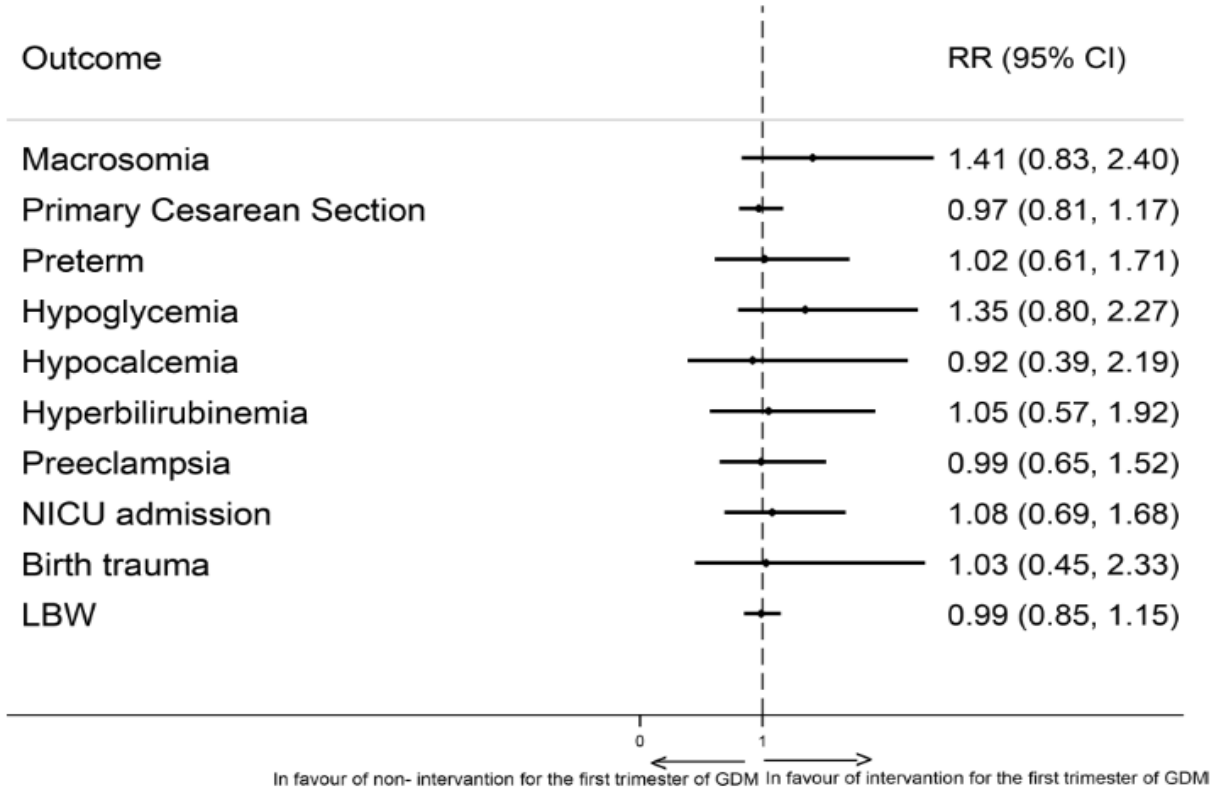


FIGURE 2
Adjusted risk ratio plot for pregnancy outcomes comparing intervention group and controls.

CLINICAL TRIAL article
Front. Endocrinol., 02 June 2023
Sec. Reproduction
Volume 14 - 2023 |

Result

Is the Etiological Mechanism for This GDM From Early Pregnancy the Same as for GDM Developing Later?

Depending on the setting, screening approach,

and diagnostic criteria used, a high proportion (15–70%) of women with GDM have hyperglycemia detectable in early pregnancy

Women who develop GDM in early pregnancy appear to be more insulin resistant, with greater waist circumference, higher blood pressure, and higher triglycerides than women who develop GDM

*Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and meta-analysis. Curr Diab Rep 2017;17:115

How Should We Diagnose and Manage GDM From Early Pregnancy?

New studies contributed to a growing shift in paradigm that women with higher glucose levels early in pregnancy, below overt diabetes, should be treated for their dysglycemia but further research is needed !

Standards of Care in Diabetes—2023

The American Diabetes Association recommends those with "pre-diabetes" be treated as if they have hyperglycemia , but there may be a risk of overtreatment early in pregnancy

2.26b Before 15 weeks of gestation, test individuals with risk factors **B** and consider testing all individuals **E** for undiagnosed diabetes at the first prenatal visit using standard diagnostic criteria if not screened preconception.

2.26d Before 15 weeks of gestation, screen for abnormal glucose metabolism to identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes, are more likely to need insulin, and are at high risk of a later gestational diabetes mellitus diagnosis. **B** Treatment may provide some benefit. **E**

ADA

Table 2.7—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in individuals not previously diagnosed with diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in individuals not previously diagnosed with diabetes.

If the plasma glucose level measured 1 h after the load is ≥130, 135, or 140 mg/dL (7.2, 7.5, or 7.8 mmol/L, respectively), proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting.

The diagnosis of GDM is made when at least two* of the following four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria [251]):

- Fasting: 95 mg/dL (5.3 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 155 mg/dL (8.6 mmol/L)
- 3 h: 140 mg/dL (7.8 mmol/L)

GDM, gestational diabetes mellitus; GLT, glucose load test; OGTT, oral glucose tolerance test. *American College of Obstetricians and Gynecologists notes that one elevated value can be used for diagnosis (247).

2.26e Screen for early abnormal glucose metabolism using fasting glucose of 110–125 mg/dL (6.1 mmol/L) or A1C 5.9–6.4% (41–47 mmol/mol). **B**

2.27 Screen for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant individuals not previously found to have diabetes or high-risk abnormal glucose metabolism detected earlier in the current

admission (213). If individuals are not screened prior to pregnancy, universal early screening at <15 weeks of gestation for undiagnosed diabetes may be considered over selective screening (**Table 2.3**), particularly in populations with high prevalence of risk factors and undiagnosed diabetes in people of childbearing age. Strong racial and ethnic

(209–212). Standard diagnostic criteria for identifying undiagnosed diabetes in early pregnancy are the same as those used in the nonpregnant population

If early screening is negative, individuals should be rescreened for GDM between 24 and 28 weeks of gestation

Early abnormal glucose metabolism, defined as fasting glucose threshold of 110 mg/dL (6.1 mmol/L) or an A1C of 5.9% (39 mmol/mol), may identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes

Thank you