
بسم الله الرحمن الرحیم

Diabetes Management During Pregnancy

AGENDA
Diabetes in Pregnancy

- **Definition**
- **Pathogenesis, Prevalence, Health Risks, Risk Factors**
- **Screening**
- **HAPO Study**
- **The 2013 Endocrine Society Clinical Practice Guideline**
  - Preconception care of women with diabetes
  - Gestational diabetes (GDM)
  - Glucose monitoring and glycemic targets
  - Nutrition therapy and weight gain targets for women with overt or GDM
  - Blood glucose lowering pharmacological therapy during pregnancy
  - Labor, delivery, lactation, and postpartum care
- **Pitfalls and Conclusion**

Classification of Diabetes

- Type 1 diabetes
  - β-cell destruction
- Type 2 diabetes
  - Progressive insulin secretory defect
- Other specific types of diabetes
  - Genetic defects in β-cell function, insulin action
  - Diseases of the exocrine pancreas
  - Drug- or chemical-induced
- Gestational diabetes mellitus (GDM)

GDM: Old Definition

- *"Glucose intolerance with onset or first recognition during pregnancy"*
  - whether or not insulin is used for treatment or hyperglycemia persists after pregnancy
- Criteria for the diagnosis were initially established about 50 years ago.
- With minor modifications, remained in use for more than 40 years.

O'sullivan JB. Criteria for oral glucose tolerance test in pregnancy. Diabetes 1964;13:278–285

Diabetes in Pregnancy: Current Definitions (IADPSG & ADA)

- Overt
- Gestational

Overt diabetes (type 1 or 2) in initial visit:

- FPG ≥126 *mg/dl*
- A_{1C} ≥ 6.5%
- Random PG ≥200 *mg/dl*

these women are at increased risk of having a child with a **congenital anomaly** and may be at increased risk of **complications** from diabetes.

Gestational diabetes:

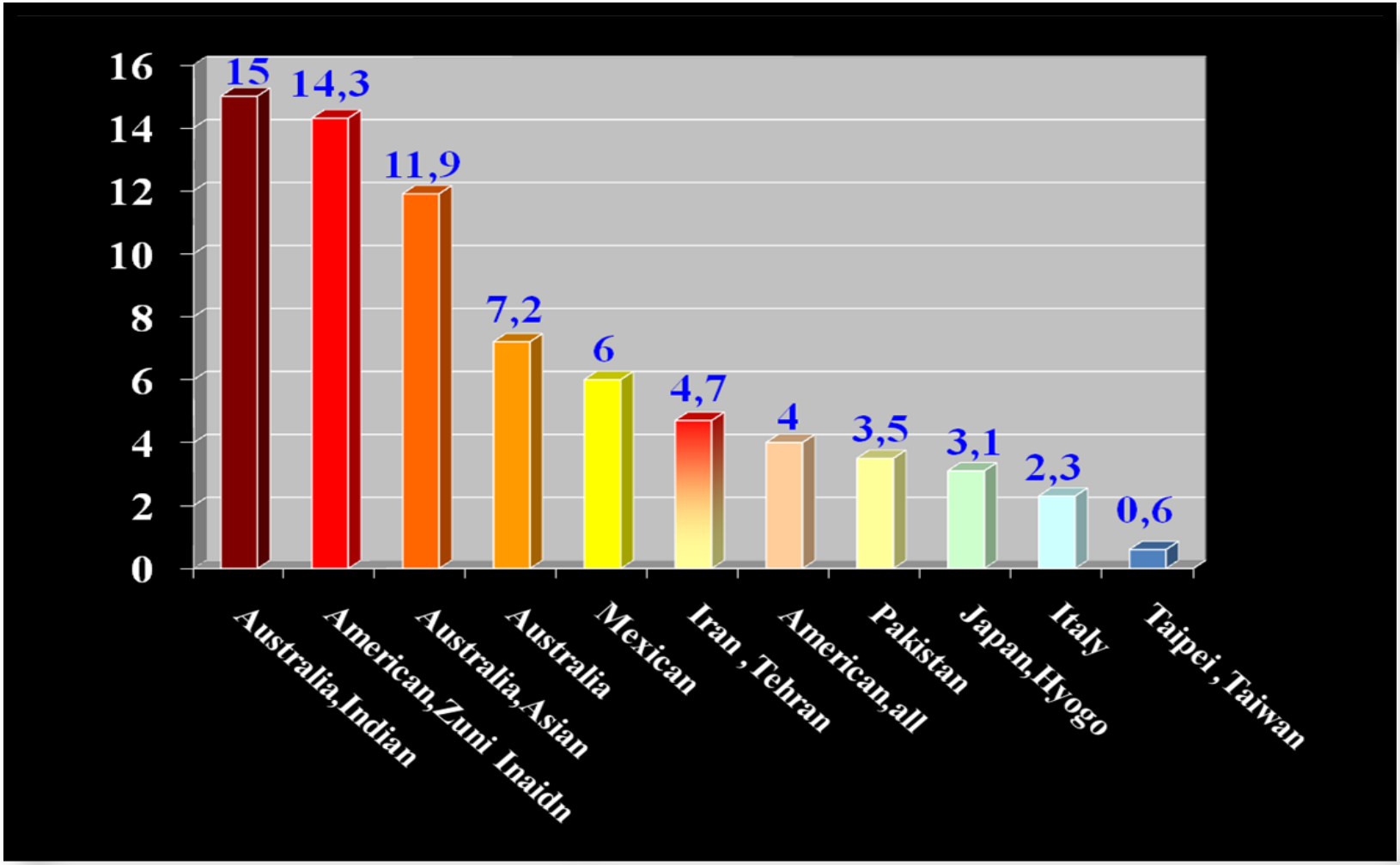
- 92 ≤ FPG <126 *mg/dl* at any gestational age
- At 24-28 weeks of gestation: 75 gr 2-hr OGTT with any of the below:
  - FPG ≥92 *mg/dl*
  - 1-hr ≥180 *mg/dl*
  - 2-hr ≥153 *mg/dl*

NIH & ACOG still believe on 2 step approach & old criteria.

GDM Pathogenesis

- Pregnancy is characterized by insulin resistance and hyperinsulinemia due to:
  - placental secretion of diabetogenic hormones including:
    - GH
    - CRH
    - Human placental lactogen (hPL)
    - Progesterone
  - increased maternal adipose deposition
  - decreased exercise
  - increased caloric intake
- These and other endocrinologic and metabolic changes ensure that the fetus has an ample supply of fuel and nutrients at all times.
- GDM occurs when pancreatic function is not sufficient to overcome the insulin resistance created by changes in diabetogenic hormones during pregnancy.

Prevalence of GDM



Epidemiology of glucose intolerance and GDM in women of child bearing age, Diabetes Care, 21, 1998

Overall Prevalence of Pregnancy Complicated by DM

- Pre-GDM: 0.8 % in 1999
  1.8 % in 2005

- The prevalence of GDM remained constant at about 7.5% during the same interval. [1]

- Using new diagnostic IADPSG criteria: 18% [2]

1. Lawrence JM, et al. Trends in the prevalence of preexisting diabetes and GDM among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care 2008; 31:899
2. C.D.C 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs

GDM: a doubly important health problem

- A great impact on the health of the woman:
  - not only during pregnancy but also later on.
  - one of the most predictive factors for the development of T_2DM later in life.

- GDM also affects the health of the baby.

Health Risks of Gestational Diabetes

Mother	Fetus	Newborn	Child/Adult
Birth trauma	Hyperinsulinemia	Hypoglycemia	Obesity
Increased cesarean delivery	Cardiomyopathy	Respiratory distress syndrome	Type 2 diabetes
Preeclampsia/ Gestational hypertension	Fetal organomegaly	Hypocalcemia	Metabolic syndrome
Type 2 diabetes	Hydramnios Stillbirth	Hyperviscosity Hypomagnesemia	impaired fine and gross motor functions
Metabolic syndrome	LGA/ macrosomia	Cardiomyopathy Hyperbilirubinemia Perinatal mortality	higher rates of inattention and/or hyperactivity
	Birth trauma	Polycythemia	

Diabetes Care 2008; 31:340.
Obstet Gynecol Clin N Am 2010; 37:255–67.

Risk Factors for Gestational Diabetes

Risk Factor	Odds Ratio	References
Prior GDM	23	*McGuire et al*
South East Asian	7.6[a]	*Dornhorst et al*
Sibling with Diabetes	7.1	*Kim et al*
Severe Obesity	7	*Torloni et al; Chu et al*
Obesity	3.7	*Torloni et al; Chu et al*
Prior Macrosomic Infant	3.3	*McGuire et al*
Parent with Diabetes	3.2	*Kim et al*
PCOS	2.9	*Toulis et al*
Periodontal Disease	2.6	*Xiong et al*
Hispanic	2.4[a]	*Dooley et al*
Maternal Age Greater than 35 y	2.3	*Xiong et al*
Multiple Gestation	2.2	*Rauh-Hain et al*
Overweight	2	*Torloni et al; Chu et al*
Low Maternal Birth Weight	1.9	*Seghieri et al*
African American	1.8[a]	*Dooley et al*
Maternal Age > 25 y	1.4	*Cypryk et al*

[a] Relative risk compared with white race

Obstet Gynecol Clin N Am 2010; 37:255–67.

Screening For GDM

- GDM has been a very hot topic; its screening has been a topic of debate for many years, and different screening strategies have been proposed over the years.

SCREENING

- Selective *vs.* Universal?

- One step *vs.* two step?

SCREENING

Whom to be screened ?

- **low risks of GDM should have all below criteria:**
  - <25 yrs
  - non-Hispanic white
  - BMI <25 kg/m^2
  - no history of previous glucose intolerance or adverse pregnancy outcomes associated with GDM
  - no first degree relative with diabetes
- Only 10% of the general obstetric population meets all of these criteria.
- 2.7-20% of women diagnosed with GDM have no risk factors.

Thus, universal screening is recommended.

Obstet Gynecol 2013; 122:406.

Old Screening for GDM

Two approaches may be followed for GDM screening at 24–28 weeks:

✦ **Two-step approach:**

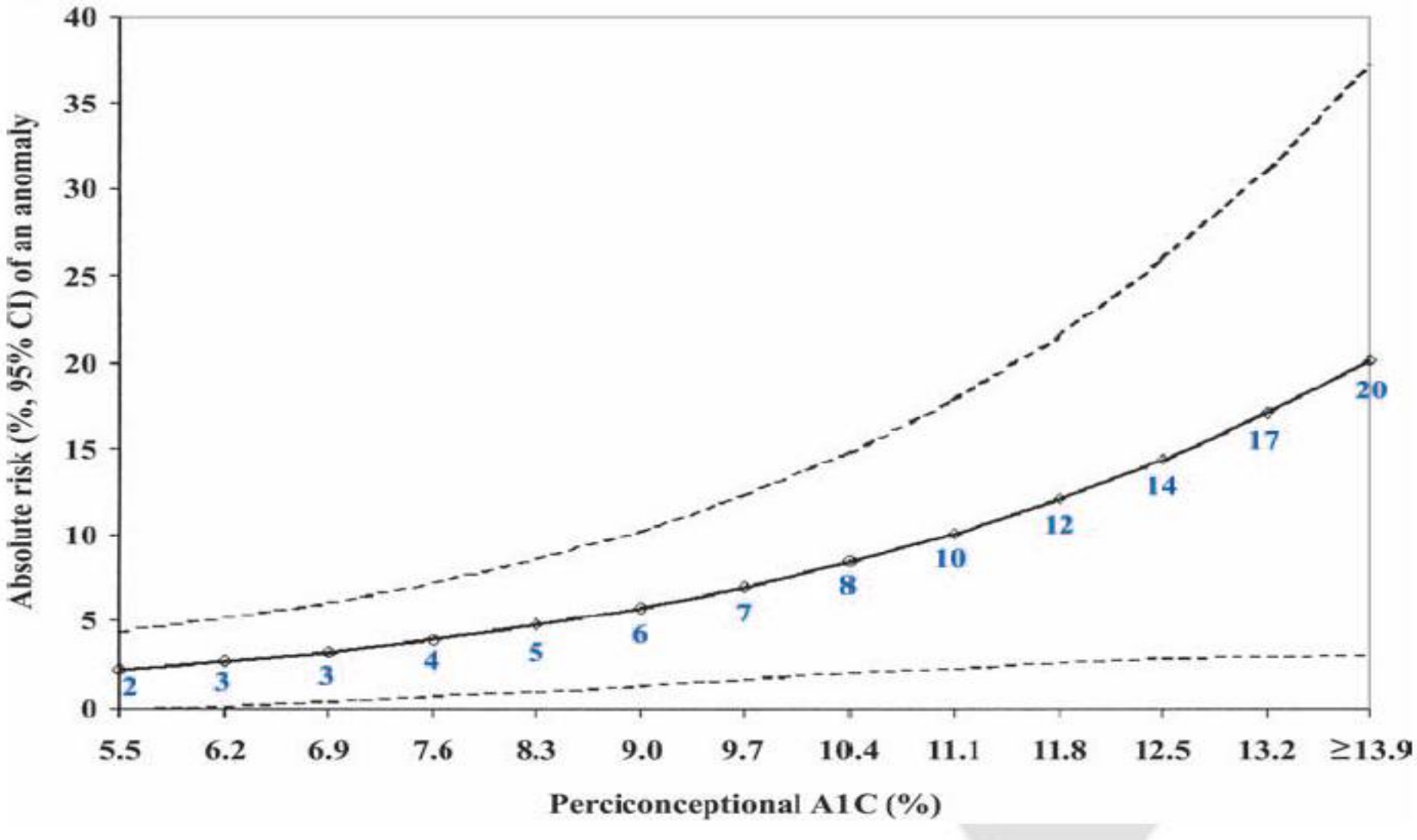
- **A.** Perform initial screening by measuring plasma or serum glucose 1 h after 50-g load (GCT). 1-hPG of >140 mg/dl identifies 80% of women with GDM, while the sensitivity is further increased to 90% by a threshold of >130 mg/dl.
- **B.** Perform diagnostic 100-g OGTT on a separate day in women who exceed the chosen threshold on 50-g screening.

✦ **One-step approach:**

- Perform a diagnostic 70-g OGTT in all women to be tested at 24–28 weeks.
- May be preferred in clinics with high prevalence of GDM.

Diabetes Care 2010; 33 (Suppl 1): S16

Risk of Fetal Anomaly Relative to Periconceptional HbA_{1C}



Guerin A et al. *Diabetes Care* 2007;30:1-6.

Diagnosis of GDM: which criteria to be used?

- Are there clear threshold glucose levels above which the risk of adverse neonatal or maternal outcomes increases?

IADPSG Consensus

Reviews/Commentaries/ADA Statements

REVIEW ARTICLE

International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy

Diabetes Care 2010; 33(3): 676-82

International Association of Diabetes and Pregnancy Study Groups (IADPSG)

- Was formed in 1998; 225 conferees from 40 countries.
- The principal objectives of IADPSG are to foster an international approach to enhancing the quality of care, facilitating research, and advancing education in the field of diabetes in pregnancy.

Diabetes Care 2010; 33(3): 676-82

Hyperglycemia and Adverse Pregnancy Outcome study (HAPO)

- 25,505 pregnant women at 15 centers in nine countries

✦ Primary outcomes

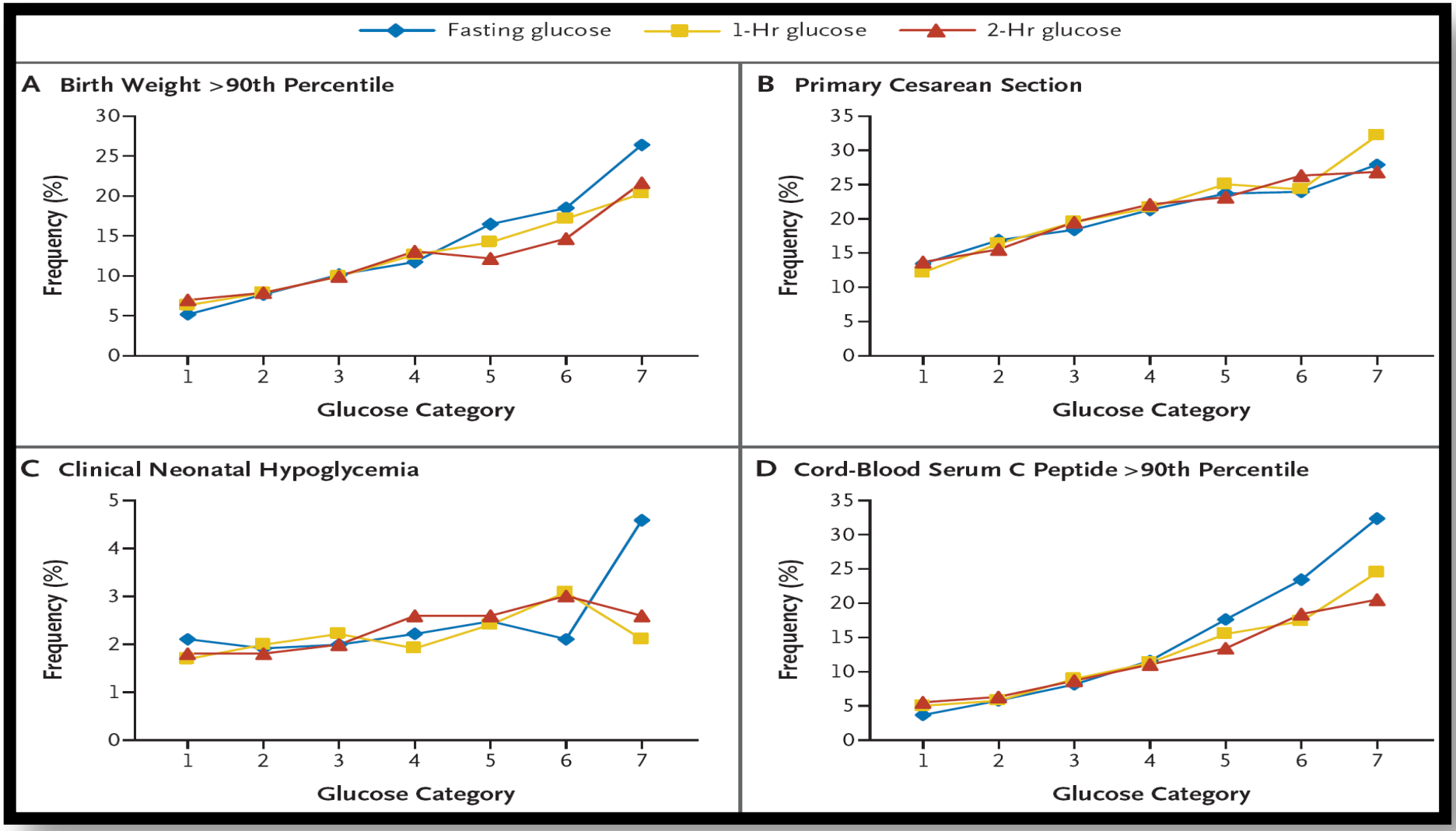
- birth weight > 90th percentile for gestational age
- primary cesarean delivery
- clinically diagnosed neonatal hypoglycemia
- cord-blood serum C-peptide level > 90th percentile

✦ Secondary outcomes

- delivery before 37 wks of gestation
- shoulder dystocia or birth injury
- need for intensive neonatal care
- hyperbilirubinemia
- preeclampsia

N Engl J Med 2008; 358:1991-2002

HAPO Primary Outcomes



N Engl J Med 2008; 358:1991-2002

Adjusted OR 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)

* Odds ratios were for an increase in the glucose level of 1 SD (6.9 mg per deciliter [0.4 mmol per liter] for the fasting plasma glucose level, 30.9 mg per deciliter [1.7 mmol per liter] for the 1-hr plasma glucose level, and 23.5 mg per deciliter [1.3 mmol per liter] for the 2-hr plasma glucose level). The model for preeclampsia did not include adjustment for hospitalization or mean arterial pressure, and presence or absence of family history of hypertension or prenatal urinary tract infection was included in the model for preeclampsia only. See Table 2 for other details about adjustments in each model.

† Data for women who had had a previous cesarean section were excluded.

‡ The P value for the quadratic (nonlinear) association was 0.013.

N Engl J Med 2008; 358:1991-2002

Diagnosis of GDM: which criteria to be used?

- Are there clear threshold glucose levels above which the risk of adverse neonatal or maternal outcomes increases?

NO

HAPO Key Messages

- Based on **odds ratio** of **1.75** for primary outcome:
  - The frequency of birth weight, C-peptide, preeclampsia, or percent infant body fat >90th percentile was approximately twofold greater when any of the glucose values were greater than or equal to the threshold.
  - The frequencies of preterm delivery and primary C/S were >45% higher when one or more glucose values met or exceeded threshold.

Diabetes Care 2010; 33(3): 676-82

IADPSG Consensus Threshold Values for Diagnosis of GDM *(≥1 Value is Diagnostic)*

Glucose measure with a 75 g OGTT	*Glucose threshold (mg/dL)*	*Proportion of HAPO cohort above threshold (%)*
FPG	92	8.3
1-h PG	***180***	***14.0***
2-h PG	153	16.1

Based on OR of **1.75** for primary outcome

OGTT = Oral Glucose Tolerance Test
HAPO = Hyperglycemia and Adverse Pregnancy Outcomes study
IADPSG. Diabetes Care 2010;22:676-682

Threshold Values for Diagnosis of GDM or Overt Diabetes in Pregnancy

Glucose measure	Glucose concentration threshold* (mg/dl)
FPG	92
1-h plasma glucose	180
2-h plasma glucose	153
To diagnose overt diabetes in pregnancy	
FPG‡	≥126 mg/dl
A1C‡	≥6.5% (DCCT/UKPDS standardized)
Random plasma glucose	≥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.

•‡ One of these must be met to identify the patient as having overt diabetes in pregnancy.

§ If a random PG 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.

Diabetes Care 2010; 33(3): 676-82.

The Diagnosis Still Remains a Controversial Topic …

Perspectives on the Proposed Gestational Diabetes Mellitus Diagnostic Criteria

Oded Langer, MD, PhD, Jason G. Umans, MD, PhD, and Menachem Miodovnik, MD

(Obstet Gynecol 2013;121:177–82)

Review Article

Proposed new diagnostic criteria for gestational diabetes – a pause for thought?

T. Cundy

Diabet. Med. 29, 176–180 (2012)

Diagnosing gestational diabetes

E. A. Ryan

Diabetologia (2011) 54:480–486

Diabetes and Pregnancy: An Endocrine Society Clinical Practice Guideline

Ian Blumer, Eran Hadar, David R. Hadden, Lois Jovanovič, Jorge H. Mestman, M. Hassan Murad, and Yariv Yogev

Charles H. Best Diabetes Centre (I.B.), Whitby, Ontario, Canada L1M 1Z5; Helen Schneider Hospital for Women (E.H., Y.Y.), Petach Tikva 49100, Israel; Royal Victoria Hospital (D.R.H.), Belfast BT12 6BA, Northern Ireland, United Kingdom; Sansum Diabetes Research Institute (L.J.), Santa Barbara, California 93105; University of Southern California (J. H. M.), Los Angeles, California 90089; and Knowledge and Evaluation Research Unit, Mayo Clinic (M. H. M.), Rochester, Minnesota 55905

Objective: Our objective was to formulate a clinical practice guideline for the management of the pregnant woman with diabetes.

Participants: The Task Force was composed of a chair, selected by the Clinical Guidelines Subcommittee of The Endocrine Society, 5 additional experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe both the strength of recommendations and the quality of evidence.

Consensus Process: One group meeting, several conference calls, and innumerable e-mail communications enabled consensus for all recommendations save one with a majority decision being employed for this single exception.

Conclusions: Using an evidence-based approach, this Diabetes and Pregnancy Clinical Practice Guideline addresses important clinical issues in the contemporary management of women with type 1 or type 2 diabetes preconceptionally, during pregnancy, and in the postpartum setting and in the diagnosis and management of women with gestational diabetes during and after pregnancy.

J Clin Endocrinol Metab, November 2013, 98(11):4227–4249

1.0.
Preconception care of women with diabetes

1.1. Preconception Counseling

- We recommend that preconception counseling be provided to all women with diabetes who are considering pregnancy. (1 ⨁⨁OO)

1.2. Preconception Glycemic Control

- We suggest that women with diabetes seeking to conceive strive to achieve blood glucose and HbA_{1C} levels as close to normal as possible when they can be safely achieved without undue hypoglycemia. (2 ⊕⊕OO)

- Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, and other complications. B

1.3. Insulin Therapy-1
Regimens

- **a.** We recommend that insulin-treated women with diabetes seeking to conceive be treated with **multiple daily doses of insulin** or **continuous sc insulin infusion** in preference to split-dose, premixed insulin therapy, because the former are:
  - more likely to allow for the achievement and maintenance of target blood glucose levels preconceptionally.
  - in the event of pregnancy, are more likely to allow for sufficient flexibility or precise adjustment of insulin therapy. (1 ⊕⊕◯◯)

1.3. Insulin Therapy-2
Change Time

- **b.** We suggest that a change to a woman's insulin regimen, particularly when she starts continuous sc insulin infusion, be undertaken well in advance of withdrawing contraceptive measures or otherwise trying to conceive to allow the patient to acquire expertise in, and the optimization of, the chosen insulin regimen. (Ungraded recommendation)

1.3. Insulin Therapy-3
Analogues

- **c.** We suggest that insulin-treated women with diabetes seeking to conceive **be treated with** rapid-acting insulin analog therapy (with insulin **aspart** or insulin lispro) in preference to regular insulin. (2 ⊕⊕OO)

- **d.** We suggest that women with diabetes successfully using the long-acting insulin analogs insulin detemir **or** insulin **glargine** preconceptionally **may continue** with this therapy before and then during pregnancy. (2 ⊕⊕OO)

1.4. Folic Acid Supplementation

- We recommend that beginning 3 months before withdrawing contraceptive measures or otherwise trying to conceive, a woman with diabetes take a daily folic acid supplement to reduce the risk of neural tube defects. (1 ⨁⨁◯OO)
  - We suggest a daily dose of 5 mg based on this dose's theoretical benefits. (2⨁⨁OO)

1.5. Ocular Care:
Preconception, During pregnancy, & Postpartum

- **a.** We recommend that all women with diabetes who are seeking pregnancy have a detailed ocular assessment by a suitably trained and qualified eye care professional in advance of withdrawing contraceptive measures or otherwise trying to conceive. (1 ⊕⊕⊕⊕)
  - If retinopathy is documented, the patient should be apprised of the specific risks to her of this worsening during pregnancy.
  - If the degree of retinopathy warrants therapy, we recommend deferring conception until the retinopathy has been treated and found to have stabilized. (1 ⊕⊕⊕⊕)

- **b.** We recommend that women with **established retinopathy** be **seen** by their eye specialist **every trimester, then within 3 months of delivering**, and then as needed. (1 OOO) ⊕

- **c.** We suggest that pregnant women with diabetes not known to have retinopathy have ocular assessment performed soon after conception and then periodically as indicated during pregnancy. (2 OO⊕⊕)

2.0.
Gestational diabetes (GDM)

2.1. Testing for overt diabetes in early pregnancy

- We recommend **universal testing** for diabetes with a FPG, HbA_{1C}, or an untimed random PG at the first prenatal visit (before 13 weeks gestation or as soon as possible thereafter) for those women not known to already have diabetes. (1 OO) ⊕⊕
  - In the case of overt diabetes, but not GDM, a second test (either a FPG, untimed random plasma glucose, HbA_{1C}, or OGTT) must be performed in the absence of symptoms of hyperglycemia and found to be abnormal on another day to confirm the diagnosis.

1st Prenatal Visit
Abnormal Plasma Glucose Classification

Table 1. Diagnostic Criteria for Overt Diabetes and Gestational Diabetes at the First Prenatal Visit (Before 13 Weeks Gestation or as Soon as Possible Thereafter) for Those Women Not Known to Already Have Diabetes[a]

Diagnosis	Fasting Plasma Glucose,[b] mg/dL (mmol/L)	Untimed (Random) Plasma Glucose,[b] mg/dL (mmol/L)	HbA1C,[c] %
Overt diabetes (type 1, type 2, or other)	≥126 (≥7.0)	≥200 (≥11.1)	≥6.5%
Gestational diabetes	92–125 (5.1–6.9)	NA	NA

Abbreviation: NA, not applicable.

[a] These criteria for the diagnosis of overt diabetes in early pregnancy are congruent with those of the American Diabetes Association (56) and differ somewhat from those of the IADPSG (69).

[b] Testing should use plasma glucose analyzed at a laboratory, not capillary blood glucose analyzed with a blood glucose meter.

[c] Performed using a method that is certified by the NGSP (National Glycohemoglobin Standardization Program) and standardized to the Diabetes Control and Complications Trial (DCCT) (39) reference assay.

2.2. Testing for GDM at 24-28 weeks gestation-1

- We recommend that pregnant women not previously identified with overt diabetes or GDM be **tested for GDM** (Table 2) by having a **2-hr, 75-g OGTT** performed at **24-28 weeks** gestation. (1 ⊕⊕⊕◯)
  - We recommend that GDM be diagnosed on this test using the IADPSG criteria (majority opinion of this committee). (1 ⊕⊕⊕◯)

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)

Abbreviation: NA, not applicable.

[a] These criteria for diagnosing overt diabetes based on the results of the 24- to 28-week glucose tolerance test differ somewhat from those of the American Diabetes Association (56) and the IADPSG (69).

[b] Testing should use plasma glucose analyzed at a laboratory, not capillary blood glucose analyzed with a blood glucose meter.

2.2. Testing for GDM at 24-28 weeks gestation-2

- The 75-g OGTT should be performed after an overnight fast of at least 8 hrs (but not >14 hrs) and **without** having reduced usual carbohydrate intake for the preceding several days.
  - The test should be performed with the patient seated, and the patient should not smoke during the test.

- One or more abnormal values establishes the diagnosis.
  - The exception is that in the case of overt diabetes, but not GDM, a second test (either a FPG, untimed random PG, HbA1C, or OGTT), in the absence of symptoms of hyperglycemia, must be performed and found to be abnormal on another day to confirm the diagnosis of overt diabetes.

2.3. Management of Elevated Blood Glucose

- **a.** We recommend that women with **GDM target** blood glucose levels **as close to normal as possible**. (1 ⊕⊕○)

- **b.** We recommend that the **initial treatment** of GDM should consist of MNT and daily **moderate exercise** for **≥30 minutes**. (1 ⊕⊕⊕)

- **c.** We recommend using blood glucose-lowering pharmacological therapy if lifestyle therapy is insufficient to maintain normoglycemia in women with GDM. (1 ⊕⊕⊕⊕)

2.4. Postpartum Care-1

- **a.** We recommend that postpartum care for women who have had GDM should include measurement of FPG or fasting SMBG for 24-72 hrs after delivery to rule out ongoing hyperglycemia. (1 OOO) ⊕

- **b.** We recommend that a 2-hr, 75-gOGTT should be undertaken 6-12 weeks after delivery in women with GDM to rule out prediabetes or diabetes. (1 ⊕⊕⊕O)
  - If results are normal, we recommend this or other diagnostic tests for diabetes should be repeated periodically as well as before future pregnancies. (1 ⊕⊕OO)

2.4. Postpartum Care-2

- **c.** We suggest the child's birth weight and whether or not the child was born to a mother with GDM become part of the child's permanent medical record. (Ungraded recommendation)

- **d.** We recommend that all women who have had GDM receive counseling on lifestyle measures to reduce the risk of type 2 diabetes, the need for future pregnancies to be planned, and the need for regular diabetes screening, especially before any future pregnancies. (1 ⊕OOO)

- **e.** We suggest blood glucose-lowering medication should be discontinued immediately after delivery for women with GDM unless overt diabetes is suspected.
  - in which case the decision to continue such medication should be made on a case-by-case basis. (2 ⊕⊕OO)

3.0.
Glucose Monitoring and Glycemic Targets

3.1. Self-monitoring of blood glucose (SMBG)

- We recommend SMBG in all pregnant women with GDM or overt diabetes (1 ⨁⨁⨁◯, and suggest testing before and either 1 or 2 hours after the start of each meal (choosing the post meal time when it is estimated that peak postprandial blood glucose is most likely to occur) and, as indicated, at bedtime and during the night. (2 ⨁⨁◯◯

3.2. Glycemic Targets-1
FPG

- **a.** We recommend pregnant women with overt or GDM strive to achieve a target **pre-prandial** blood glucose **95 mg/dl**. (1QQOO for fasting target, 1QOOO for other meals)
  - **b.** We suggest that an even lower FPG target of 90 mg/dl be strived for (2QOOO) if this can be **safely** achieved without undue hypoglycemia.

3.2. Glycemic Targets-2
Post Prandials

- **c.** We suggest pregnant women with overt or GDM strive to achieve target blood glucose levels 1 hr after the start of a meal 140 mg/dl and **2 hrs after the start of a meal 120 mg/dl** (2QOOO) when these targets can be safely achieved without undue hypoglycemia.

- **d.** We suggest pregnant women with **overt diabetes** strive to achieve a **HbA_{1C} 7% (ideally 6.5%)**. (2QOOO)

3.2. Glycemic Targets-3

Table 3. Glycemic Targets Preconceptionally for Women with Overt Diabetes and During Pregnancy for Women With Either Overt Diabetes or Gestational Diabetes[a]

	Target Value, mg/dL (mmol/L)
Preprandial blood glucose	≤95 (5.3)[b]
1 h after the start of a meal	≤140 (7.8)
2 h after the start of a meal	≤120 (6.7)

[a] Note that blood glucose meters use capillary blood but display corrected results equivalent to plasma glucose levels.

[b] Target preprandial blood glucose is ≤90 mg/dL (5.0 mmol/L) if this can be safely achieved without undue hypoglycemia.

3.3. Continuous Glucose Monitoring System (CGMS)

- We suggest that CGMS be used during pregnancy in women with overt or GDM when SMBG levels (or, in the case of the woman with overt diabetes, HbA_{1C} values) are not sufficient to assess glycemic control (including both hyperglycemia and hypoglycemia). (2 ⊕⊕OO)

4.0.
Nutrition Therapy And Weight Gain Targets For Women With Overt Or GDM

4.1. Nutrition Therapy

- We recommend MNT for all pregnant women with overt or GDM to help achieve and maintain desired glycemic control while providing essential nutrient requirements. (1⊕⊕OO)

4.2.Weight Management

- **a.** We suggest that women with overt or GDM follow the Institute of Medicine revised guidelines for weight gain during pregnancy (Table 4). (Ungraded recommendation)
- **b.** We suggest obese women with overt or GDM reduce their calorie intake by approximately one-third (compared with their usual intake before pregnancy) while maintaining a minimum intake of 1600-1800 kcal/d. (2QQOO)

Table 4. 2009 Institute of Medicine Recommendations for Total Weight Gain and Rate of Weight Gain During Pregnancy, by Prepregnancy BMI (129)

	Total Weight Gain		Rates of Weight Gain in Second and Third Trimester[a]	
Prepregnancy BMI	Range, kg	Range, lb	Mean (Range), kg/wk	Mean (Range), lb/wk
Underweight (<18.5 kg/m^2)	12.5–18	28–40	0.51 (0.44–0.58)	1 (1–1.3)
Normal weight (18.5–24.9 kg/m^2)	11.5–16	25–35	0.42 (0.35–0.50)	1 (0.8–1)
Overweight (25.0–29.9 kg/m^2)	7–11.5	15–25	0.28 (0.23–0.33)	0.6 (0.5–0.7)
Obese (≥30.0 kg/m^2)	5–9	11–20	0.22 (0.17–0.27)	0.5 (0.4–0.6)

[a] Calculations assume a 0.5- to 2-kg (1.1–4.4 lb) weight gain in the first trimester.

4.3. Carbohydrate Intake

- We suggest women with overt or GDM limit carbohydrate intake to 35-45% of total calories, distributed in
  - 3 small- to moderate-sized meals

    &
  - 2-4 snacks including an evening snack. (2QQOO)

4.4. Nutritional Supplements

- We recommend pregnant women with overt or GDM should follow the same guidelines for the intake of minerals and vitamins as for women without diabetes (1QQEE), with the exception of taking folic acid 5mg daily beginning 3 months before withdrawing contraceptive measures or otherwise trying to conceive.
  - We suggest that at 12 weeks gestation, the dose of folic acid be reduced to 0.4-1.0 mg/d, which should be continued until the completion of breastfeeding. (2QQOO)

5.0.
Blood Glucose Lowering Pharmacological Therapy During Pregnancy

5.1. Insulin Therapy-1
Basal Insulin Analogues

- **a.** We suggest that the insulin analog detemir may be initiated during pregnancy for those women who require basal insulin and for whom NPH insulin, in appropriate doses, has previously resulted in, or for whom it is thought NPH insulin may result in, problematic hypoglycemia.
  - Insulin detemir may be continued in those women with diabetes already successfully taking insulin detemir before pregnancy. (2QQQQ)

- **b.** We suggest that those pregnant women successfully using insulin glargine before pregnancy may continue it during pregnancy. (2QQOO)

5.1. Insulin Therapy-2
Prandial Insulins

- **c.** We suggest that insulin analogs lispro and **aspart** be used **in preference to regular** insulin in pregnant women with diabetes. (2QQQO)

- **d.** We recommend the ongoing use of CSII during pregnancy in women with diabetes when this has been initiated before pregnancy. (1QQQO)
  - but suggest that CSII not be initiated during pregnancy unless other insulin strategies including multiple daily doses of insulin have first been tried and proven unsuccessful. (2QQOO)

5.2. Noninsulin Anti-hyperglycemic Agent Therapy

- **a**. We suggest that **Glibenclamide** is a suitable alternative to insulin therapy for glycemic control in women with GDM who fail to achieve sufficient glycemic control after a 1-week trial of MNT and exercise, **except for:**
  - **a diagnosis of GDM before 25 weeks gestation**
  - **FPG levels 110 mg/dl**

  in which case insulin therapy is preferred. (2QQOO)

- **b**. We suggest that **metformin** therapy be used for glycemic control only for those women with GDM who do not have satisfactory glycemic control despite MNT and who **refuse or cannot use insulin or glyburide** and are **not in the 1st trimester**. (2QQOO)

- 14.13 Lifestyle behavior change is an essential component of management of gestational diabetes mellitus and may suffice for the treatment of many women. Insulin should be added if needed to achieve glycemic targets. A
- 14.14 Insulin is the preferred medication for treating hyperglycemia in gestational diabetes mellitus. Metformin and glyburide should not be used as first-line agents, as both cross the placenta to the fetus. A Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data.
- 14.15 Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester. A

- Women with type 1 or type 2 diabetes should be prescribed low-dose aspirin 100–150 mg/day starting at 12 to 16 weeks of gestation to lower the risk of preeclampsia. E A dosage of 162mg/day may be acceptable; currently in the U.S., low-dose aspirin is available in 81-mg tablets. A

6.0.
Labor, Delivery, Lactation, and Postpartum Care

6.1. Blood Glucose Targets During Labor and Delivery

- We suggest target blood glucose levels of 72-126 mg/dl during labor and delivery for pregnant women with overt or GDM. (2⊕⊕OO)

6.2. Lactation

- **a.** We recommend whenever possible women with overt or GDM should breastfeed their infant. (1 

- **b.** We recommend that breastfeeding women with overt diabetes successfully using metformin or glyburide therapy during pregnancy should continue to use these medications, when necessary, during breastfeeding. (1) 

6.3. Postpartum Contraception

- We recommend that the choice of a contraceptive method for a woman with overt diabetes or a history of GDM should not be influenced by virtue of having overt diabetes or a history of GDM. (1 ⊕⊕⊕)

6.4. Screening for Postpartum Thyroiditis

- We suggest that women with type 1 diabetes be screened for postpartum thyroiditis with a TSH at 3 and 6 months postpartum. (2 ⊕⊕◯◯)

Treatment of infertility in PCOS

Legro RS. Diagnosis and Treatment of PCOS: An Endocrine Society Clinical Practice Guideline. JCEM 2013; 98: 4565–92.

- The routine use of metformin during pregnancy in women with PCOS is unwarranted, although it may be useful to treat GDM [1].
  - A meta-analysis of RCTs demonstrated no effect of metformin on abortion rate *(OR: 0.89; $CI_{95\%}$: 0.59–1.75; P: 0.9)* [2].
  - A large RCT demonstrated no difference in the prevalence of pre-eclampsia, preterm delivery, or GDM in women with PCOS treated with metformin during pregnancy [3].
  - Metformin was associated with a significantly higher incidence of GI disturbance, but no serious maternal or fetal adverse effects [3,4].

1. Metformin vs. insulin for the treatment of GDM. ***NEJM* 2008**;358:2003–15.
2. Effect of preconceptional metformin on abortion risk in PCOS: a systematic review and meta-analysis of RCTs. ***Fertil Steril.* 2009**;92:1646–58.
3. Metformin vs. placebo from 1st trimester to delivery in PCOS: a randomized, controlled multicenter study. ***JCEM* 2010**;95:E448–55.
4. Insulin sensitising drugs for women with PCOS, oligo amenorrhoea and subfertility. ***Cochrane Database Syst Rev.* 2010**;1:CD003053.


Thanks for your attention