Gestational Diabetes Mellitus

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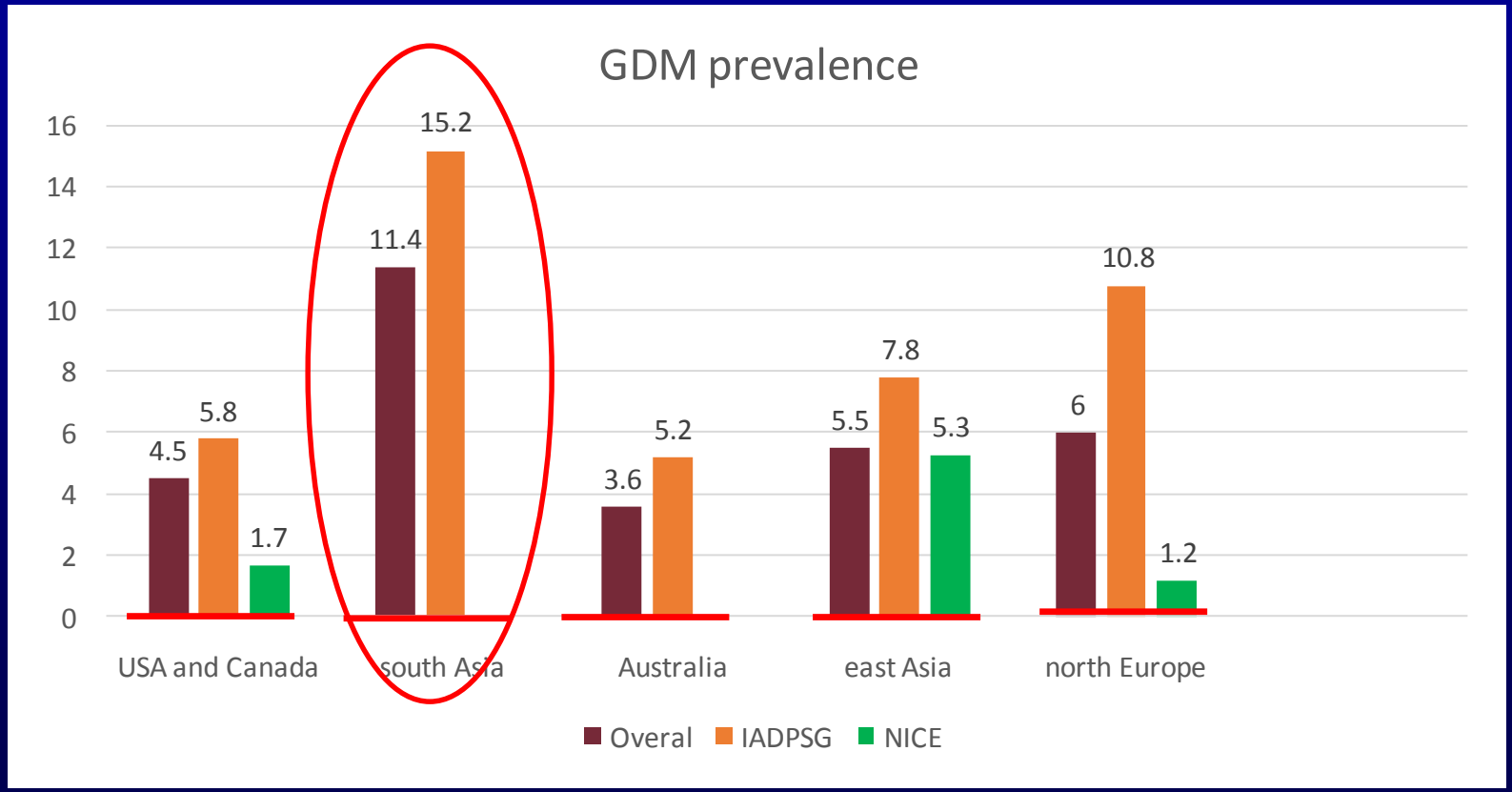
Prevalence of GDM

- Gestational diabetes mellitus (GDM), is one of the most common endocrinopathies during pregnancy which is defined as glucose intolerance, with onset or first recognition during pregnancy

- GDM affecting between 4% and 18% of pregnancies

Endocrinol Metab Clin, 2019

Worldwide prevalence of GDM: Meta-analysis of population based studies



Endocrinol Metab Clin, 2019

Prevalence of GDM in Iran

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Iran J Public Health. 2015 Aug; 44(8): 1036–1044.

PMCID: PMC4645723
PMID: 26587467

Prevalence and Risk Factors of Gestational Diabetes in Iran: A Systematic Review and Meta-Analysis

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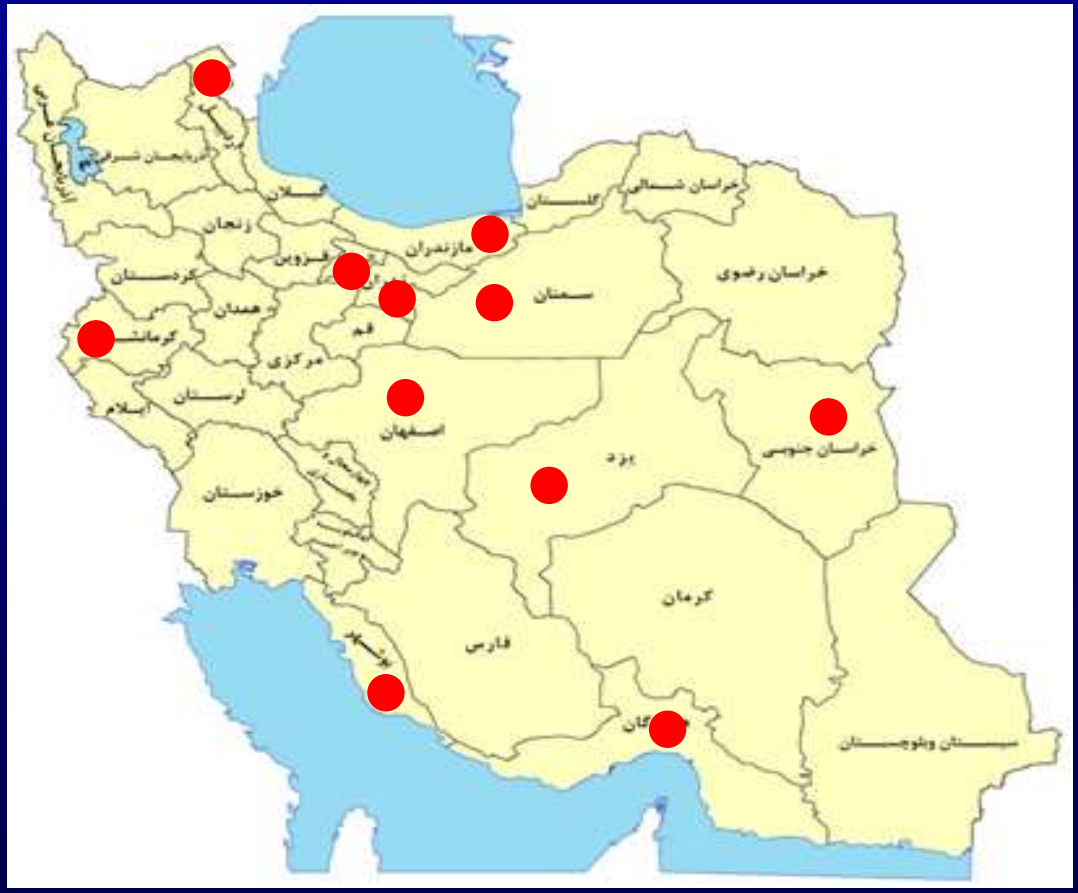
Prevalence of GDM in Iran



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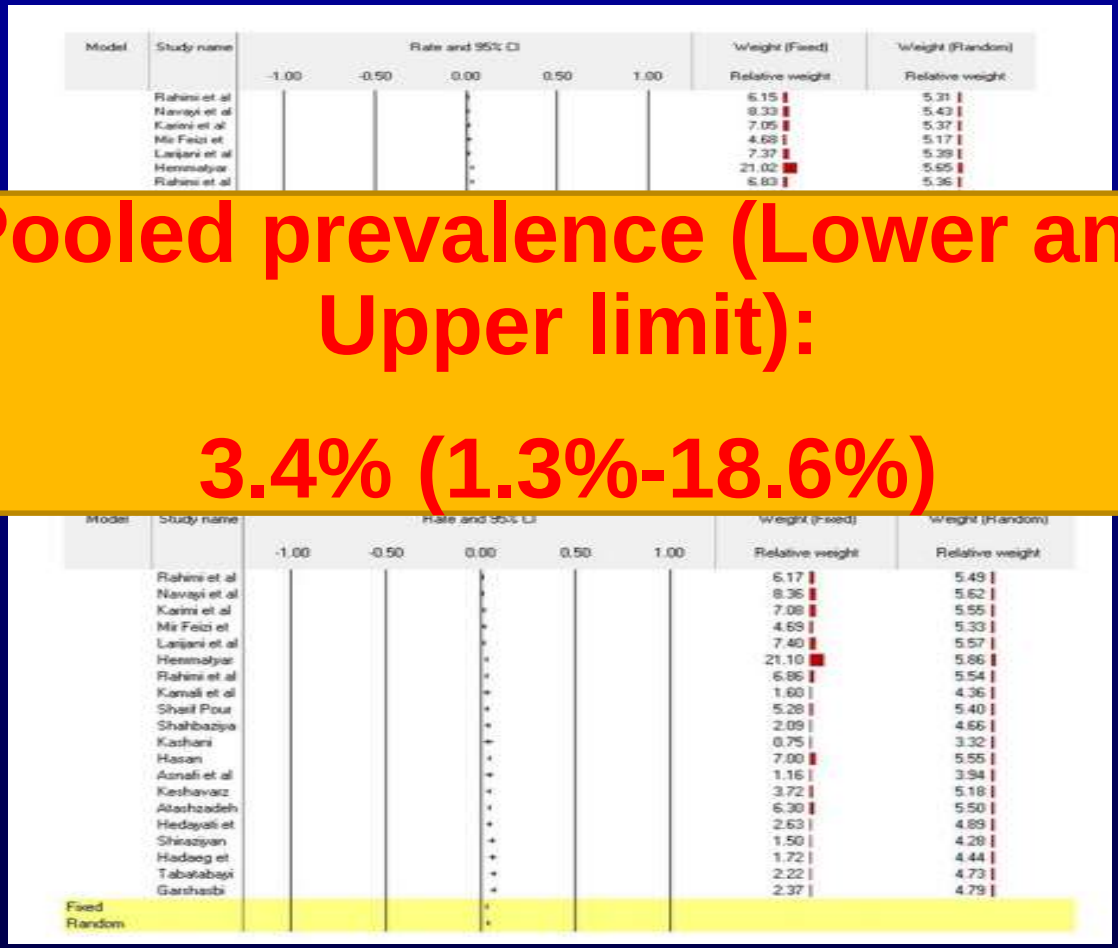
Prevalence of GDM in Iran



Pooled prevalence (Lower and Upper limit):

3.4% (1.3%-18.6%)

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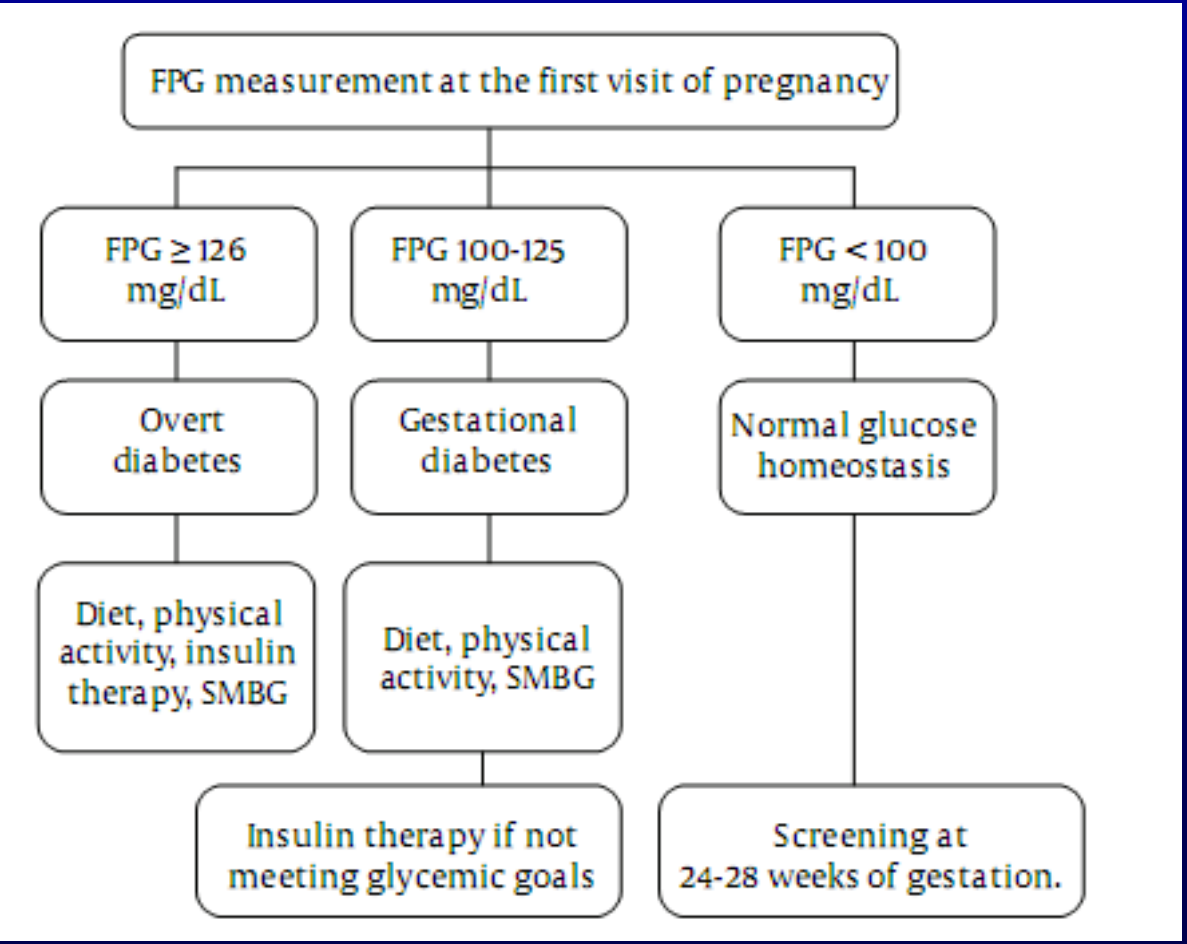
GDM Diagnosis



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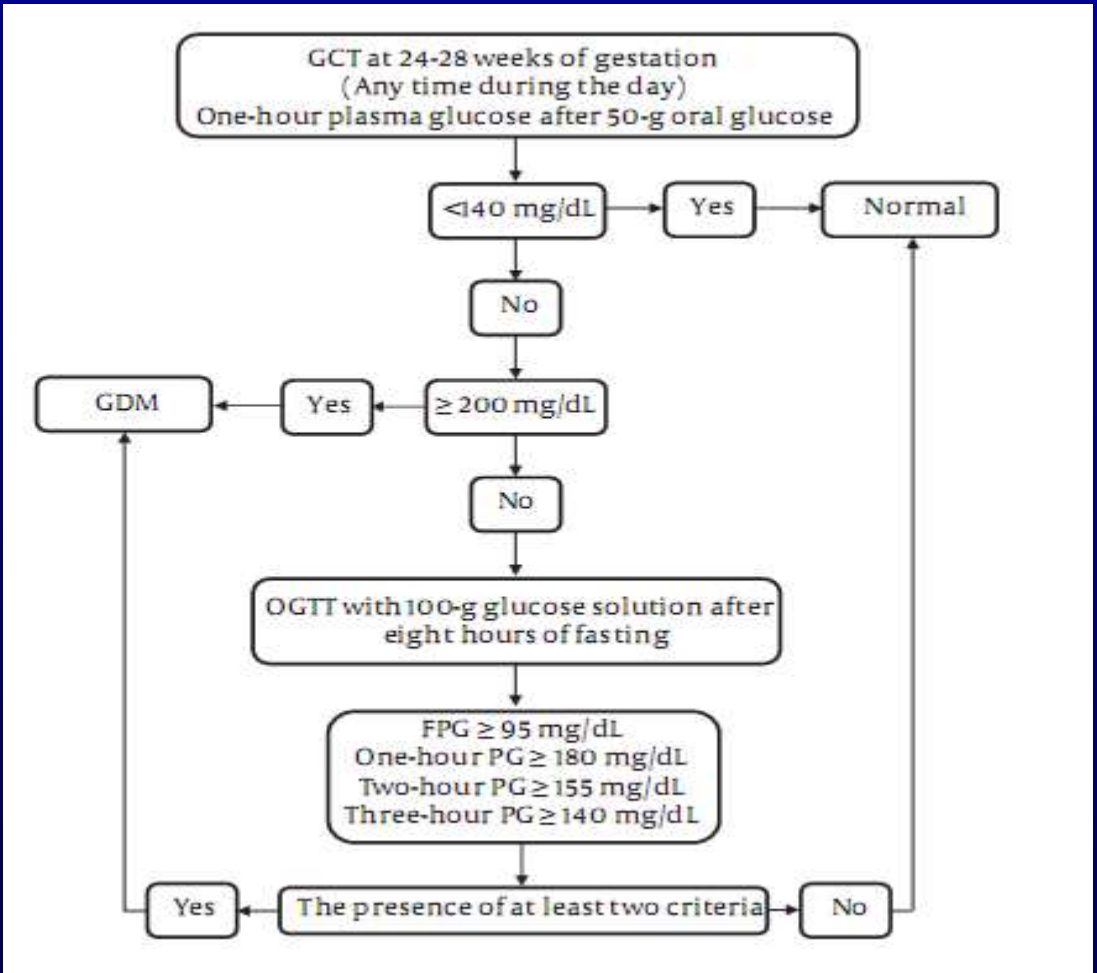
GDM Diagnosis



Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of GDM, 2021

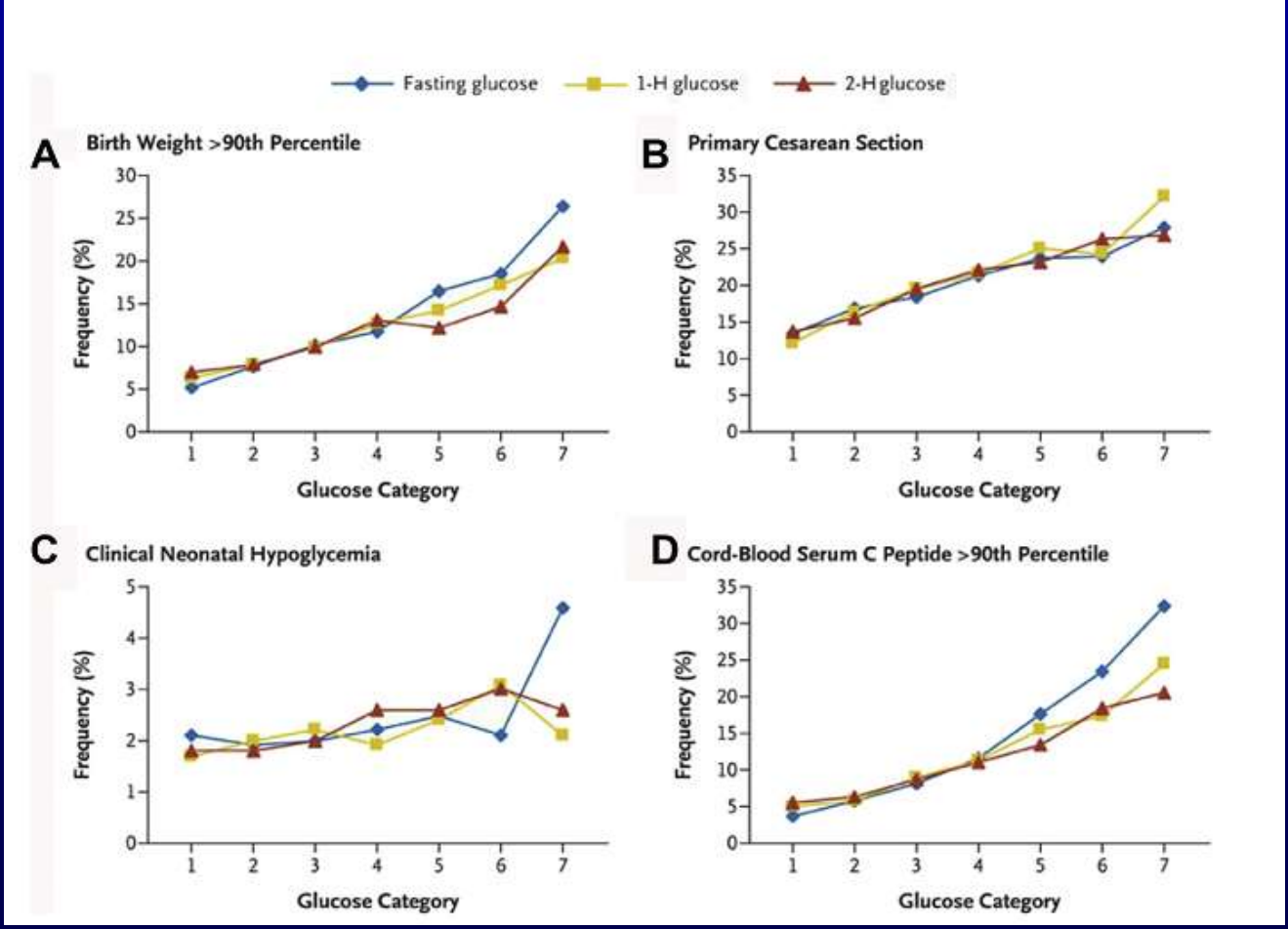
GDM Diagnosis

Table 3
Diagnosis of gestational diabetes

Glucose Value, mg/dL	100 g Oral Glucose Load[a]			75 g Oral Glucose Load
	O'Sullivan-Mahan[1] Whole Blood[b]	NDDG[4] Plasma-Autoanalyzer[c]	Carpenter-Coustan[14] Plasma-Glucose Oxidase[d]	IADPSG[15] Plasma Enzymatic[e]
Fasting	90	105	95	92
1-h	165	190	180	180
2-h	145	165	155	153
3-h	125	145	140	NA

2016 European Society of Endocrinology

Frequency of primary outcomes across the glucose categories



Endocrinol Metab Clin, 2019

Frequency of primary outcomes across the glucose categories

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)

Endocrinol Metab Clin, 2019

Paradigm Shifts in the Management of Diabetes in Pregnancy

- 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”)

- The management of women with type 2 diabetes in pregnancy is often complicated by severe insulin resistance

- The proposition that GDM is heterogenous (including early vs. late) is important , as it may suggest different GDM preventive and treatment strategies for different types of GDM

Diabetes Care 2021

Paradigm Shifts in the Management of Diabetes in 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 later in pregnancy

- Most importantly, a meta-analysis of 13 cohort studies showed that perinatal mortality (relative risk 3.58 [95% CI 1.91–6 .7 1]), neonatal hypoglycemia (RR 1.6), and insulin use (RR 1.7) were greater among women with early GDM compared with those with GDM diagnosed later inthe pregnancy

Diabetes Care 2021

Paradigm Shifts in the Management of Diabetes in Pregnancy

- Screening for undiagnosed diabetes early in pregnancy also identifies women with hyperglycemia less than overt diabetes, yet at increased risk of adverse pregnancy outcomes

- Such women are more insulin resistant—with higher blood pressure, triglycerides, perinatal mortality, and neonatal hypoglycemia with a greater need for insulin treatment—than those with GDM diagnosed at 24 –28 weeks ’ gestation

Diabetes Care 2021

Glycemic Targets

Preprandial blood glucose	95 mg/dl or less
1 h after the start of a meal	140 mg/dl or less
2 h after the start of a meal	120 mg/dl or less

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Self-monitoring of blood glucose

- It is recommend in all pregnant women with gestational or overt diabetes
- It is suggested to test before and either 1 or 2 h after the each meal
- It may be needed at bedtime and during the night as indicated
- if not possible, at least 4 - 8 times a week, after achieving the goals of therapy

Journal of Clinical Endocrinology and Metabolism 2014

CGM in Pregnancy

- There is a mild improvement in A1C without an increase in hypoglycemia and reductions in large-for-gestational-age in pregnant women with DM1
- TIR(63-140) should be at least 70% in DM1 and pregnancy
- There are no data to support the use of TIR in women with type 2 DM or GDM
- Continuous glucose monitoring may be used when SMBG levels are not sufficient to assess glycemic control

ADA, 2021

HbA1C in Pregnancy

- At present, the measurement of HbA1c is not recommended for the diagnosis of GDM

- HbA1c may be helpful for glucose monitoring in pregnancy as the second measure after SMBG (Weak recommendation, low-quality evidence)

ADA, 2021

HbA1C in Pregnancy

- In a normal pregnancy, theHbA1c level is lower because of increased red blood cell turnover
- It is suggested to maintain HbA1c in pregnancy < 6% if it can be achieved without significant hypoglycemia
- It should be noted that most data on this subject are related to pregnant women with pregestational diabetes

ADA, 2021

Management of GDM

General Principles for Management of Diabetes in Pregnancy

- Potentially teratogenic medications (ACE inhibitors, statins, etc.) should be avoided in sexually active women of childbearing age who are not using reliable contraception. **B**
- Fasting, preprandial, and postprandial self-monitoring of blood glucose are recommended in both gestational diabetes mellitus and pregestational diabetes in pregnancy to achieve glycemic control. **B**
- Due to increased red blood cell turnover, A1C is lower in normal pregnancy than in normal nonpregnant women. The A1C target in pregnancy is 6–6.5% (42–48 mmol/mol); <6% (42 mmol/mol) may be optimal if this can be achieved without significant hypoglycemia, but the target may be relaxed to <7% (53 mmol/mol) if necessary to prevent hypoglycemia. **B**

ADA, 2021

Non Medical Management

Nutrition therapy is recommend for all pregnant women

Carbohydrate controlled meal plan

- appropriate weight gain
- normoglycemia
- adequate nutrition
- absence of ketosis

Optimal Total Weight Gain in GDM

Prepregnancy BMI	Total Weight Gain (kg)
less than 18.5	12.5-18
18.5 - 24.9	11.5-16
25 – 29.9	7-11.5
more than 30	5-9

Journal of Clinical Endocrinology and Metabolism 2014

Non Medical Management

- Reducing calorie intake by approximately one-third
- maintaining a minimum intake of 1600 to 1800 kcal/d
- Moderate energy restriction (1600 –1800 kcal/d) improves mean glycemia and fasting insulinemia without inhibiting fetal growth

Journal of Clinical Endocrinology and Metabolism 2014

Non Medical Management

- It is recommended to receive 20% of calorie intake from proteins, 50% from carbohydrates, and 30% from fat with a proper distribution

- Total carbohydrate intake should be divided into three main courses and three snacks

Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of GDM, 2021

Non Medical Management

- Individuals under insulin therapy should receive15% carbohydrate in the morning, 10 -15% in the first snack, 20 - 25% in the lunch meal, 10 -15% in the second snack, 20 - 25% in the dinner meal, and 15% in the dinner snack

- Individuals who are managed without insulin therapy should receive 15% in the morning, 10 -15% in the first snack, 20-25% in the lunch meal, 10-15% CHO in the second snack, 20 - 25% in the dinner meal, and 10% in the dinner snack

Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of GDM, 2021

Non Medical Management

- For each 1000 calorie intake, 14 g of fiber should be received, including five units from vegetables, four units from fruits, and one unit from cereals

- Simple sugars can account for up to 10% of calorie intake; however, it is more favorable to limit the intake of simple sugars to 5% of calorie intake

Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of GDM, 2021

Non Medical Management

- Moderate physical activity is recommended for all pregnant women with GDM, and there are no exercise restrictions for controlling blood glucose

- Although aerobic training is more favorable, endurance training may be also helpful. Moderate-intensity training is recommended for at least 30 minutes daily, four to five days a week

- Women without physical fitness should start physical activity at low intensity (15 minutes daily) and gradually increase the duration of training

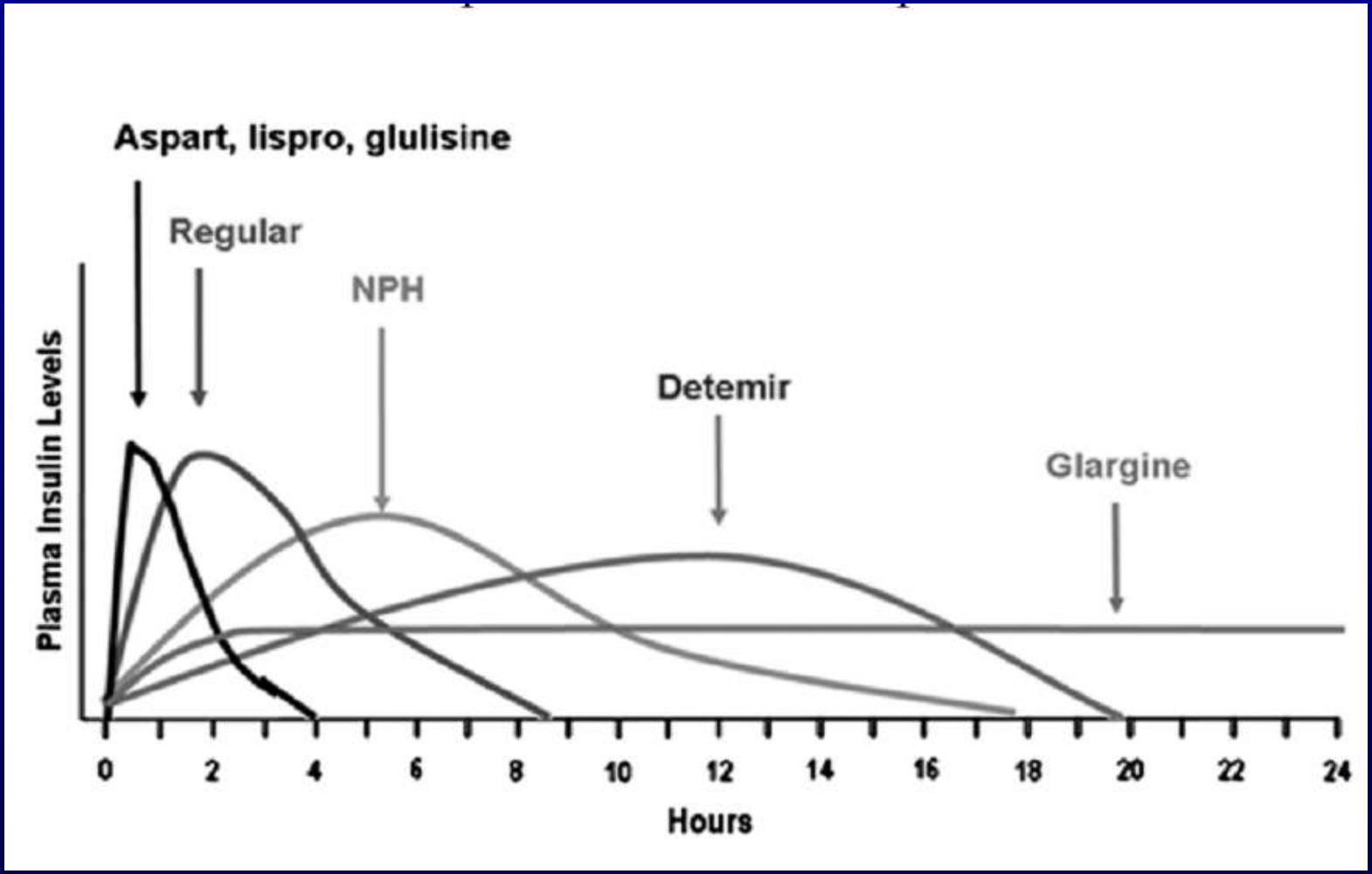
Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of GDM, 2021

Pharmacologic Profiles of Insulins and Insulin Analogues

	Onset of Action	Peak Action	Duration of Action (h)
Standard			
Regular	30-60 min	2-3 h	8-10
Neutral protamine hagedorn	2-4 h	4-10 h	12-18
Rapid-acting analogues			
Lispro	5-15 min	30-90 min	4-6
Aspart	5-15 min	30-90 min	4-6
Glulisine	5-15 min	30-90 min	4-6
Long-acting analogues			
Glargine	2-4 h	None	20-24
Detemir	3-4 h	None	20

Journal of Clinical Endocrinology and Metabolism 2014

Pharmacologic Profiles of Insulins and Insulin Analogues



2016 European Society of Endocrinology

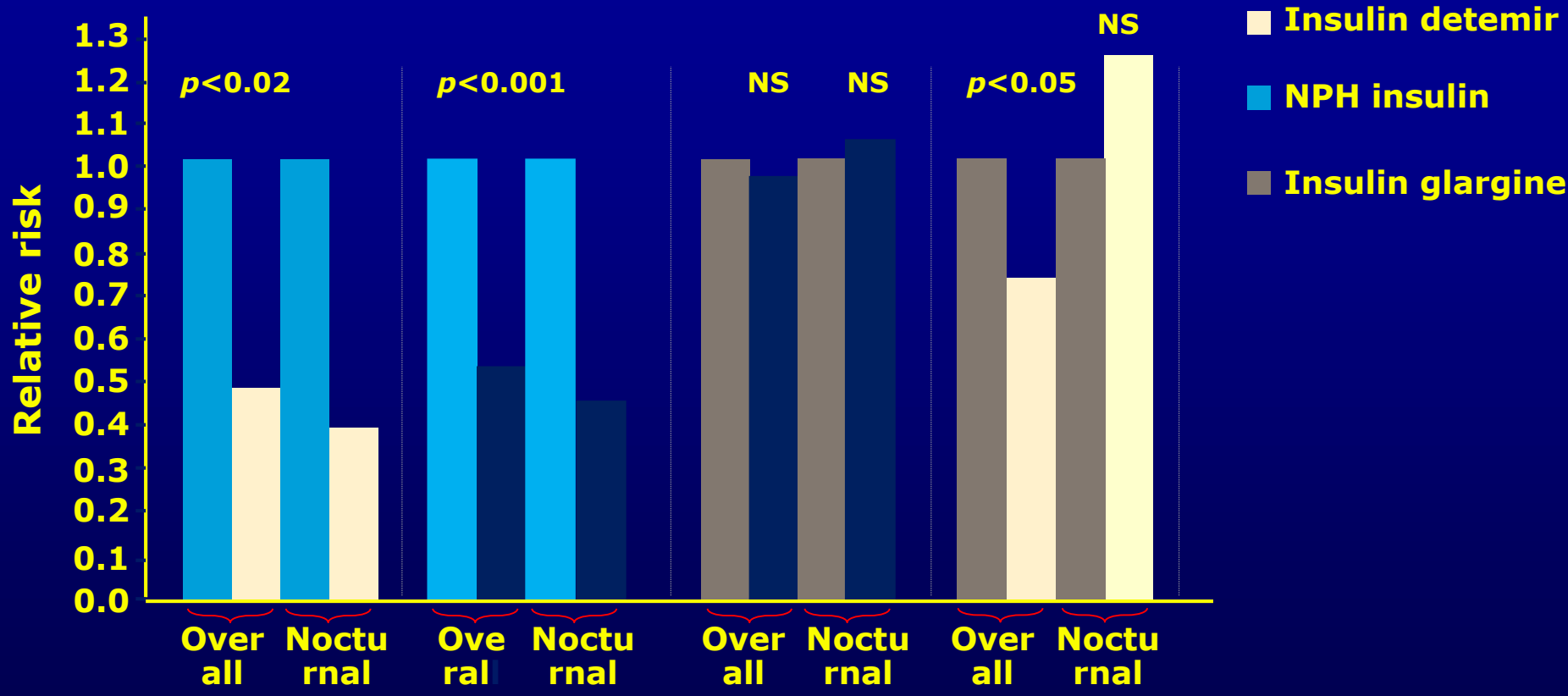
Pharmacological therapy : Insulin

Basal insulin
- glargine
- NPH
- detemir

Rapid-acting insulin
- aspart
- lispro

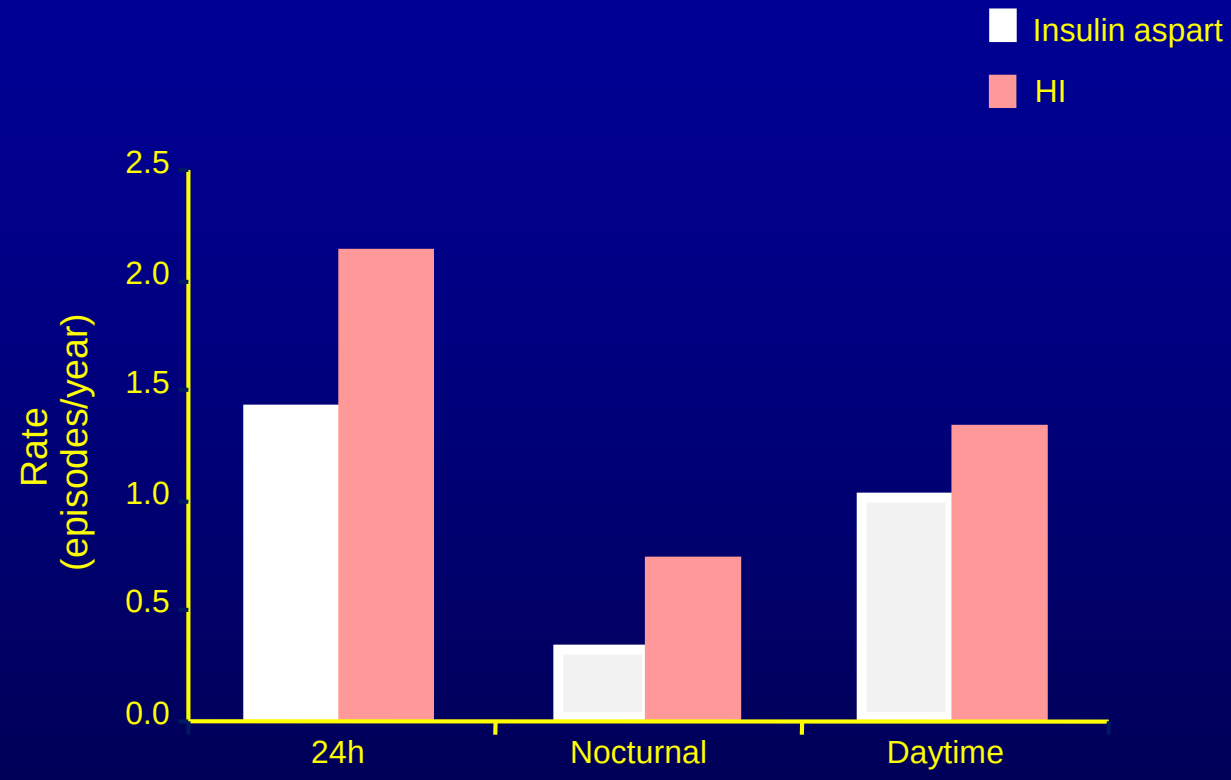
Type 2 diabetes: basal–oral – hypoglycaemia

Significantly less hypoglycaemia compared with NPH insulin



Based on biochemically confirmed events: plasma glucose <3.1 mmol/L
NPH, neutral protamine Hagedorn; NS, not significant

Major hypoglycaemic episodes during pregnancy



Of 322 pregnant subjects, 73 subjects experienced 287 major hypoglycaemic episodes

HI, human insulin

Mathiesen *et al. Diabetes Care* 2007;30:771–6

Insulin aspart versus HI

In pregnant women, insulin aspart compared with human insulin showed:

- Better postprandial control
- Better overall treatment satisfaction
- Trend towards lower risk of overall major hypoglycaemia
- Similar pregnancy outcomes (foetal loss, congenital malformations)
- Trend towards fewer foetal losses and pre-term deliveries
- Higher peak concentrations

Pharmacological therapy : Insulin

If more than 20% of postprandial values are > target

↓

Initiate 4-8 unit of rapid acting before that meal

If more than 10% of fasting values are > target

↓

Initiate 6-8 unit of NPH or detemir

Pharmacological therapy : Oral agents

- Prescription of oral antidiabetic agents is not recommended during the first trimester of pregnancy
- Oral anti-diabetic agents, especially metformin, can be used after 24 weeks of gestation in women with FPG 110 mg/dL (Weak recommendation, moderate-quality evidence).
- Metformin is suggested for women with mild GDM (FPG < 110 mg/dL), unwilling to use insulin
- However, 30% of these women need to shift to insulin in the next weeks of gestation

Pharmacological therapy : Oral agents

- Glibenclamide (glyburide) should be considered as the last option due to the possible increase in neonatal hypoglycemia, overweight, and macrosomia

- As mentioned earlier, therapy with oral antidiabetic drugs is not recommended during early pregnancy

- Nevertheless, if a pregnant woman is treated with metformin due to other reasons before pregnancy, therapy with metformin can be continued

Pharmacological therapy : Oral agents

Glibenclamide

may be suitable after 25w and FPG less than 110

Metformin

may be considered but not in the first trimester

Other oral agents are not recommended

Metformin

Potential Benefits

- less weight gain
- lower postprandial glucose
- less pregnancy induced HTN
- less sever neonatal hypoglycemia

Potential Harms

- More spontaneous preterm delivery
- GI adverse effects

Metformin

- No short term adverse fetal outcomes, including fetal malformations have been described in GDM

- However, the long term effects of metformin on offspring remains uncertain

GDM and use of glucocorticoids

- In pregnant women under insulin therapy, who require glucocorticoids for fetal lung maturation, the insulin dose should be increased accordingly. In these cases, hospitalization and blood glucose monitoring are highly recommended (Strong recommendation, low-quality evidence)

- In women with GDM and acceptable glycemic control without insulin therapy, warning about the risk of hyperglycemia and closer monitoring of blood glucose is advisable if glucocorticoid would be prescribed

Endocrinol Metab Clin, 2019

Postpartum Follow-up

- Gestational diabetes mellitus usually resolves after delivery, as hormones secreted from the placenta, as the main source of insulin resistance, are removed from the body

- Therefore, the need for drug therapy mostly resolves after delivery although these patients are at risk of type 2 diabetes, which may occur in 50% of women in the next 20 years

- Women who develop GDM at younger gestational ages or those who require a higher insulin dosage are at a higher risk of type 2 diabetes. Therefore, pregnant women with GDM should be followed up after delivery

ADA, 2021

Postpartum Follow-up

- The OGTT is recommended over A1C at the 4 to 12 week postpartum visit because A1C may be persistently impacted (lowered) by the increased red blood cell turn over related to pregnancy or blood loss at delivery

- In women with normal OGTT after delivery, the annual measurement of FPG is recommended

- For all prediabetic women diagnosed after delivery, lifestyle modifications (exercise and diet), with or without metformin therapy, are recommended

ADA, 2021