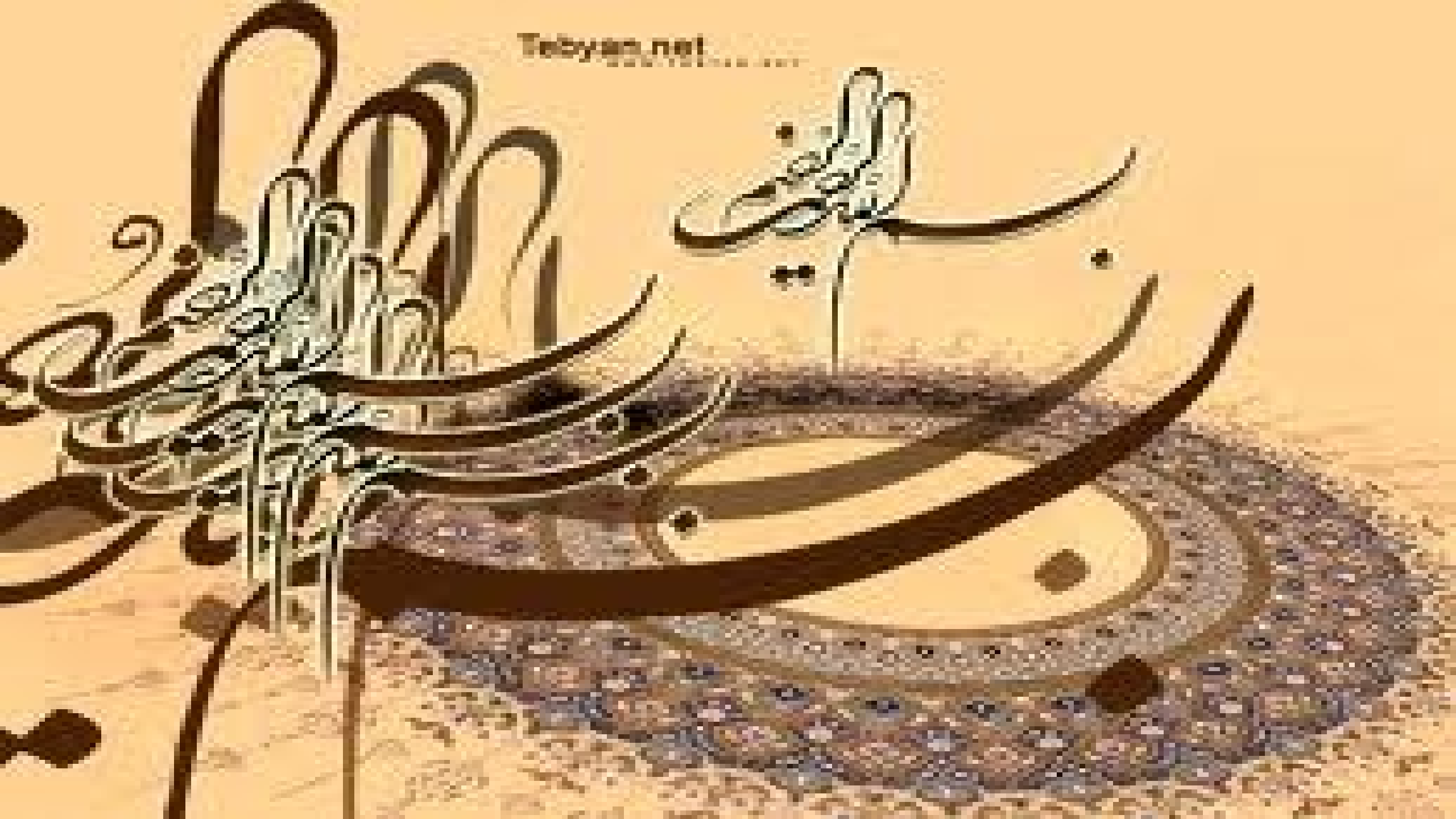

Hyperglycemia management in pregnancy

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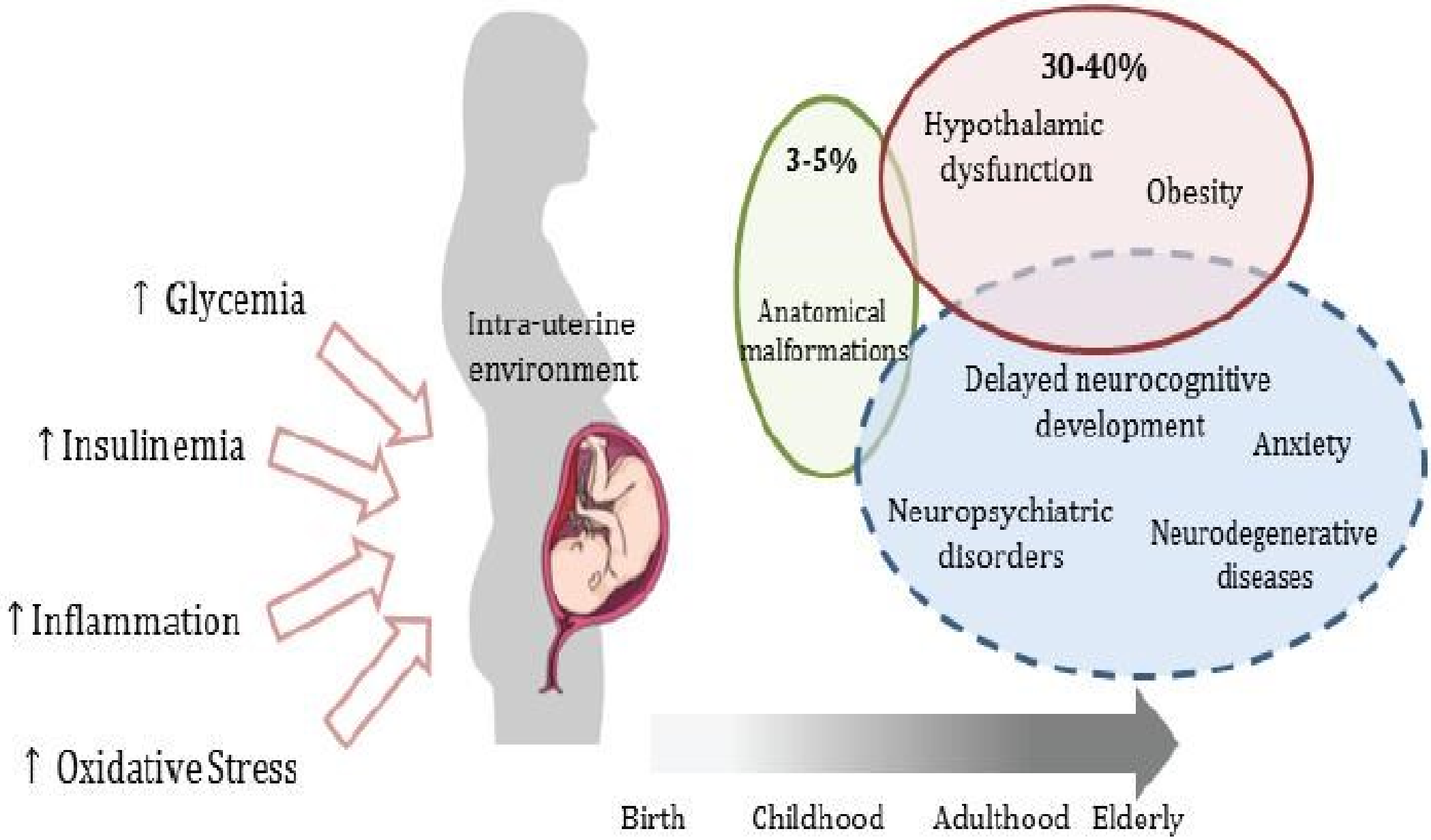
1402

Common problem in GDM

- **Definition**
- **Who should be screened in early pregnancy**
- **What is goal of therapy in each trimester**
- **Oral agent benefit or harm**
- **When to deliver**


↑ Glycemia
↑ Insulinemia
↑ Inflammation
↑ Oxidative Stress
Intra-uterine environment
30-40%
Hypothalamic dysfunction
Obesity
3-5%
Anatomical malformations
Delayed neurocognitive development
Anxiety
Neuropsychiatric disorders
Neurodegenerative diseases
Birth
Childhood
Adulthood
Elderly

Preventive Care in Nursing and Midwifery Journal
2023; 13(1): 35-49

Prevalence of Gestational Diabetes in Iran: A Systematic Review and Meta-analysis

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Abstract

Background: Gestational diabetes mellitus (GDM) is the most common complication of pregnancy and an important public health concern. Several studies have investigated the prevalence of gestational diabetes in different parts of Iran with different results.

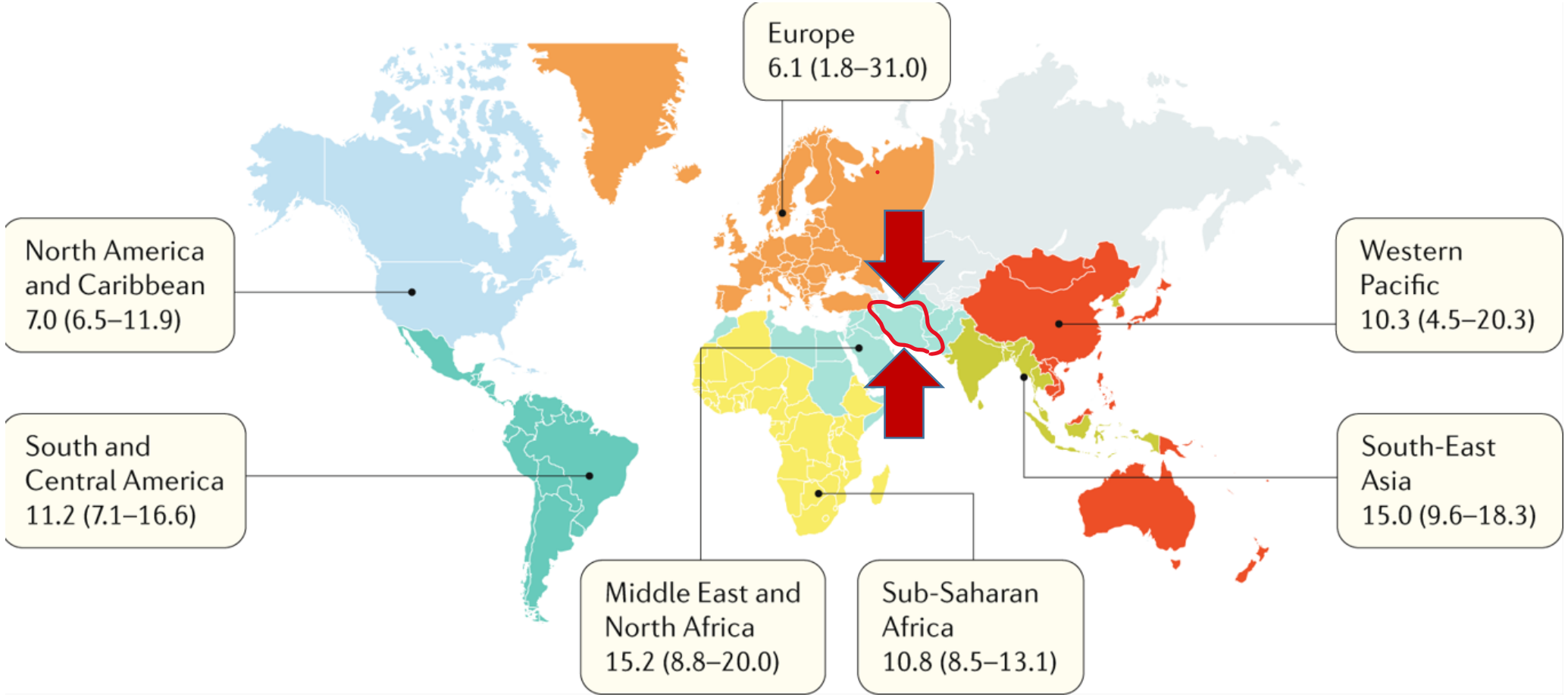
Objectives: The present study aimed to review studies on gestational diabetes prevalence and estimate the prevalence of gestational diabetes in Iran.

Methods: A search on gestational diabetes mellitus and related synonyms was conducted using global and national databases, including PubMed, Science Direct, Scopus, Web of Sciences, Google Scholar, SID, IranMedex, Magiran, Irandoc, Medlib. Moreover, gray literature and reference checks and a library search were conducted. Keywords included: prevalence, Iran, gestational diabetes mellitus (GDM), and their synonyms. The inclusion criteria were observational studies (cross-sectional, prospective cohorts, and retrospective cohorts) published in Persian or English between 2000 and 2020 on the prevalence or incidence of gestational diabetes in Iran, a sample size of more than 100 people, and availably of full texts. The selected articles were thoroughly reviewed, and after quality assessment, the required information was extracted and included in the meta-analysis.

Results: From 907 articles, 48 were included in the meta-analysis according to the inclusion criteria, which included 51,259 patients with an average age (standard deviation) of 27.05 years (1.83). The overall prevalence of GDM in Iran was 10% (11,9: 95% confidence interval). The prevalence of GDM had increased in recent years, from 4% before 2005 to 16% in 2016 to 2020 (20,12: 95% CI). There was significant heterogeneity between studies, and the I-square index was 98%.

Conclusion: The prevalence of gestational diabetes in Iran is slowly increasing. The increasing prevalence of gestational diabetes can seriously threaten the health of mothers, fetuses, and newborns in the near future.

Keywords: *prevalence, gestational diabetes, meta-analysis, Iran*


Europe
6.1 (1.8–31.0)
North America and Caribbean
7.0 (6.5–11.9)
Western Pacific
10.3 (4.5–20.3)
South and Central America
11.2 (7.1–16.6)
South-East Asia
15.0 (9.6–18.3)
Middle East and North Africa
15.2 (8.8–20.0)
Sub-Saharan Africa
10.8 (8.5–13.1)

Diabetes in Pregnancy: 2 Categories

Pregestational diabetes	Gestational diabetes
Pregnancy in pre-existing diabetes • Type 1 diabetes • Type 2 diabetes	Diabetes diagnosed in pregnancy

In contrast to patients with pregestational diabetes, patients with true GDM are not at increased risk of congenital anomalies in offspring because the onset of the disorder is after the major period of organogenesis. Similarly, they should not experience diabetes-related vasculopathy because of the short duration of the disorder

NEW TERMINOLOGY AND DIAGNOSTIC CRITERIA :

- The term "***gestational diabetes***" has been used to define women with onset or first recognition of abnormal glucose tolerance during pregnancy

- GDM is diabetes that is first diagnosed in the ***second or third trimester*** of pregnancy that is not clearly either preexisting type 1 or type 2 diabetes

Classification and Diagnosis of Diabetes:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;46(Suppl. 1):S19-S40

Mother

Pregnancy

↑ Pre-eclampsia

Labor

↑ Induction of labor
↑ Cesarean section
↑ Operative deliveries
↑ Labor complications

Postpartum and beyond

↑ Recurrent GDM
↑ Type 2 diabetes

Offspring

Congenital

– CNS
– Cardiac
Fetal programming
– ↑ LGA
– ↑ Macrosomia
– Increased fat mass

Neonatal complications

Prematurity
Perinatal asphyxia
Respiratory distress
Metabolic complications (hypoglycemia and hypocalcemia)
Polycythemia and hyperviscosity
Low iron stores
Hyperbilirubinemia
Cardiomyopathy

Long-term outcome

↑ Obesity
↑ Type 1 diabetes
↑ Type 2 diabetes
↑ Metabolic syndrome

Who Should be Screened Early?

- 2.26a In individuals who are planning pregnancy, screen those with risk factors B and consider testing all individuals of childbearing potential for undiagnosed diabetes. E

- 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

Classification and Diagnosis of Diabetes:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;46(Suppl. 1):S19-S40

Gestational Diabetes Mellitus (continued)

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 pregnancy. A

Classification and Diagnosis of Diabetes:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;46(Suppl. 1):S19-S40

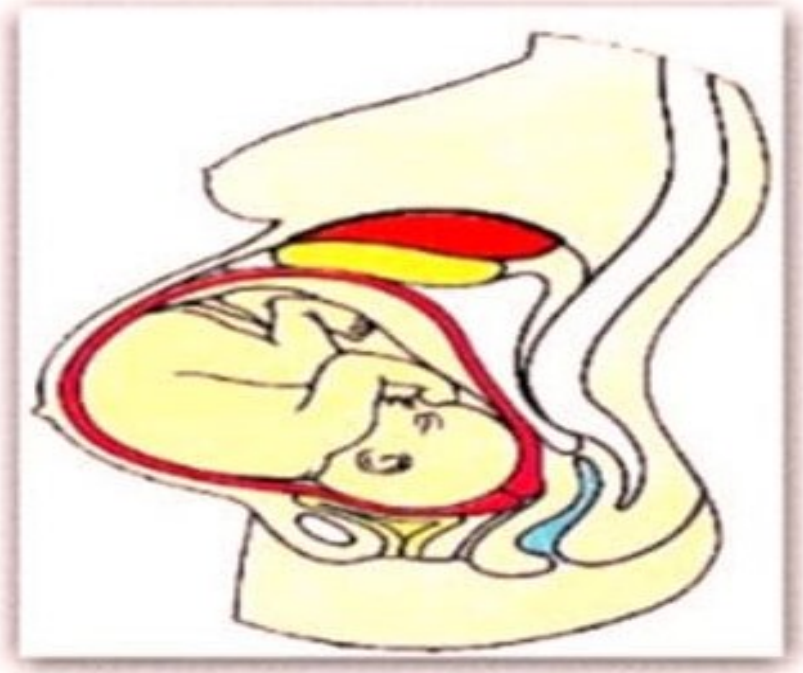
Table 2.3—Criteria for screening for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in adults with overweight or obesity (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian American individuals) who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Individuals with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. People with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. People who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other people, testing should begin at age 35 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
6. People with HIV

CVD, cardiovascular disease; GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Classification and Diagnosis of Diabetes:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;46(Suppl. 1):S19-S40

Gestational diabetes



Gestational Diabetes Mellitus, GDM) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy.

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).

This one-step strategy was anticipated to significantly increase the incidence of GDM (from5–6% to15–20%), primarily because only one abnormal value not two , became sufficient to make the diagnosis(233).

Classification and Diagnosis of Diabetes:
Standards of Care in Diabetes - 2023. Diabetes Care 2023;46(Suppl. 1):S19-S40

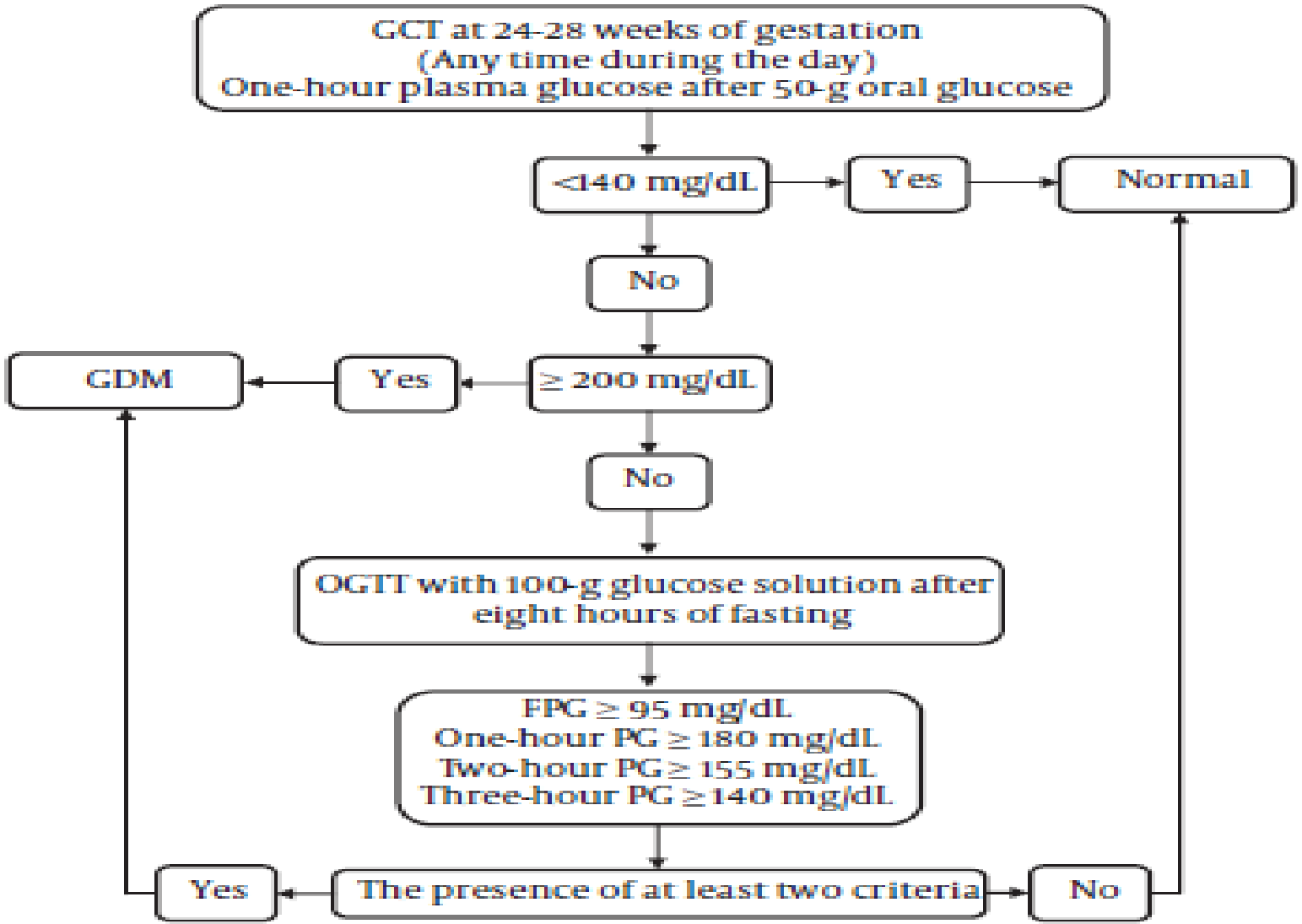


Figure 2. The two-step approach for GDM screening at 24 - 28 weeks of gestation. Abbreviations: GCT, Glucose Challenge Test; OGTT, Oral Glucose Tolerance Test; FPG, Fasting Plasma Glucose; GDM, Gestational Diabetes Mellitus.

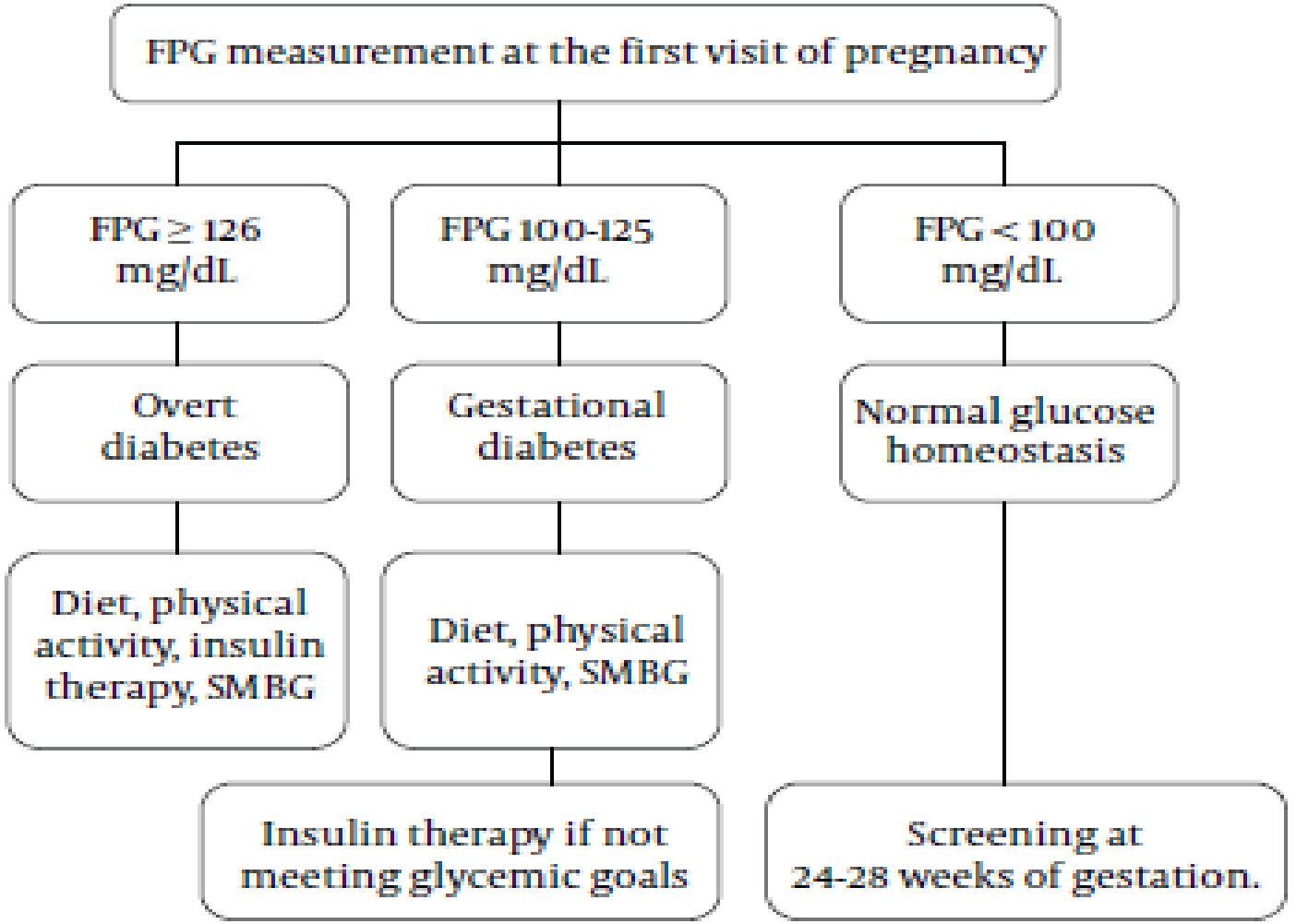


Figure 1. Algorithm for the screening of diabetes at the first visit of pregnancy. Abbreviations: FPG, fasting plasma glucose; SMBG, self-monitoring of blood glucose.

Iranian Endocrine Society Guidelines for Screening, Diagnosis , and Management of Gestational Diabetes Mellitus, Int J Endocrinol Metab. 2021 January; 19(1):e107906.

Do you recommend Repeated GTT?

- **We don’t recommended repeated GTT routinely unless:**
- Macrosomia
- Polyhydramnios
- Fetal waist circumference>90%
- In these patients we prefer one step GTT

Iranian Endocrine Society Guidelines for Screening, Diagnosis , and Management of Gestational Diabetes Mellitus, Int J Endocrinol Metab. 2021 January; 19(1):e107906.

Diabetes
.co.in

HOW TO CONTROL AND MANAGE

GESTATIONAL DIABETES

EXERCISE

DIABETIC DIET

CLASSIFICATION/TERMINOLOGY

- Patients with GDM are classified into two groups , which have been associated with pregnancy risk and thus guide obstetric management:
- ●A1: glycemic control achieved **without** medication
- ●A2: glycemic control achieved **with** medication

NUTRITIONAL THERAPY

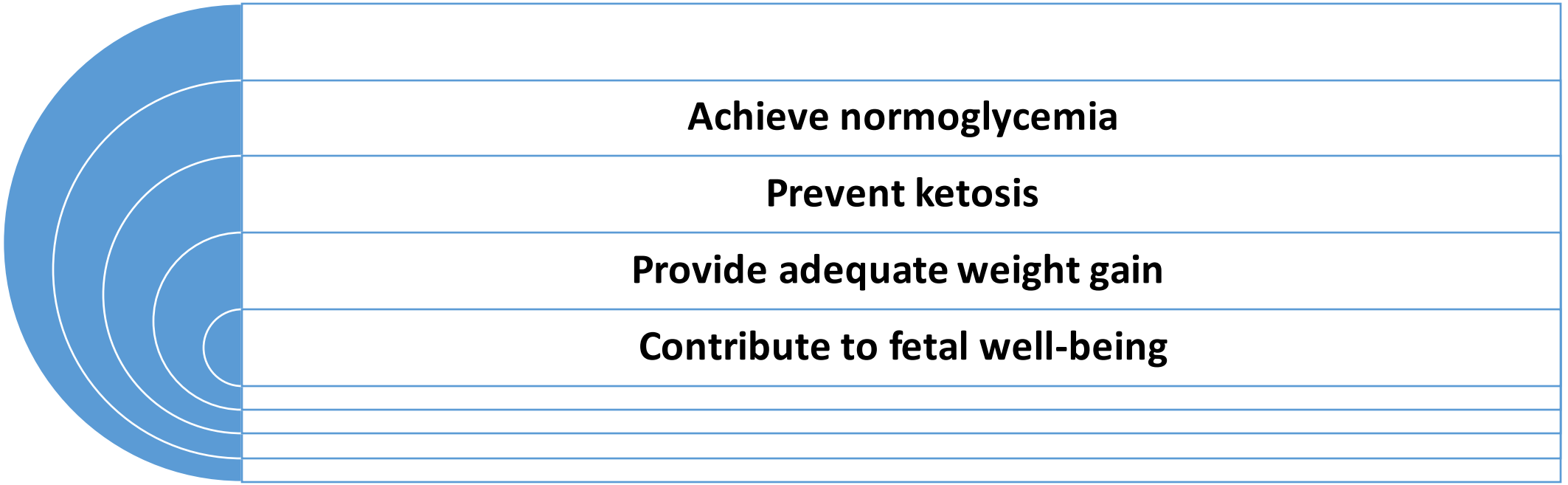
Diet and Exercise

- Nutritional assessment and plan
  - Counseling by registered dietician/nutritional team if available
  - ***Recommend complex carbohydrates, 3 meals and 2 snacks to limit glucose fluctuations***
    - **Ideal caloric distribution between carbohydrates, fat and protein not yet known**
- 30 minutes of moderate-intensity aerobic exercise at least 5 days a week or minimum 150 minutes per week
  - Improvement seen with walking 10 to 15 minutes after each meal

- **The recommended dietary reference intake for all pregnant people :**
- **Minimum of 175 g of carbohydrate, or 35% of a 2,000-calorie diet**
- **Minimum of 71 g of protein**
- **Liberalizing higher quality, nutrient-dense carbohydrates results in controlled fasting/postprandial glucose, lower free fatty acids, improved insulin action, and vascular benefits and may reduce excess infant adiposity**
- **28 g of fiber**

Standards of Care in Diabetes - 2023. Diabetes Care 2023;46(Suppl. 1):S19-S40

The goals of medical nutritional therapy are to:



Most patients (up to 85 percent) with GDM based on Carpenter and Coustan criteria can achieve target glucose levels with lifestyle modification alone

- **Receive nutrition counseling**
  - Moderate carbohydrate restriction: 3 meals + 3 snacks
  - Targets not met within 2 weeks→ start insulin
  - Avoid hypocaloric diet → weight loss + ketosis

For individuals with a pre pregnancy BMI in the healthy range, caloric requirements in the first trimester are the same as before pregnancy and generally increase by 340 calories per day in the second trimester and 452 calories per day in the third trimester

Glycemic Targets in Pregnancy

14.8 Due to increased red blood cell turnover, A1C is slightly lower in normal pregnancy than in normal nonpregnant women. Ideally, the A1C target in pregnancy is <6% (42 mmol/mol) if this can be achieved without significant hypoglycemia, but the target may be relaxed to <7% (53mmol/mol) if necessary to prevent hypoglycemia. B

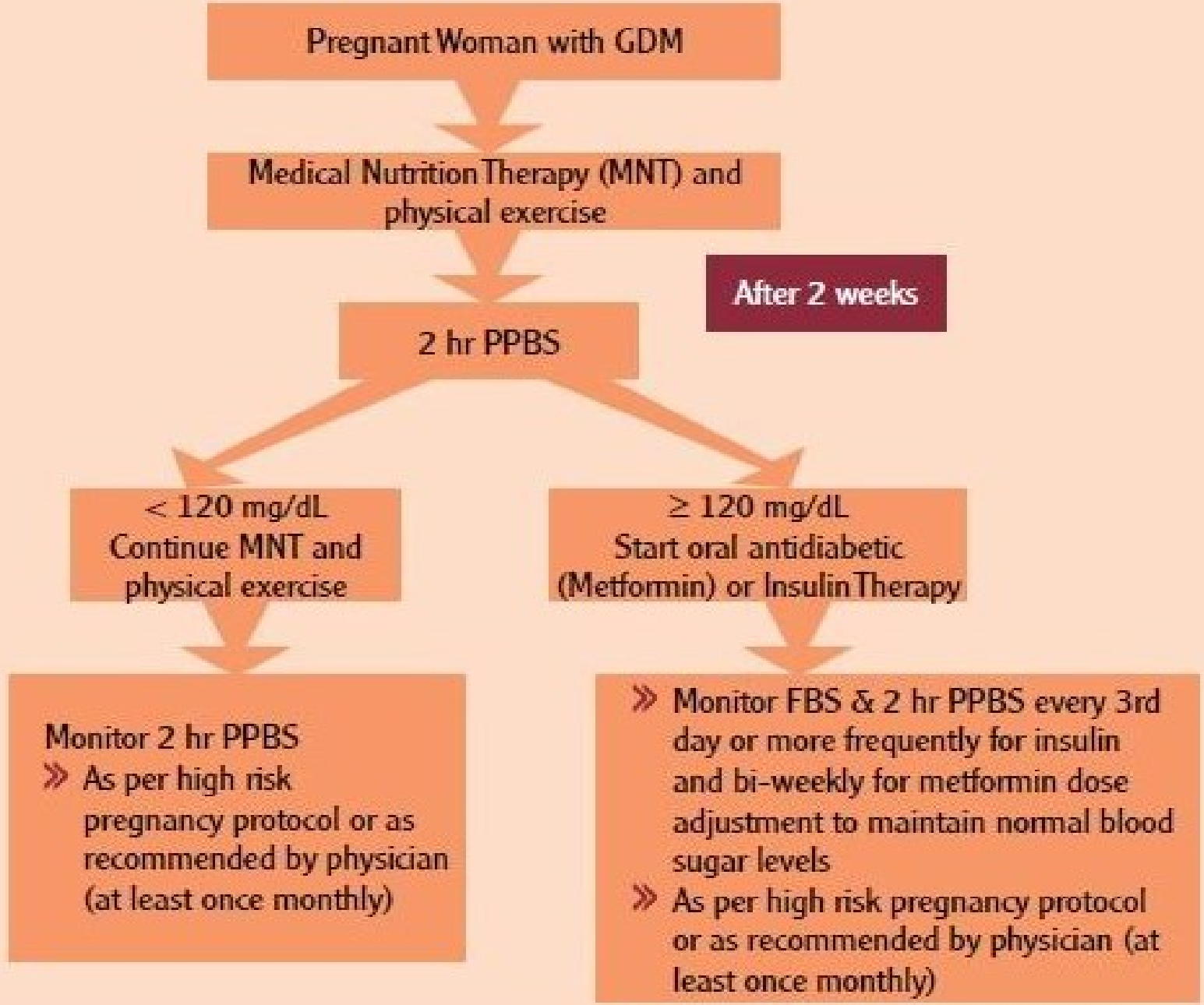
Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;43(Suppl. 1) S254-S266

Similar to the targets recommended by ACOG (the same as for GDM), the ADA-recommended targets for women with type 1 or type 2 diabetes are as follows:

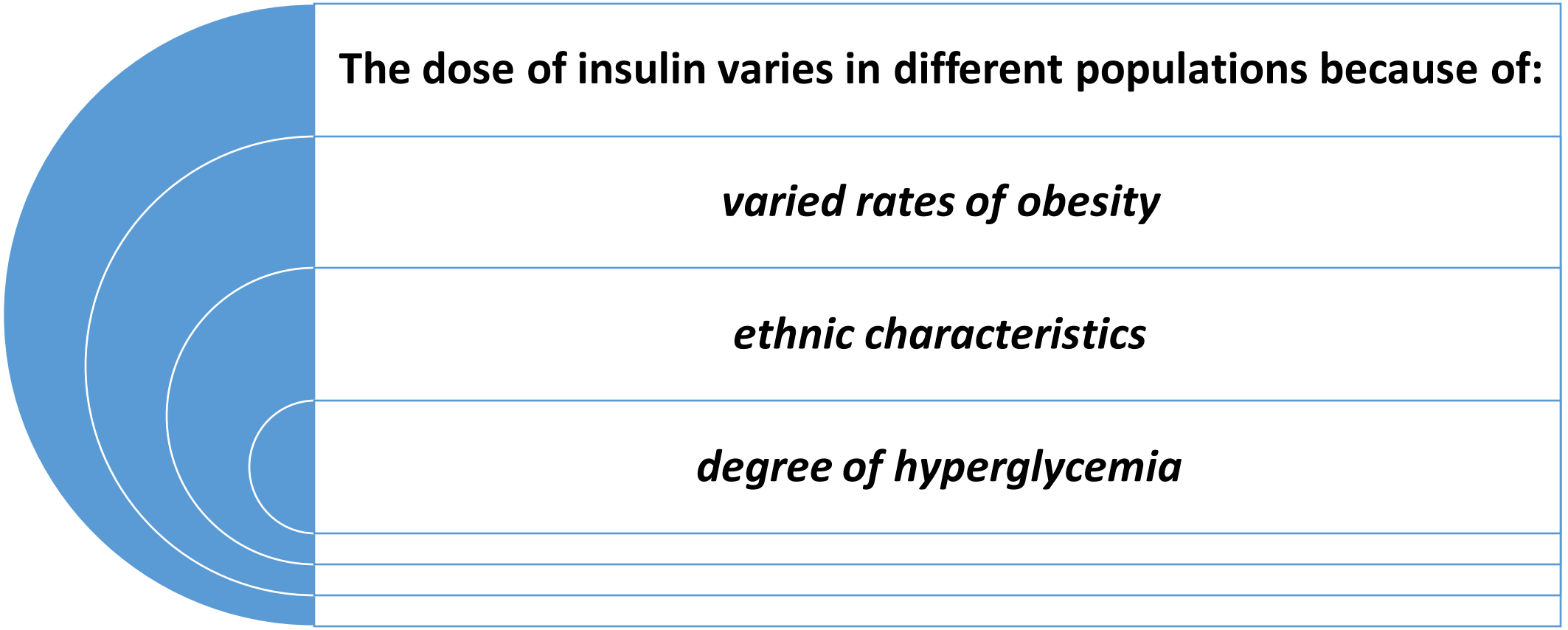
- **Fasting glucose 70–95 mg/dL (3.9–5.3mmol/L)**
- **One-hour postprandial glucose 110–140 mg/dL (6.1–7.8 mmol/L)**
- **Two-hour postprandial glucose 100–120 mg/dL (5.6–6.7 mmol/L)**

Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;43(Suppl. 1) S254-S266

Management of Pregnant Woman with GDM



INSULIN RX


The dose of insulin varies in different populations because of:
varied rates of obesity
ethnic characteristics
degree of hyperglycemia

Diabetes in Pregnancy: Insulin Dosing

AACE 2013

Insulin Dosing Guidelines During Pregnancy and Postpartum[1]	
Weeks gestation	**Total daily dose (TDD) of insulin†**
1-13 weeks	**(0.7 x weight in kg) or (0.30 x weight [lbs])**
14-26 weeks	**(0.8 x weight in kg) or (0.35 x weight [lbs])**
27-37 weeks	**(0.9 x weight in kg) or (0.40 x weight [lbs])**
38 weeks to delivery	**(1.0 x weight in kg) or (0.45 x weight [lbs])**
Postpartum (and lactation)‡	**(0.55 x weight in kg) or (0.25 x weight [lbs])**

1. Castorino K, Jovanovic L. *Clin Chem*. 2011;57(2):221-30.
2. Kitzmiller JL, et al. *Diabetes Care*. 2008;31(5):1060-79.

Protocol 1

Typically, regardless of body weight, a patient whose glucose elevations are ***mostly postprandial*** is prescribed a starting dose of ***30 units (20 units of intermediate acting insulin and 10 units of rapid acting insulin) in the morning prior to breakfast.***

If the GDM is diagnosed and therapy instituted ***prior to the third trimester***:

generally start with ***half this dose((15 units: (10 units of intermediate acting insulin and 5 units of rapid acting insulin)) in the morning prior to breakfast.***

If the ***post-dinner glucose level remains elevated,*** then an additional injection of ***rapid acting insulin*** is given just prior to dinner.

If ***fasting glucose*** is elevated, ***intermediate acting insulin*** can be given along with the dinner dose of rapid acting insulin, or can be administered separately at bedtime.

Sometimes an additional dose of rapid acting insulin is necessary to maintain euglycemia after lunch, so that a total of four injections per day are needed

Adjustments in insulin dosage in response to high glucose values are typically in the range of ***10 to 20 percent***, particularly in obese patients with GDM who are unlikely to develop hypoglycemia unless a meal is omitted after insulin is given.

- ***Twin gestations complicated by GDM may require an approximate doubling of the insulin requirement throughout pregnancy.***

Protocol 2

If insulin is required because the ***fasting blood glucose concentration is high***, an intermediate-acting insulin, such as ***NPH*** insulin, is given before bedtime; an initial dose of ***0.2 unit/kg body weight*** is utilized.

Protocol 3

If ***both preprandial and postprandial blood glucose*** concentrations are high or if the woman's postprandial glucose levels can only be blunted if starvation ketosis occurs, then a ***six injection per day*** regimen is utilized.

The insulin can be divided according to the following schedule: 50 percent as intermediate-acting insulin, such as NPH (given in two equal doses before breakfast and before bedtime), and 50 percent as three preprandial rapid-acting insulin injections; however, it may be possible to omit the lunchtime dose in some patients.

Long-acting insulin analogs (insulin glargine, insulin detemir) have not been studied as extensively in pregnancy, but data from patients with preexisting diabetes and studies of placental transfer suggest that both detemir and glargine are safe and effective for use in pregnancy

Conversely, it is reasonable to:

relax self-glucose monitoring and initiation of insulin for mild hyperglycemia in women whose ***fetuses have a small abdominal circumference (<75th percentile).***

The titration is based upon frequent self-monitoring.

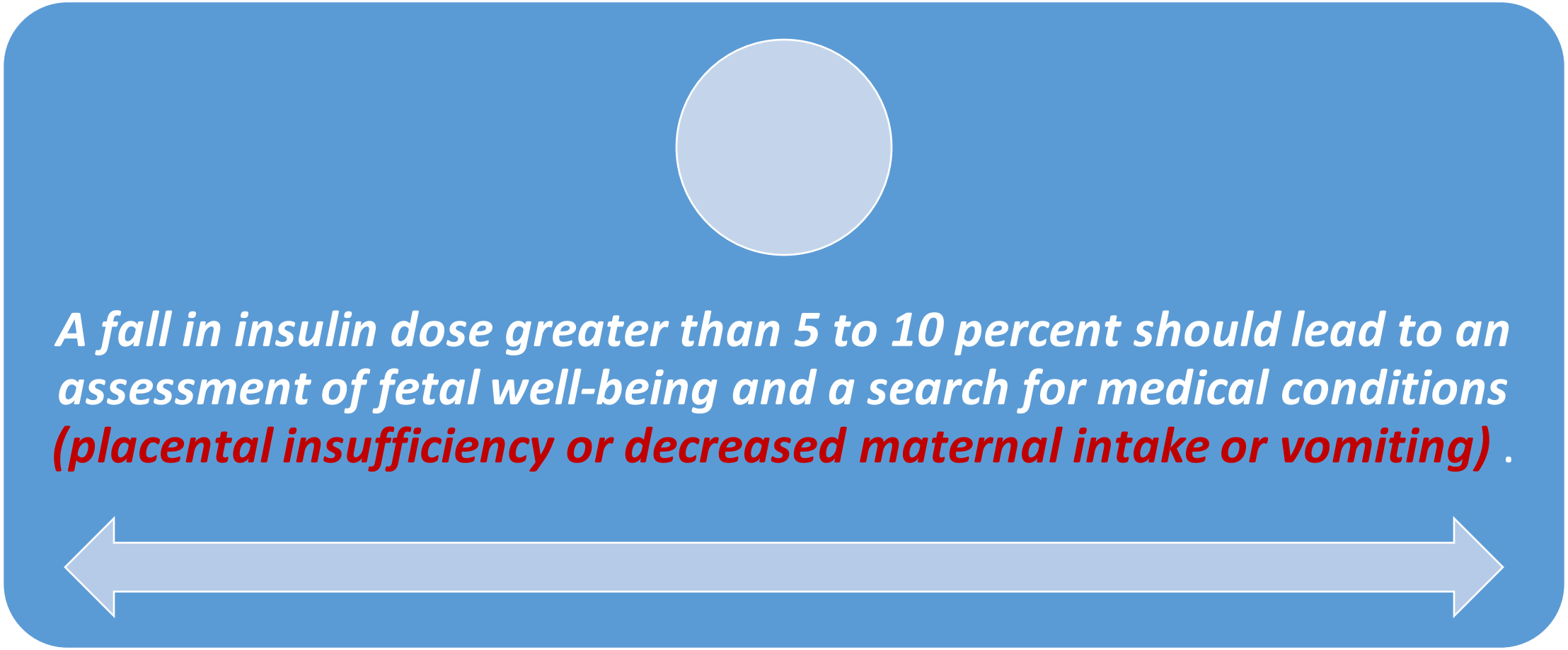
Four to six glucose measurements each day are needed to optimize therapy ***(fasting and one or two hours postprandial with the possible addition of pre-lunch and pre-dinner).***

Start insulin therapy if 30% of SMBG are above the target.

Special notes for T1DM:

- **Between *10 and 14 weeks gestation, patients with T1DM undergo a period of increased insulin sensitivity*; insulin dosage may need to be reduced accordingly during this time frame**
- ***From weeks 14 through 35 of gestation*, insulin requirements typically increase steadily**
- **After 35 weeks gestation, insulin requirements may level off or even decline[2]**

- **Obese patients may require higher insulin dosages than non-obese individuals[2]**


A fall in insulin dose greater than 5 to 10 percent should lead to an assessment of fetal well-being and a search for medical conditions (placental insufficiency or decreased maternal intake or vomiting) .

Dilated eye examinations should occur ideally ***before pregnancy or in the first trimester,*** and then patients should be monitored ***every trimester and for 1-year postpartum*** as indicated by the degree of retinopathy and as recommended by the eye care provider

Prescription of prenatal vitamins (with at least 400 µg of folic acid and 150 µg of potassium iodide) is recommended prior to conception

Preeclampsia and Aspirin

14.18 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

Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;43(Suppl. 1) S254-S266

Metformin ADA 2023

Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester

Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2023. *Diabetes Care* 2023;43(Suppl. 1) S254-S266

In randomized trials, compared with insulin, metformin:

- **Reduced gestational weight gain (mean difference -1.31 kg, 95% CI -● 2.34 to -0.27)**
- **Reduced birth weight (mean difference -74 g, 95% CI -115 to -33)**
- **Reduced risk for macrosomia (odds ratio [OR] 0.60, 95% CI 0.45-0.79)**
- **Reduced risk for neonatal hypoglycemia (risk ratio [RR] 0.63, 95% CI 0.45-0.87)**
- **Reduced risk for pregnancy-induced hypertension (RR 0.56, 95% CI 0.37-0.85)**
- **Increased offspring body mass index (BMI, by 0.8 kg/m2) and adiposity by mid-childhood**

- Differences in other outcomes were not statistically significant: large for gestational age newborn (OR 0.87, 95% CI 0.66-1.14) [69], preterm birth (RR 1.18, 95% CI 0.67-2.07), small for gestational age newborn (RR 1.20, 95% CI 0.67-2.14), perinatal mortality (RR 0.82, 95% CI 0.17-3.92), cesarean birth (RR 0.97, 95% CI 0.80-1.19) [70].

Gestational diabetes mellitus: Glycemic control and maternal Prognosis Author:Celeste Durnwald, MD,UPTODATE 2023

- If a patient cannot take insulin or declines, metformin can be used
  - Counsel about metformin risks including placental cross over and no long term studies in offspring available
    - ***May be associated with preterm birth***
  - Starting dose: 500 mg nightly for 1 week, increase to 500 twice daily
    - Check baseline creatinine
  - Adverse events include abdominal pain and diarrhea – recommend with meals
  - Maximal dose is 2,500 to 3,000 mg per day, in two or three divided doses

Gestational diabetes mellitus: Glycemic control and maternal Prognosis Author:Celeste Durnwald, MD,UPTODATE 2023

Compared with insulin, glyburide:

- **Increased mean birth weight (mean difference 290 g, 95% CI 68-511)**
- **Increased risk for macrosomia (OR 1.38, 95% CI 1.01-1.89)**
- **Increased the frequency of neonatal hypoglycemia (11 versus 7 percent; difference 5.0, 95% CI 0.5-9.5)**

- Showed trends toward an increased risk for a large for gestational age newborn (OR 2.49, 95% CI 0.79-7.81) and less maternal gestational weight gain (mean difference -0.68 kg, 95% CI -1.69 to 0.34 kg) .

Gestational diabetes mellitus: Glycemic control and maternal Prognosis Author:Celeste Durnwald, MD,UPTODATE 2023

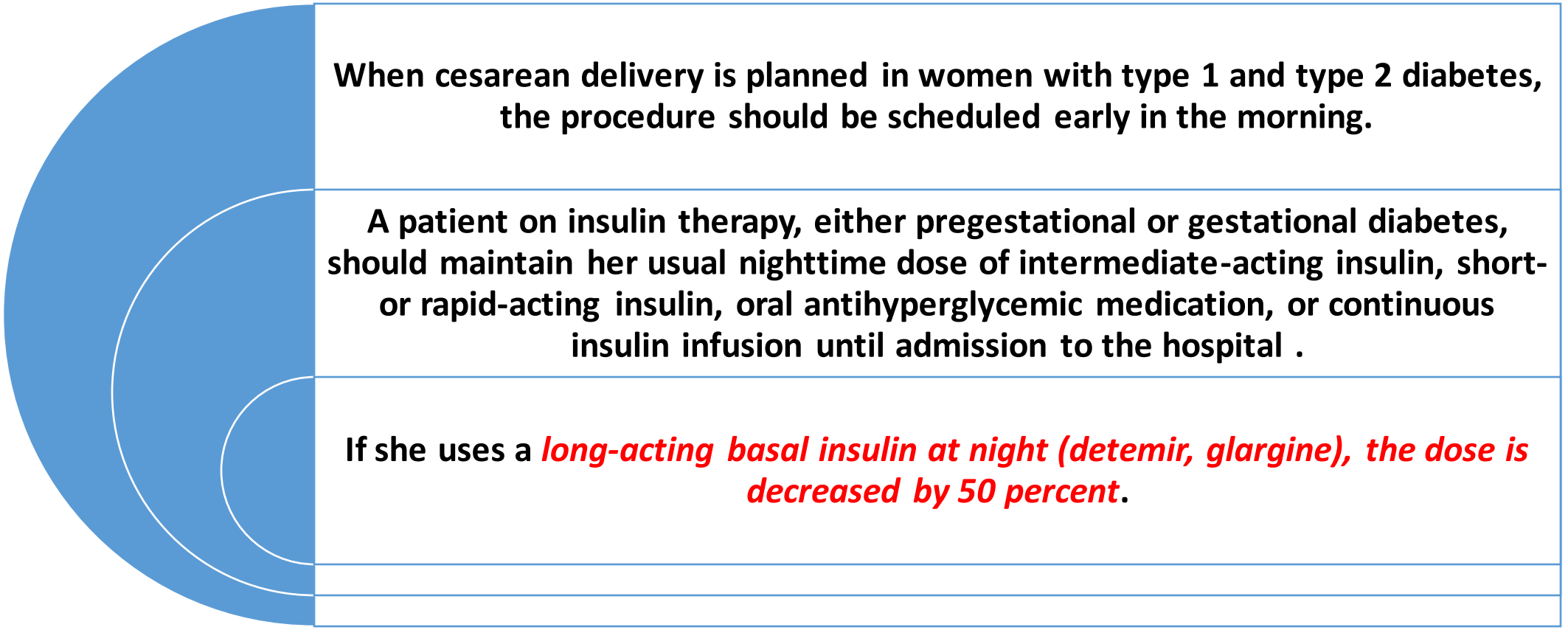
- **Glyburide** should not be used in place of insulin as studies show worse outcome, including macrosomia and birth injury
  - Starting dose is 2.5 to 20 mg per day in divided doses
  - Up to 30 mg may be necessary to obtain glycemic control
  - Long term outcome studies also still lacking, although no short term adverse events have been noted

Gestational diabetes mellitus: Glycemic control and maternal Prognosis Author:Celeste Durnwald, MD,UPTODATE 2023

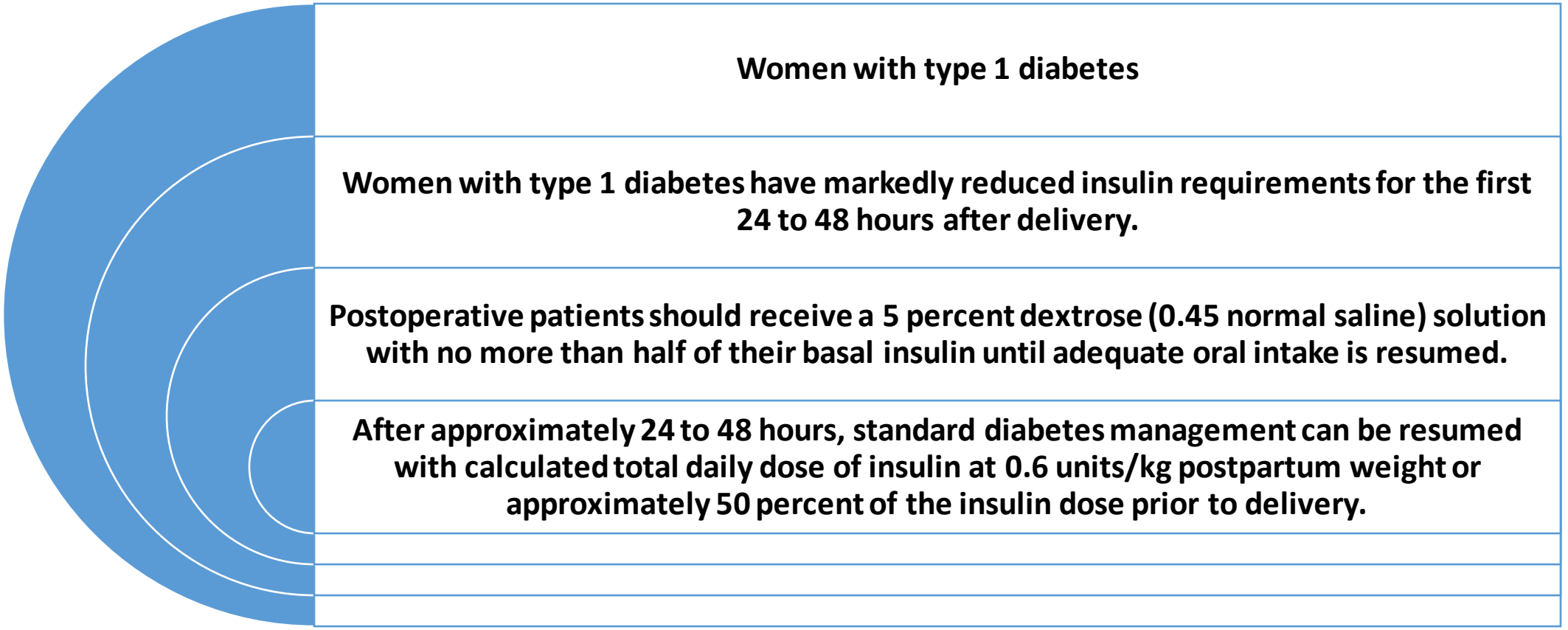
When to Deliver?

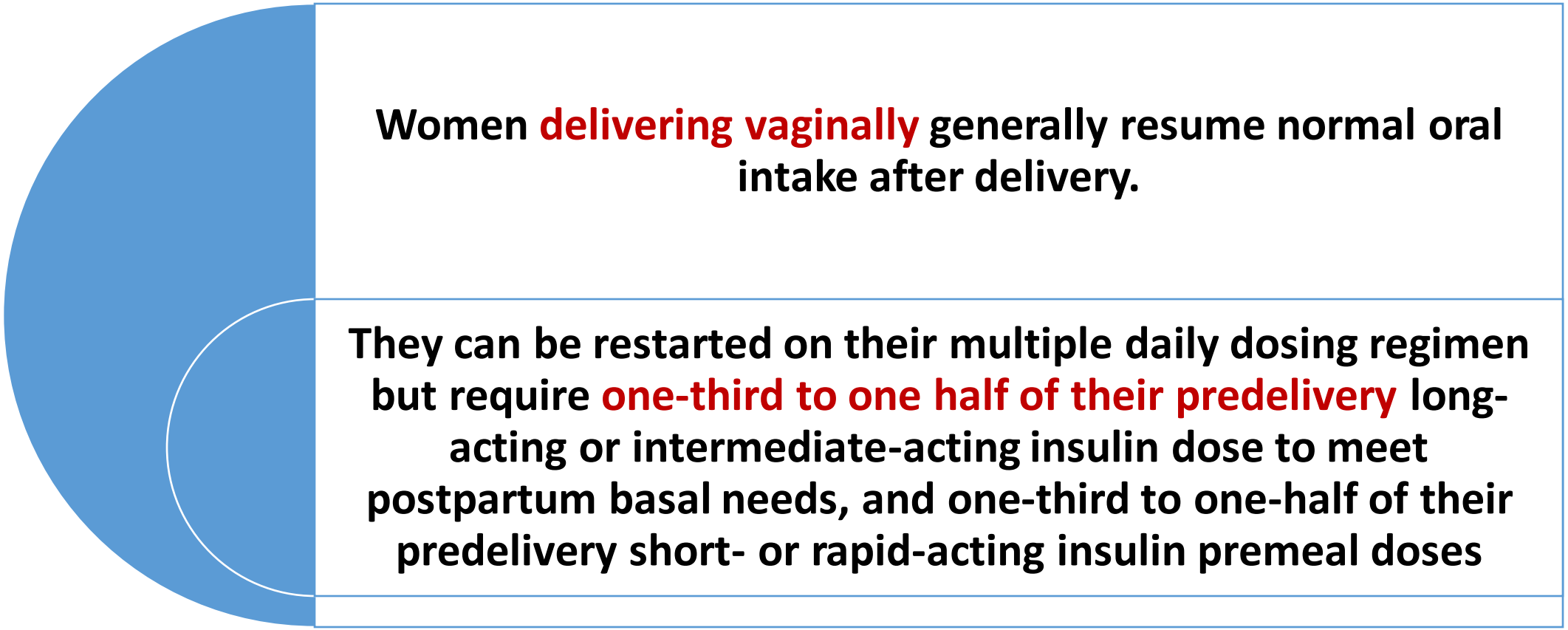
- **Controlled on diet: 39w0d to 40w6d**
  - Expectant management up to 40w6d appropriate with antepartum testing
- **Well controlled on medication: Deliver at 39w0d to 39w6d**
- **Poorly controlled: Individualize | Expert guidance supports earlier delivery but data lacking regarding precise timing**
  - Delivery between 37w0d and 38w6d may be justified
  - Delivery between 34w0d and 36w6d weeks 0 days reserved for (1) failure of in-hospital glycemic control or (2) abnormal fetal testing
- Estimated fetal weight ≥4500: Counsel regarding risks and benefits of a scheduled cesarean section

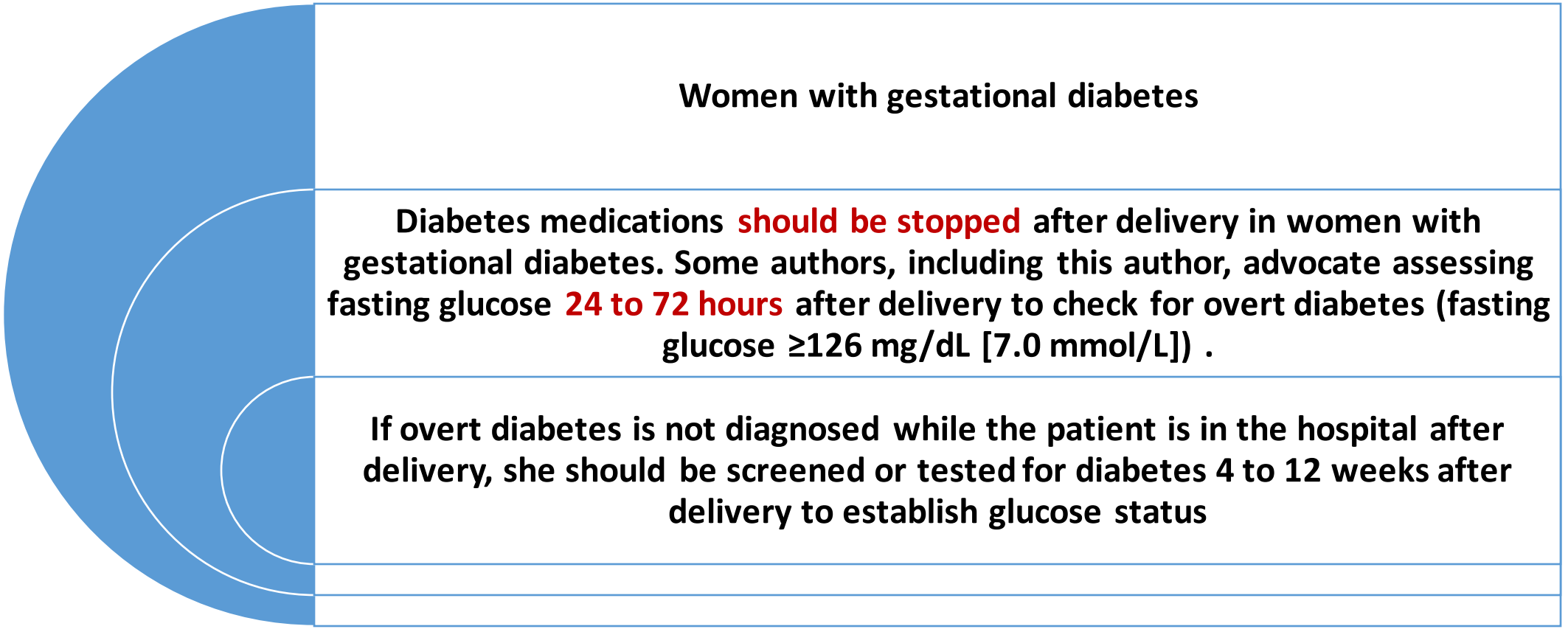
Scheduled cesarean delivery or induction: Women receiving insulin



POSTPARTUM MANAGEMENT




Women delivering vaginally generally resume normal oral intake after delivery.
They can be restarted on their multiple daily dosing regimen but require one-third to one half of their predelivery long-acting or intermediate-acting insulin dose to meet postpartum basal needs, and one-third to one-half of their predelivery short- or rapid-acting insulin premeal doses


Women with gestational diabetes
Diabetes medications should be stopped after delivery in women with gestational diabetes. Some authors, including this author, advocate assessing fasting glucose 24 to 72 hours after delivery to check for overt diabetes (fasting glucose ≥126 mg/dL [7.0 mmol/L]) .
If overt diabetes is not diagnosed while the patient is in the hospital after delivery, she should be screened or tested for diabetes 4 to 12 weeks after delivery to establish glucose status

*GDM is Diabetes that only happens during pregnancy

Urbanozo H, Isip-Tan I. JAFES November 2014
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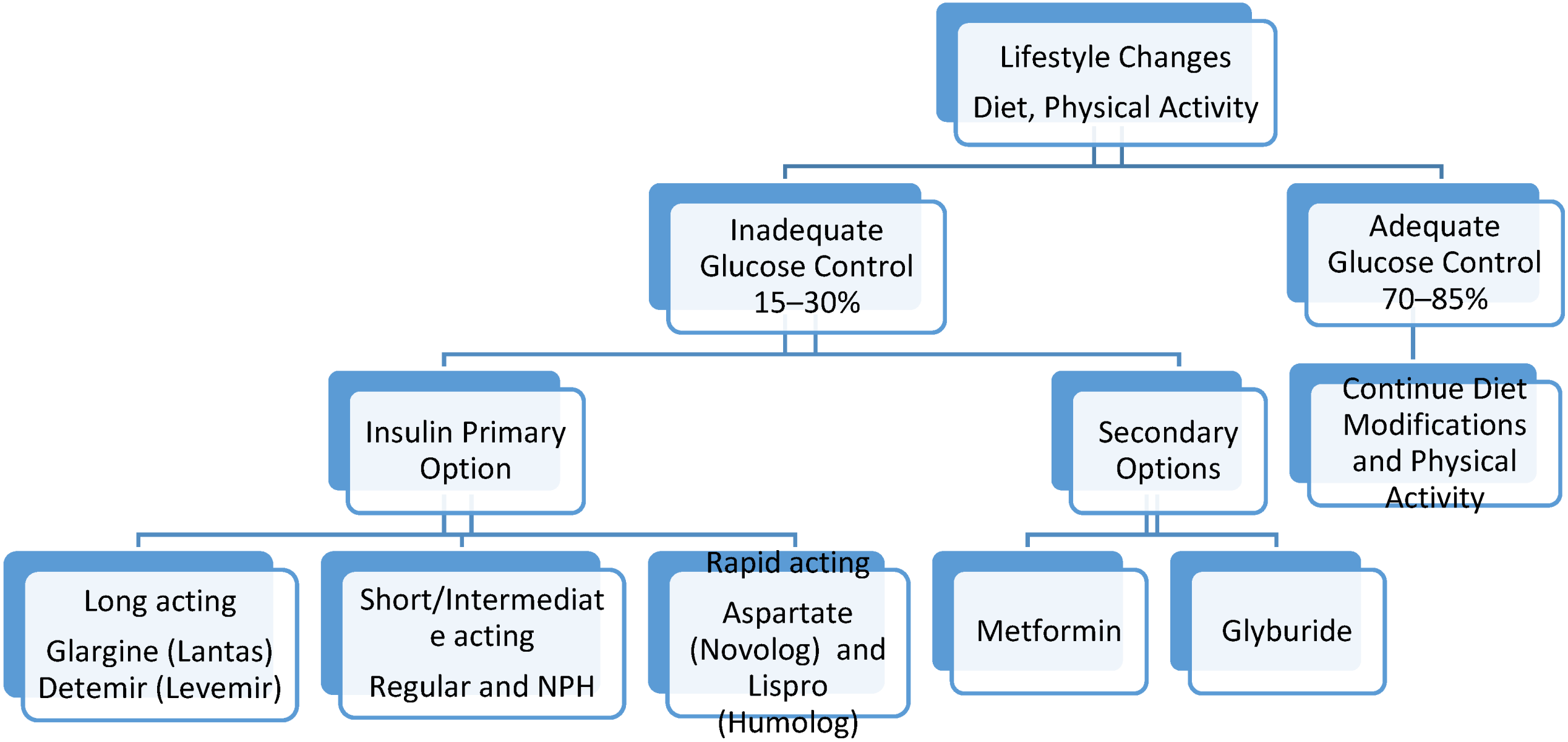
Lifestyle Changes
Diet, Physical Activity
Inadequate Glucose Control 15–30%
Adequate Glucose Control 70–85%
Insulin Primary Option
Secondary Options
Continue Diet Modifications and Physical Activity
Long acting
Glargine (Lantas)
Detemir (Levemir)
Short/Intermediate acting
Regular and NPH
Rapid acting
Aspartate (Novolog) and Lispro (Humolog)
Metformin
Glyburide

Management of Hyperglycemia in Pregnancy

St Vincent Declaration
St Vincent (Italy), 10–12 October 1989
A meeting organised by WHO and IDF in Europe

"...Achieve a pregnancy outcome in the diabetic woman that approximates that of the non-diabetic woman."