

# Diabetes and Pregnancy: Treating a Vulnerable Population

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# Acknowledgements

- Waterloo Wellington Diabetes
- Slides from 2012 CDA Clinical Practice Guidelines
- Slides from Motherrisk Educational Programme: Pharmacotherapy in Pregnancy
- Diabetes, Hypertension, Metabolic Syndrome and Pregnancy Conference, Florence, Italy-March, 2013

## Conflict of Interest

Advisory Boards: Eli Lilly; NovoNordisk; Sanofi Aventis;  
Astra Zeneca; GlaxoSmithKline; Bristol Meyers Squibb

Research: Eli Lilly; NovoNordisk; Sanofi Aventis; Canadian  
Heart Research Foundation; Bayer; Astra Zeneca;  
Novartis; GlaxoSmithKline; Eisai

Honoraria for Speaking: Eli Lilly; NovoNordisk; Sanofi  
Aventis; Merck Frosst; Astra Zeneca; GlaxoSmithKline;  
Abbott; Bristol Myers Squibb; Servier; BD.



# Learning Objectives

- To review the classification of diabetes and pregnancy.
- To discuss the epigenetics and the developmental origins of adult health and disease (DOHaD).
- To review current guidelines for diagnosis and treatment of diabetes during pregnancy.
- To review current trends in Ontario

## Quiz: True or False

1. Gestational diabetes is a time-limited disorder of pregnancy which resolves postpartum.
2. A diagnosis of gestational diabetes is secured when there are 2 or more abnormal glucose values on a 75g 2-hr gestational screen.
3. Women with gestational diabetes have an increased risk for the development of Type I diabetes.

# Classification of Diabetes in Pregnancy

Pregestational diabetes	Gestational diabetes
<p data-bbox="214 606 807 739">Pregnancy in pre-existing diabetes</p> <ul data-bbox="272 821 749 958" style="list-style-type: none"><li data-bbox="272 821 749 882">•Type 1 diabetes</li><li data-bbox="272 896 749 958">•Type 2 diabetes</li></ul>	<p data-bbox="1083 682 1721 815">Diabetes diagnosed in pregnancy</p>



## Diabetes in Pregnancy: Consider Phases

<b>Pregestational diabetes</b>	<b>Gestational diabetes</b>
1. Preconception counseling	1. Screening
2. Glycemic control during pregnancy	2. Glycemic control during pregnancy
3. Management in labour	3. Management in labour
4. Postpartum considerations	4. Postpartum considerations



# Rationale

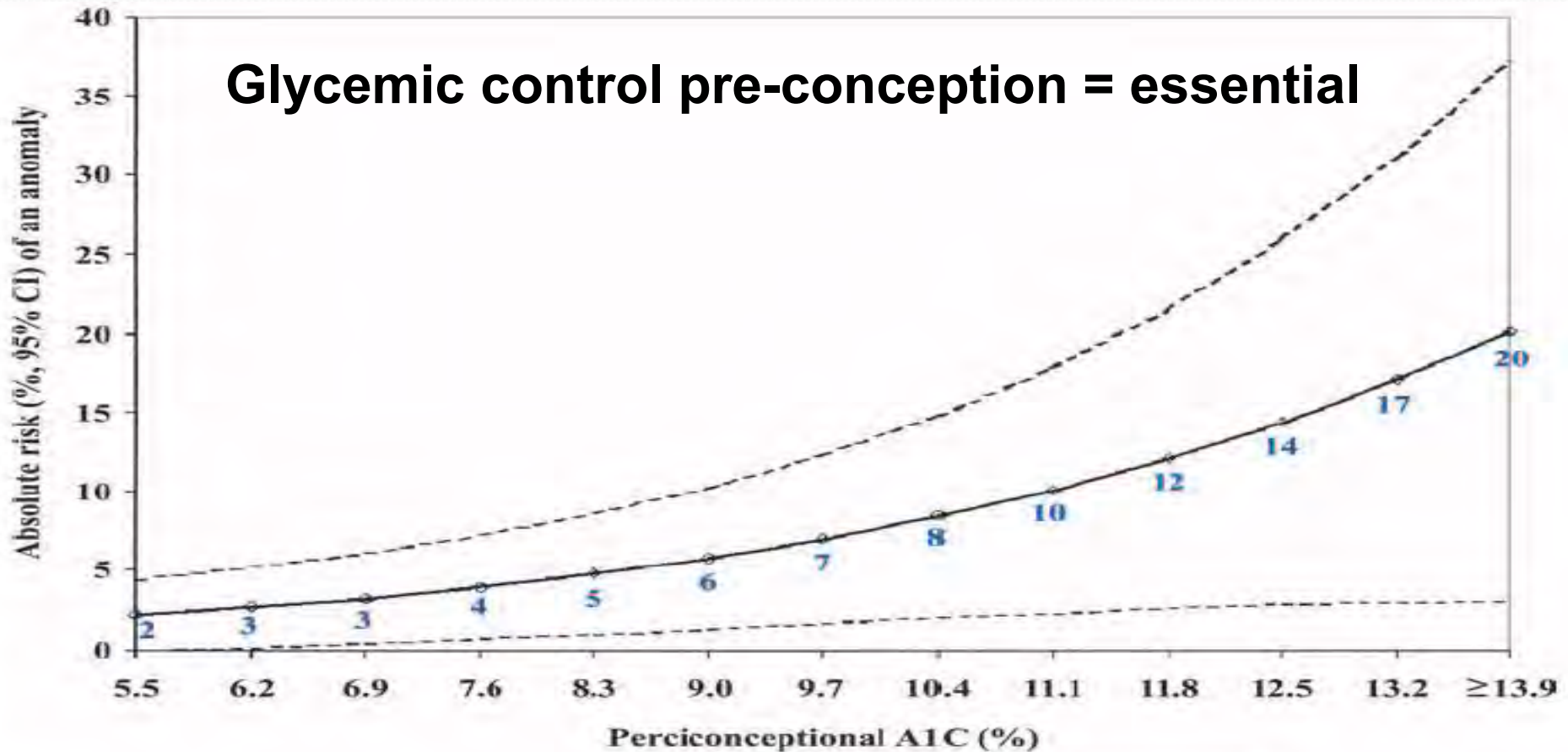


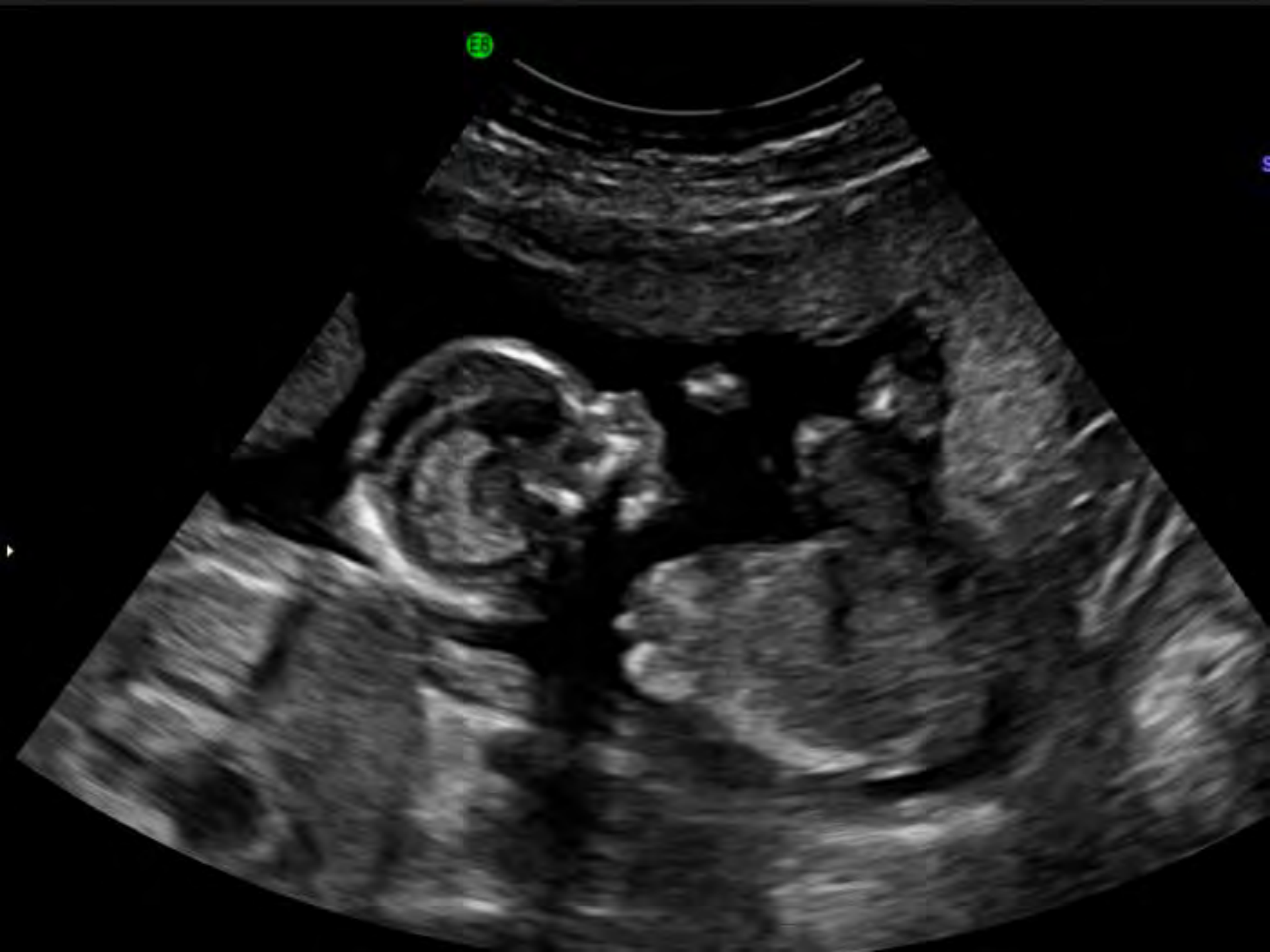
# Impact of Hyperglycemia on Pregnancy

- Elevated blood glucose levels are associated with:
  - Stillbirths
  - Macrosomia due to fetal adiposity
  - Birth trauma
  - C-section
  - Preeclampsia
  - Neonatal complications:
    - Polyhydramnios
    - Hyperbilirubinemia
    - Polycythemia
    - Hypoglycemia
    - Hypocalcemia
    - Delayed organ maturity (including lungs)

# Risk of Fetal Anomaly Relative to Periconceptional A1C

**Glycemic control pre-conception = essential**









**Epigenetics:  
The role of dysglycemia in  
long-term adverse health outcomes**

**Environment Special:**  
The oceans—why 70%  
of our planet is in danger

**The Facebook Movie:**  
The secret history of  
social networking

# TIME

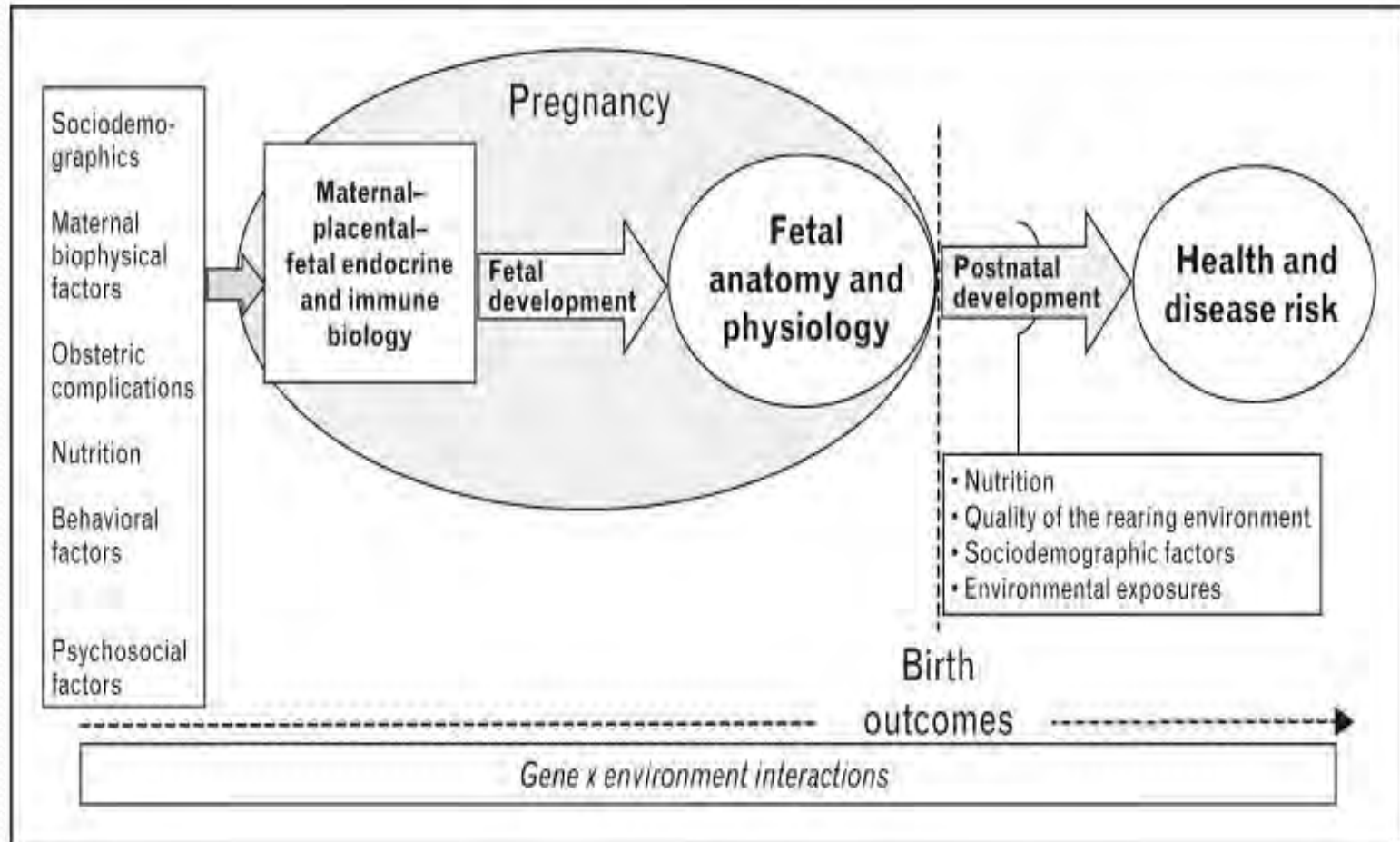


## How the first nine months shape the rest of your life

The new science  
of fetal origins

BY ANNIE MURPHY PAUL

# Epigenetics





# Epigenetics

- Fetal programming and early origins of health and disease
- DNA methylation
- Histone deacetylation/methylation/phosphorylation
- Effects on RNA
- Long period of quiet until the development of consequences in later life.
- Memory from early exposure after a period of senescence causes disease.

# Developmental Origins of Adult Health and Disease (DOHaD)

- **Barker hypothesis** (Barker & Osmond, 1986; Barker, 1995)
  - Fetal undernutrition associated with adult obesity, CVD and type II diabetes (Law et al., 1992; Sayer et al., 2004)
  - Fetal undernutrition + rapid “catch-up growth” (Ong, 2006; Stettler et al., 2003, 2005)
- **Thrifty phenotype** (Hales & Barker, 2001)
  - Adaptive response for deprived prenatals environment maladaptive for postnatal environment
- **Developmental Origins of Adult Health and Disease (DOHaD)** (Gluckman et al 2005; Taylor & Poston, 2007)
  - Fetal environment either nutritionally deprived or over-rich increases risk for child and adult obesity and its sequelae (Catalano, 2003; Oken & Gillman, 2003; Ehrenberg et al., 2004)



# Children, poverty and health





# What happens inside matters outside

- Antenatal stress associated with:
- Decreased cognitive function
  - Quebec Ice Storm -1998 - loss of electricity & water for up to 5 weeks
    - Children had lower MDI scores
    - Lower language development scores
    - These held when controlling for Ob complications, birth weight , post partum depression (LaPlante et al, 2004)
- Maternal exposure to traumatic events associated with:
  - Schizophrenia (OR – 1.5 in cohort from Dutch famine)
  - Depression in adulthood

# Mechanism

- Epigenetic modifications represent a potential way that “metabolic programming” occurs
- Alteration in the hypothalamic-pituitary-adrenal axis involving:
  - Mobilizing energy stores
  - Response to stress
  - Inhibiting inflammatory responses during stress
- Post natal stress is cumulative with prenatal stress leading to increased vulnerability to stressors
- Prenatal stress can lead to impaired fetal growth
- Attention disorders and increased anxiety observed



# Two complementary theories

- Critical periods (latency model)
  - Barker hypothesis
  - Organogenesis
    - Fewer beta cells in pancreas – type 2 diabetes
    - Fewer nephrons - hypertension
- Cumulative experiences (pathways model)
  - Allostasis and allostatic load
  - Behavioral responses



# Epigenetics

- Glucose is the enemy of pregnancy and the developing fetus.
- Women with 1 abnormality on GTT are more similar to women with gestational diabetes than women with a normal GTT.
- One abnormal value carries enough risk for intervention to be initiated.
- Long term maternal health consequences
- Opportunities for prevention

# Maternal Health

- Pregnancy is a window into a womans future health and her offsprings future.
- “The Slow Motion Disaster”:
  - Margaret Chan, Director General, WHO
- Poorer prognosis for babies of mothers with both GDM and obesity.
- Necessary to optimize early developmental environment



# Not just a local issue: Global Maternal Health

- 65% of global deaths are due to chronic, non-communicable disease
- Diabetes is one of the top 10 killers of women
- Major public health burden
- Most occurring in the developing world
- 76 million women are at risk for hyperglycemia in pregnancy.
- GDM is an unrecognized, underestimated problem





# Global Maternal Health

What kills women in pregnancy:

Hemorrhage

Hypertensive disorders

Sepsis

Obstructed labour

# Gestational Diabetes Mellitus

- Carbohydrate intolerance 1<sup>st</sup> recognised in pregnancy
- A disease in relation to insulin secretion and insulin sensitivity
- An inability to increase secretion of insulin
- An inability to overcome a decrease in insulin sensitivity

# Gestational Diabetes Mellitus

- A disease which was present before pregnancy, expresses itself during pregnancy, and remains after pregnancy.
- Gestational diabetes mellitus is Type II diabetes mellitus by another name.



# Gestational Diabetes Mellitus

- Normal pregnancy:
  - Decrease in insulin sensitivity by 47-56%
  - Increase in insulin secretion by 60-80%
- Gestational diabetes mellitus
  - Decrease in insulin sensitivity
  - Decrease in insulin secretion

## Gestational Diabetes (GDM) Diagnosis

- **Universal screening** for GDM @ 24-28 weeks Gestational Age (GA)
- **Screen earlier if risk factors for GDM:**

Previous GDM	BMI $\geq 30$ kg/m <sup>2</sup>
Prediabetes	Polycystic ovarian syndrome
High risk population (Aboriginal, Hispanic, South Asian, Asian, African)	Current fetal macrosomia or polyhydramnios
Age $\geq 35$ years	History of macrosomic infant
Corticosteroid use	Acanthosis nigricans

# Obesity

Obesity and pregnancy in non-diabetic patients:

- Increase risk of congenital malformations
- Increased risk of pregnancy induced hypertension
- Increased risk of Caesarean section
- Increased risk of stillbirth
- Increased risk of induction
- Large for gestation age and macrosomic babies
- Increased risk of gestation diabetes mellitus

BMI greater than 36 is associated with an increased risk of fetal anomalies

Obese women take longer to conceive even if they have normal menstrual cycles



# Gestational Diabetes Mellitus & Obesity

- 30-50% of women with gestational diabetes mellitus are obese
- 10% of women with GDM have metabolic syndrome
- 2-4 fold higher risk of metabolic syndrome in women with a history of gestational diabetes mellitus
- Western diet increases the risk of a GDM: red meat, processed meats, french fries and sweets, plastics, additives, genetically modified foods, etc

# Ethnicity: India's Diabetes Paradox

- Most diabetics worldwide: more than 50 million people
- Average age of onset: 42.5 years
- By 2030, it is estimated that 80 million people in India will have type II diabetes mellitus



# Ethnicity: India's Diabetes Paradox

- More than 16% of pregnant Indian women have gestational diabetes.
- Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women.
- Pregnant women age 30-39 years had greater prevalence of GDM as compared with those in the age group of 20 to 29 years.
- One third of babies born in India are low birthweight
- 80 million children under the age of 5 years are malnourished



# Low Birthweight

Is associated with an increased risk of:

Coronary artery disease

Hypertension

Stroke

Obesity

Type II diabetes

Osteoporosis

# Birthweight: LGA

- LGA infants of mothers with GDM have higher BMIs
- Macrosomia associated with lower IQ scores (10 points)
- 50% of children born to mothers with gestational diabetes mellitus are in the >90<sup>th</sup> percentile at age 8.
- Increase in metabolic syndrome at age 11 years
- 23% have an abnormal glucose tolerance test at adolescence.
- Metabolic syndrome is the #1 killer in Western societies.
- Increased risk for breast and ovarian cancers.

# Birthweight

Over and under-nutrition leads to metabolic syndrome:

- Genetic factors
- Maternal insulin sensitivity
- In utero environment



# HAPO

## Hyperglycemia And Pregnancy Outcomes

- A six-year international study that recruited approximately 25,000 pregnant women at 15 centres in 9 countries.
- What is the association of various levels of glucose intolerance during the third trimester of pregnancy?
- What is the risk of adverse outcomes and the baby?

# HAPO

## Findings:

- There is a strong linear association between higher levels of maternal plasma glucose and large babies that remains significant after adjustments for field center, maternal body mass index, height and age.
- The chances of having a larger than normal baby were up to 6 times higher across the range of fasting, one hour into our maternal plasma glucose levels.
- The chances of a baby having a C-peptide value above the highest 10% of the population (Fetal hyperinsulinemia) were up to 8 times higher across the same ranges of maternal plasma glucose.





# HAPO

International Association of Diabetes and Pregnancy Study  
Groups (IADPSG)

New guidelines for screening and diagnosis of diabetes  
in pregnancy.



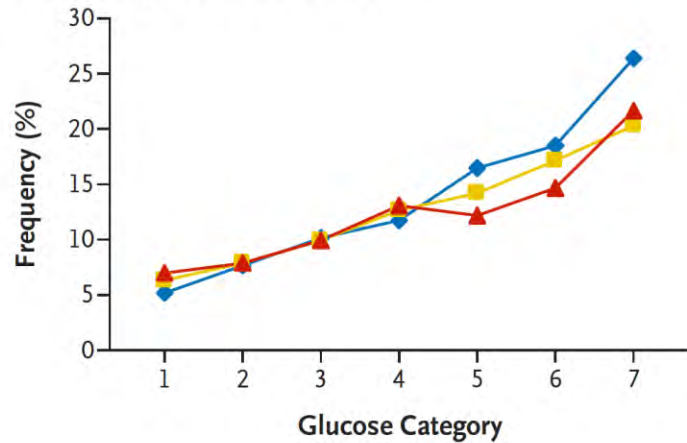
## **Diagnosis of GDM**

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

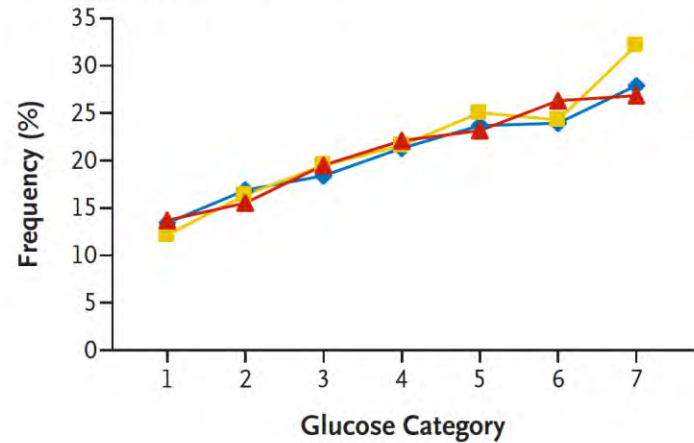
# HAPO: Incidence of Adverse Outcomes Increases Along Continuum – No Threshold

◆ Fasting glucose    ■ 1-Hr glucose    ▲ 2-Hr glucose

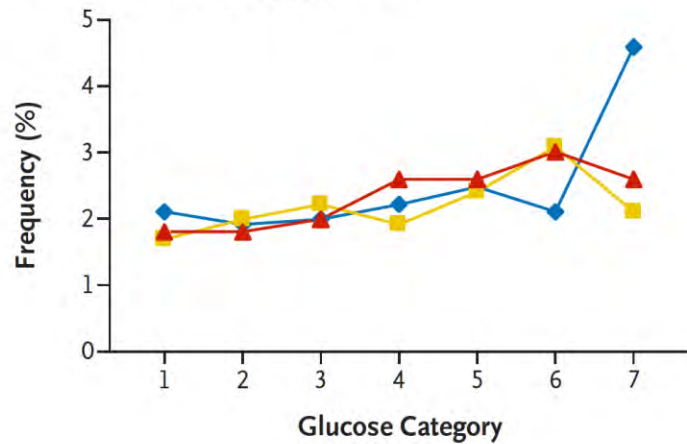
**A Birth Weight >90th Percentile**



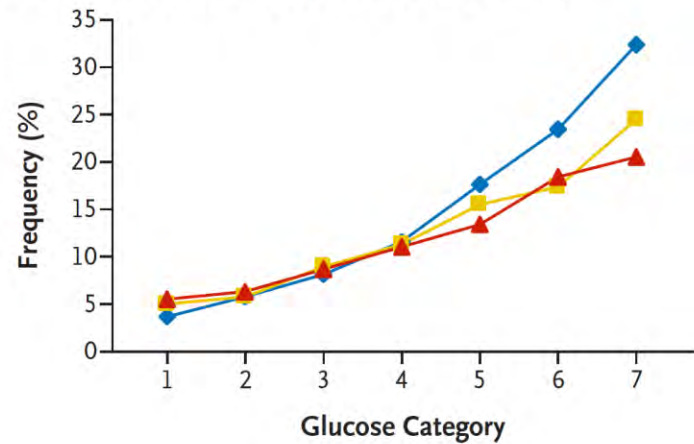
**B Primary Cesarean Section**



**C Clinical Neonatal Hypoglycemia**



**D Cord-Blood Serum C Peptide >90th Percentile**





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

**NO**



## IADPSG Consensus Threshold Values for Diagnosis of GDM ( $\geq 1$ Value is Diagnostic)

Glucose measure with a 75 g OGTT	Glucose threshold (mmol/L)	Proportion of HAPO cohort above threshold (%)
Fasting plasma glucose (FPG)	<b>5.1</b>	8.3
1-h plasma glucose	<b>10.0</b>	14.0
2-h plasma glucose	<b>8.5</b>	16.1

Based on odds ratio (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

**Remains a Controversial Topic ...**

# Perspectives on the Proposed Gestational Diabetes Mellitus Diagnostic Criteria

*(Obstet Gynecol 2013;121:177–82)*

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

## Diagnosing gestational diabetes

**E. A. Ryan**

Diabetologia (2011) 54:480–486

### **Review Article**

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

T. Cundy

Diabet. Med. 29, 176–180 (2012)

# Considerations for the CDA Adopting the IADPSG Thresholds

- How can we select an odds ratio threshold in the absence of a true threshold in the data?
- What is the impact on the patient and workload of increasing the prevalence of GDM?
- Do we have sufficient evidence with respect to treatment benefit at the various thresholds to make an informed decision?
- In the absence of clear benefit, should the diagnostic criteria be changed from 2008?



# 2013 CDA Diagnostic Criteria for GDM

2013

## **PREFERRED APPROACH (2 steps)**

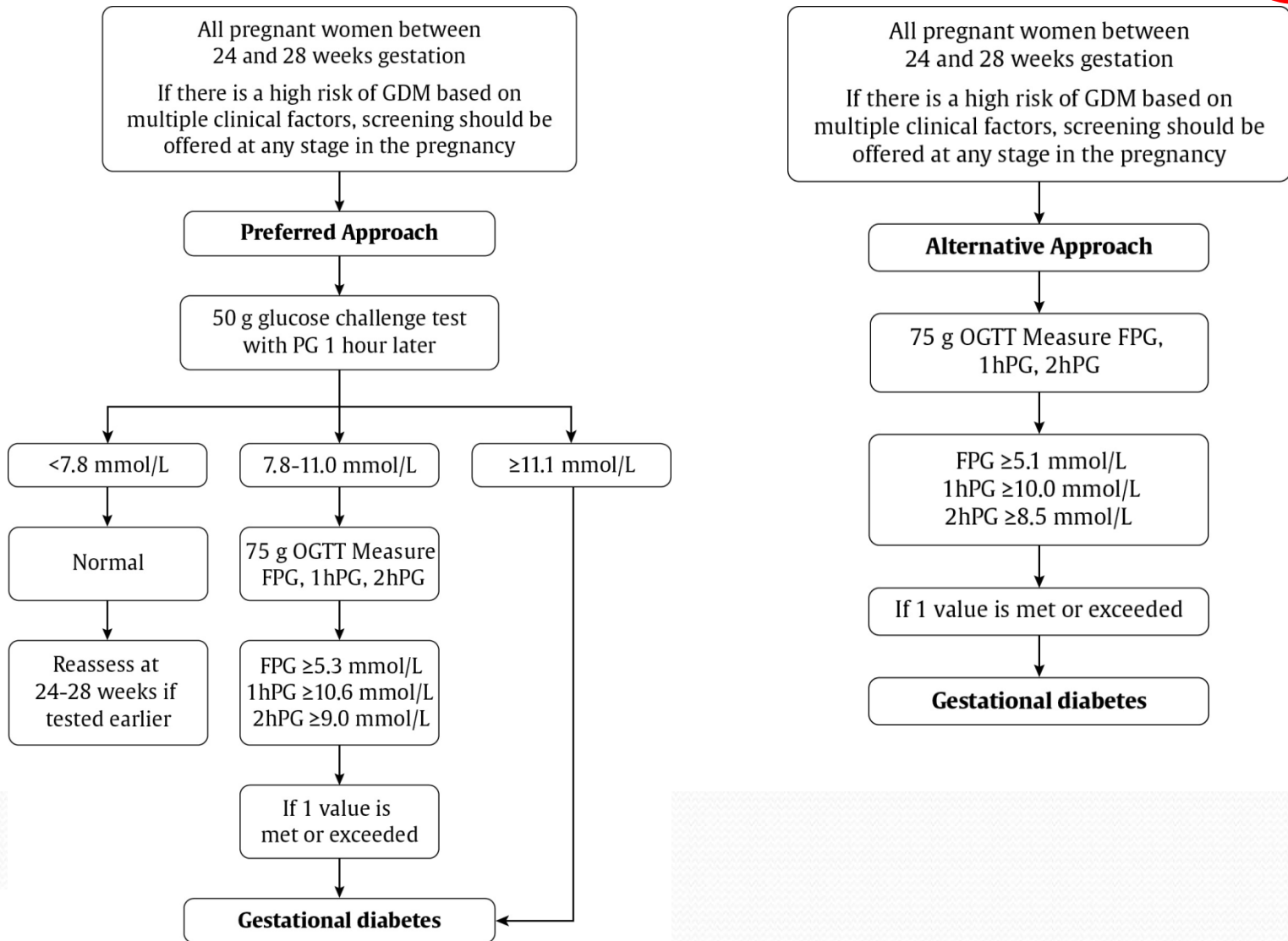
1. 50 gram glucose challenge test
  2. 75 gram oral glucose tolerance test
    - Using thresholds of OR 2.0
- 

## **ALTERNATIVE APPROACH (1 step)**

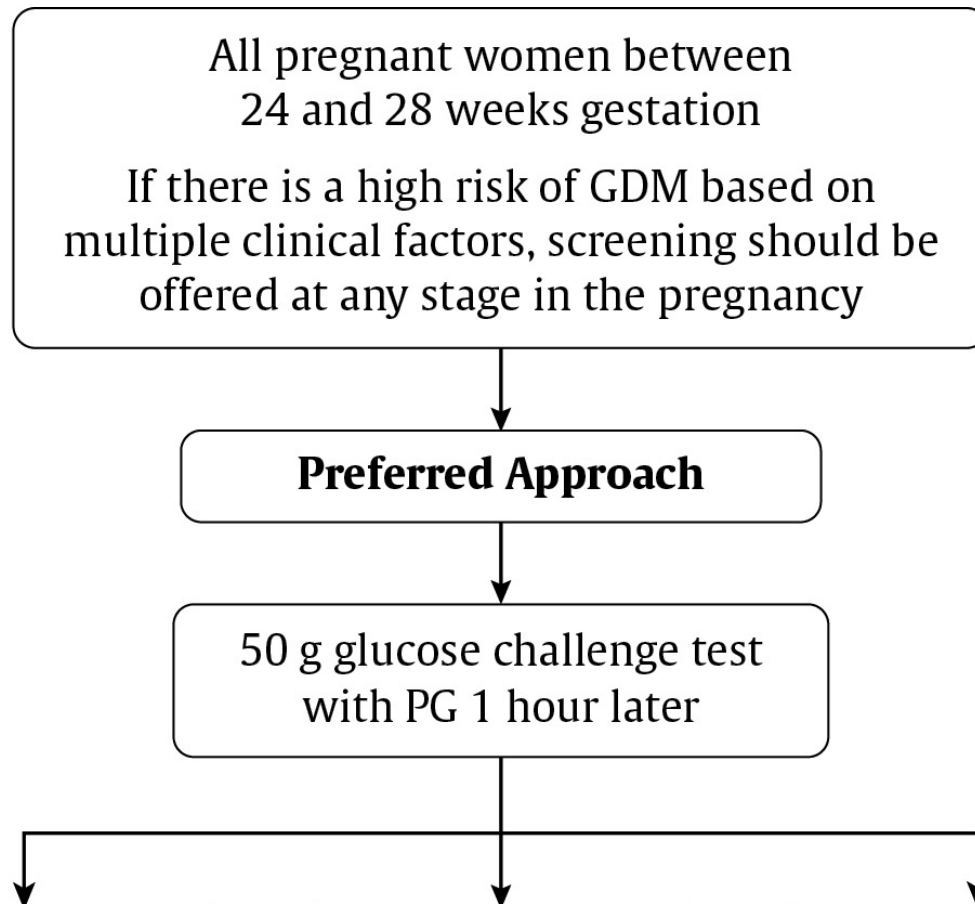
1. 75 gram oral glucose tolerance test
  - Using thresholds of OR 1.75

# 2013 GDM Diagnosis: Two Approaches

2013

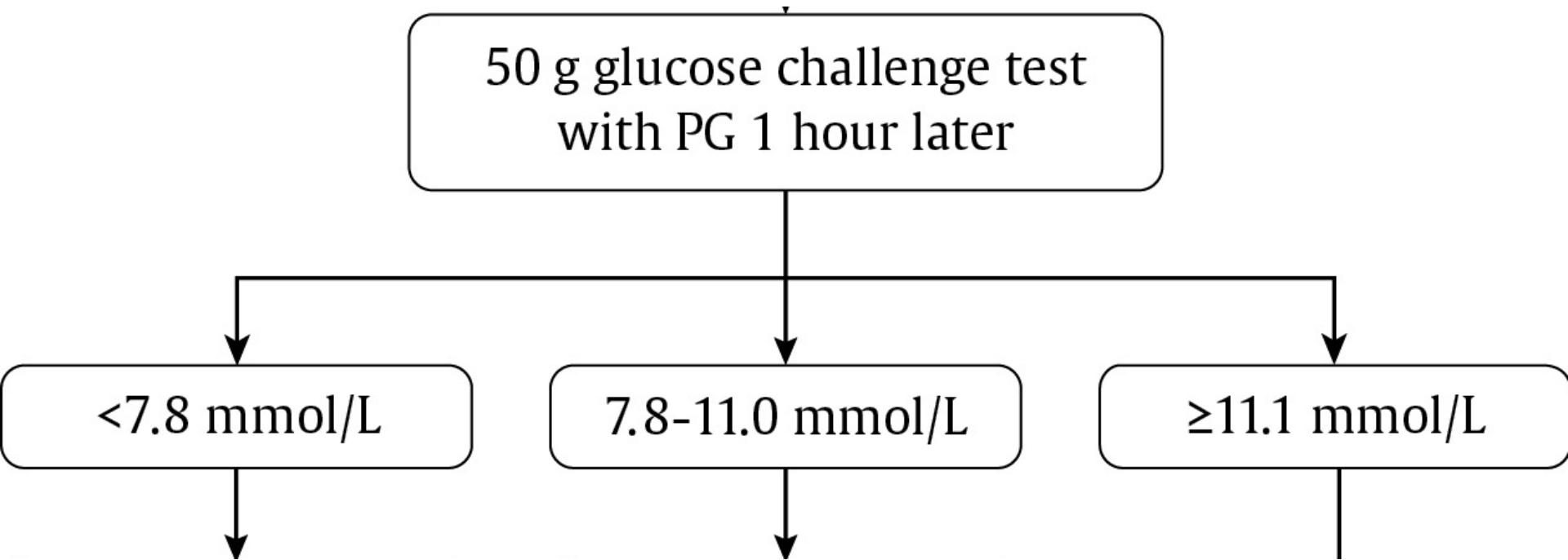


# 2013 GDM Diagnosis: Preferred Approach 2013



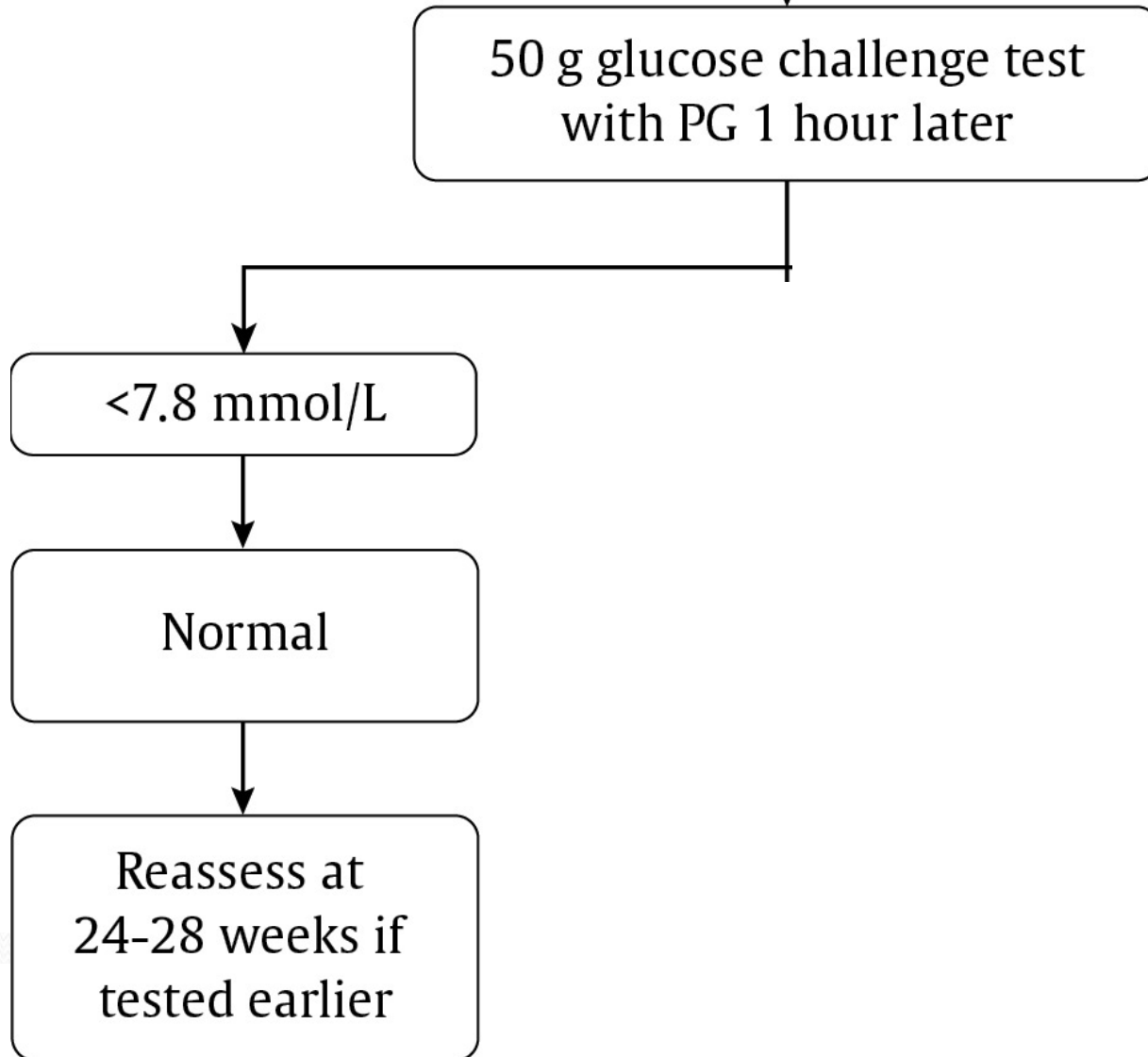


# 2013 GDM Diagnosis: Preferred Approach 2013

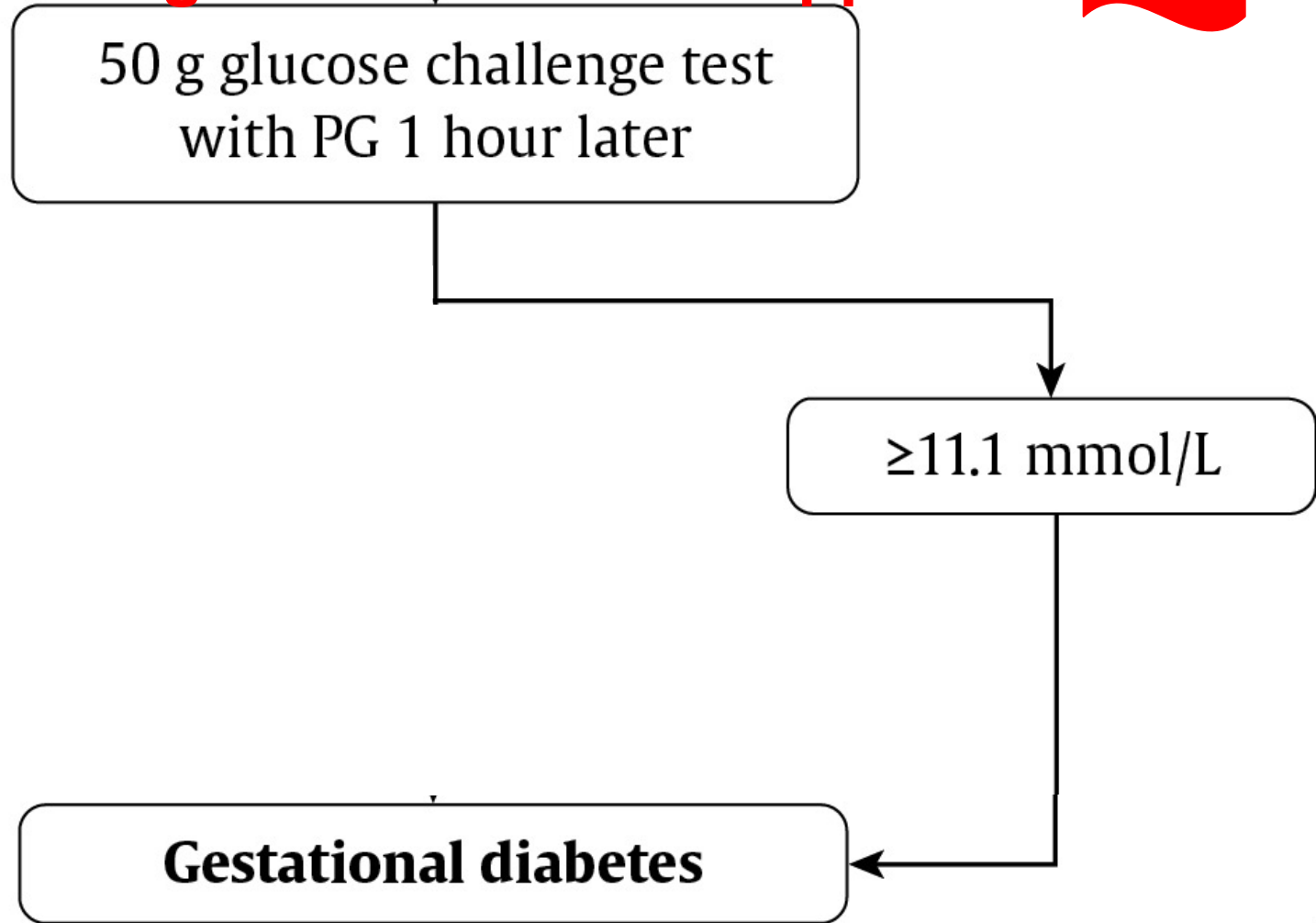


# 2013 GDM Diagnosis: Preferred Approach

2013



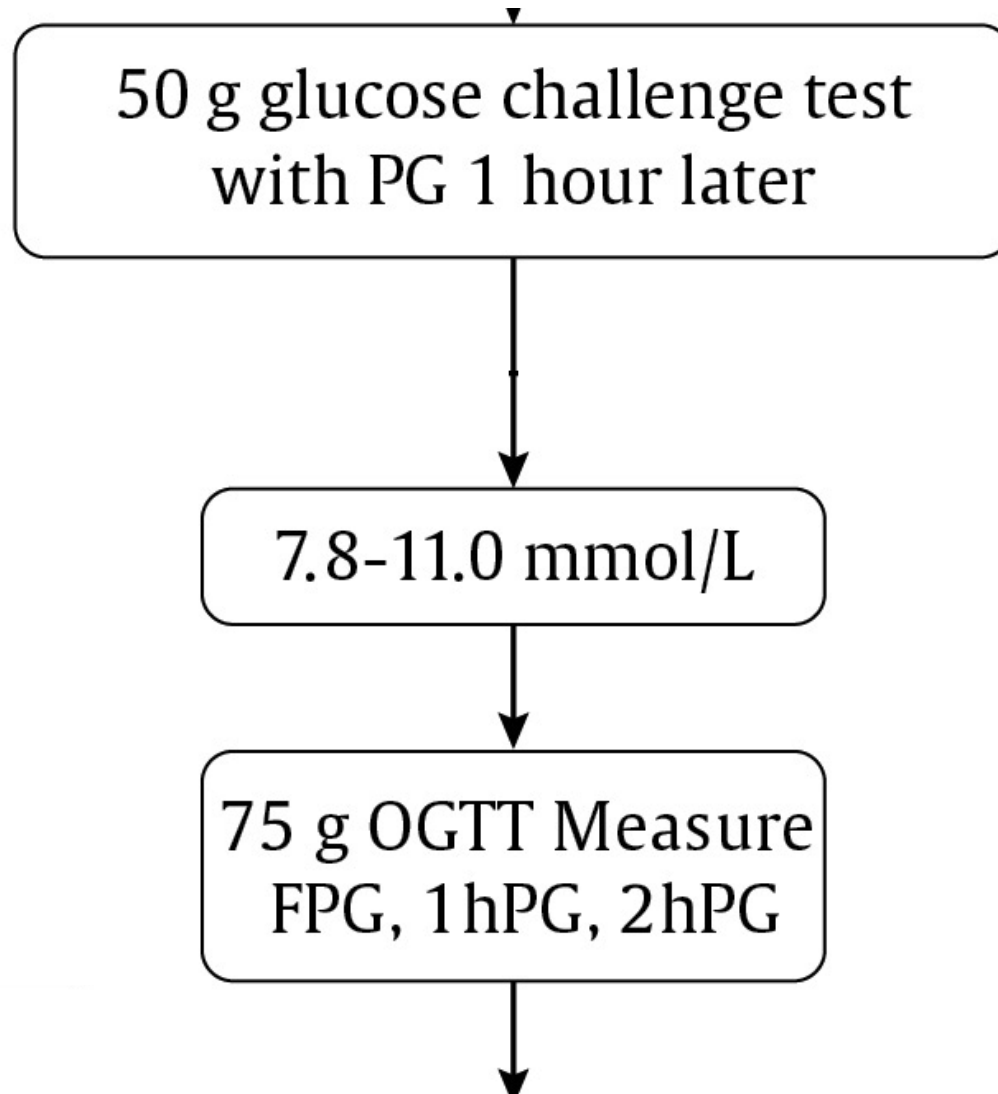
# 2013 GDM Diagnosis: Preferred Approach 2013





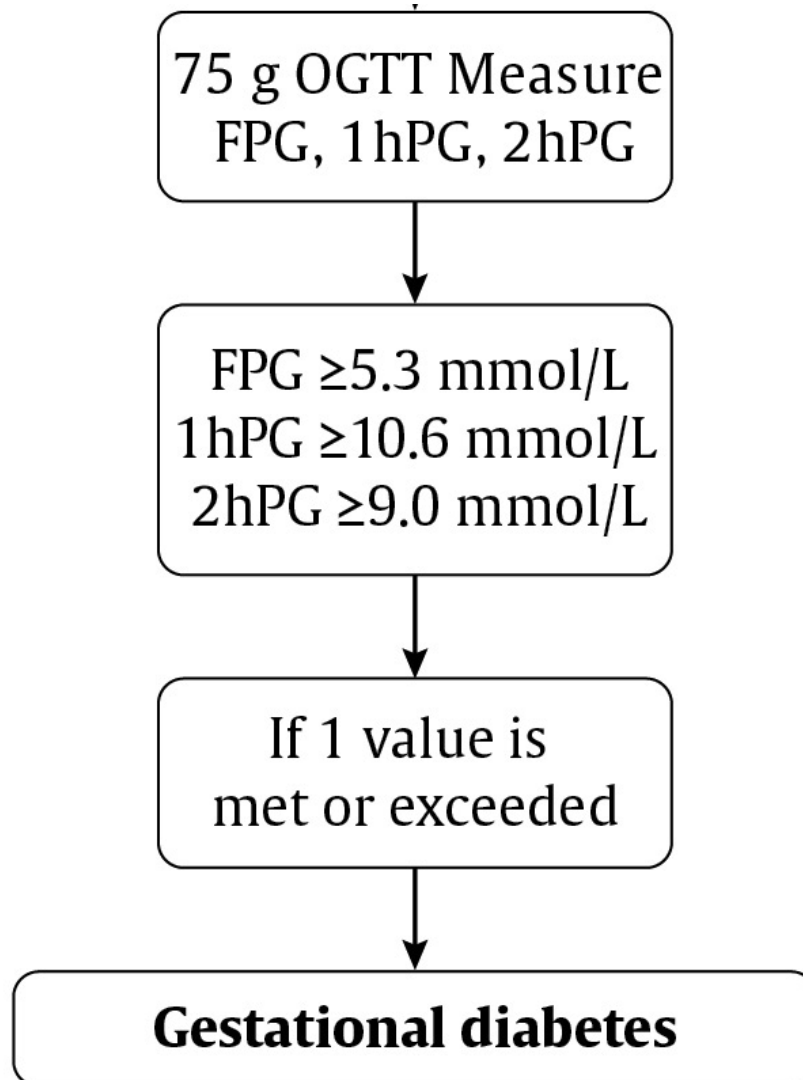
# 2013 GDM Diagnosis: Preferred Approach

2013



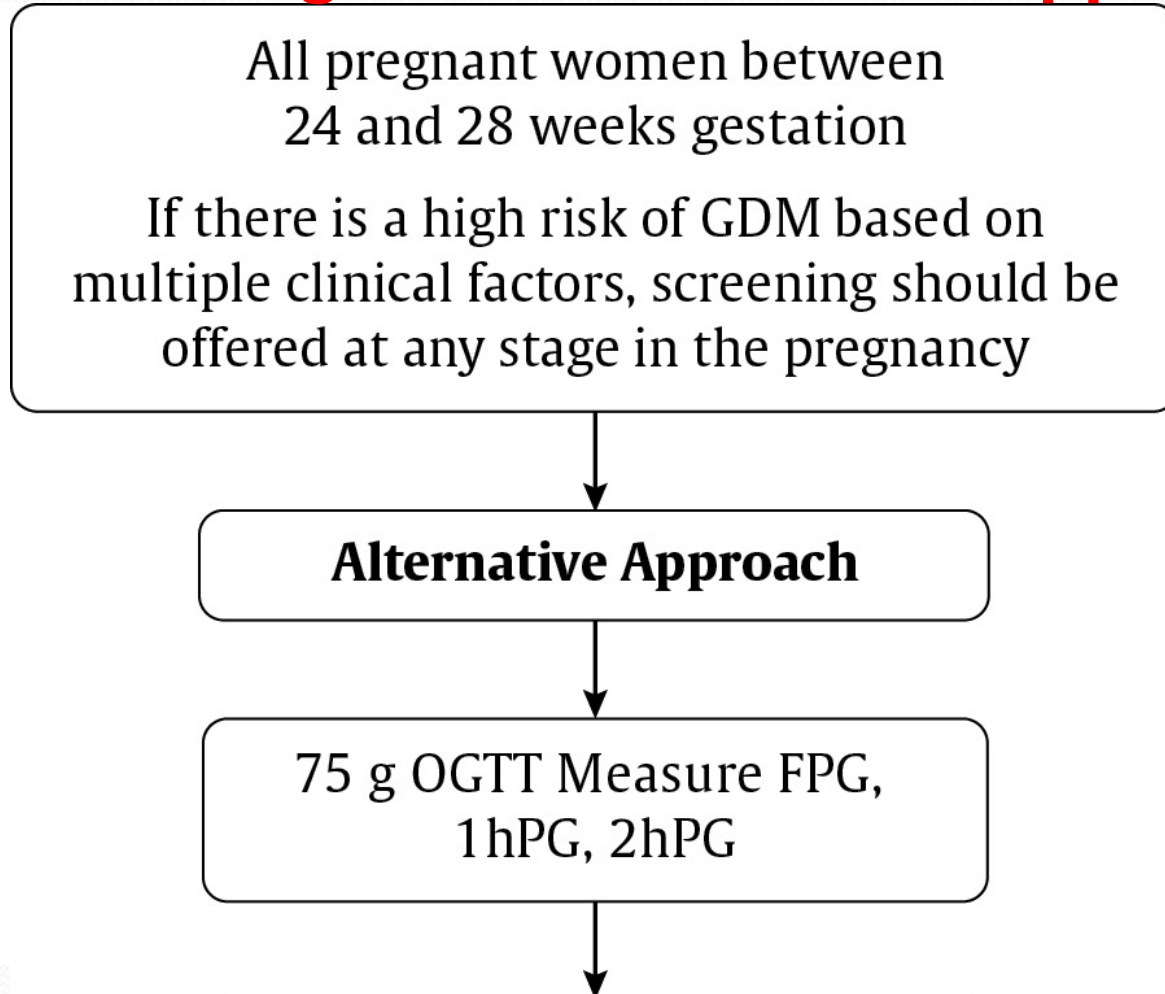
# 2013 GDM Diagnosis: Preferred Approach

2013



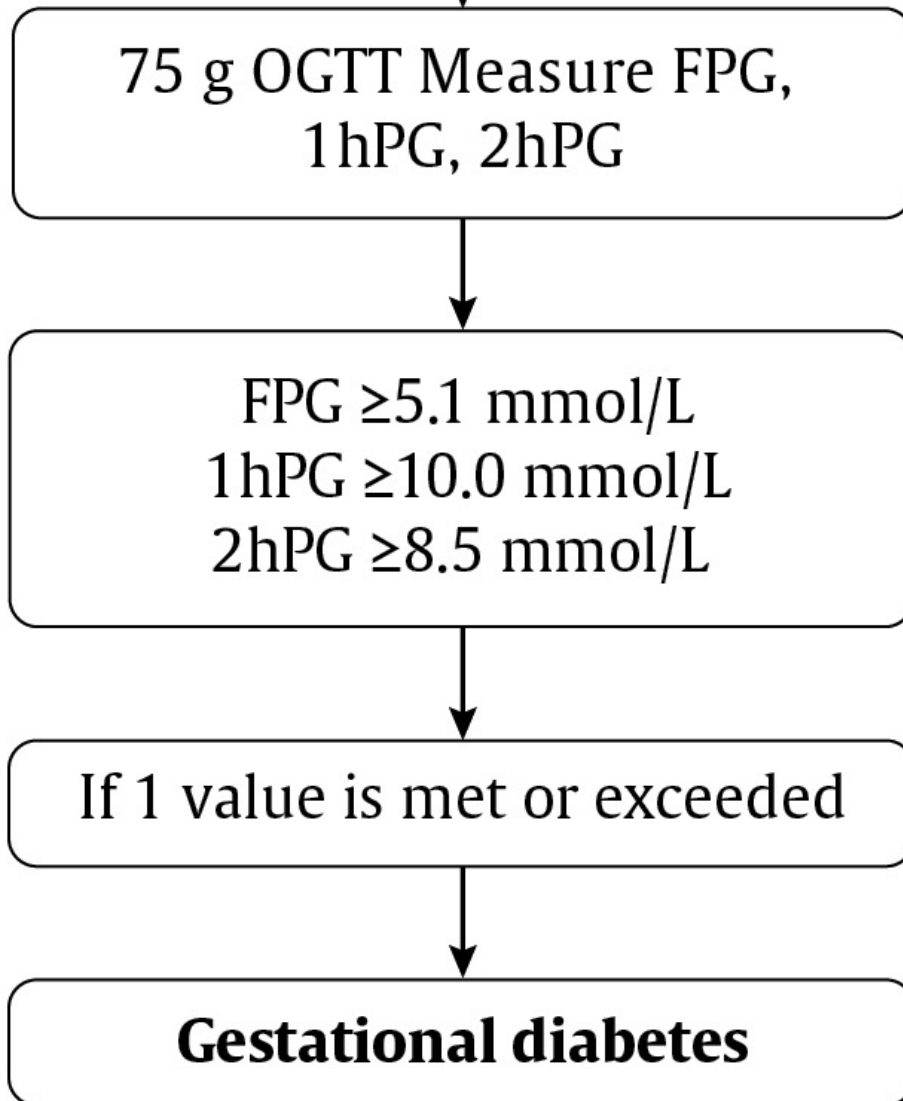
# 2013 GDM diagnosis: Alternative Approach

2013





# 2013 GDM diagnosis: Alternative Approach 2013



## Recommendations 16-17: Diagnosis of GDM

- 16. All pregnant women** should be **screened** for GDM at **24-28 weeks** of gestation [Grade C, Level 3].
17. If there is a **high risk of GDM** based on multiple clinical factors, screening should be offered at any stage in the pregnancy [Grade D, Consensus]. If the initial screening is performed **before 24 weeks** of gestation and is negative, **rescreen between 24-28 weeks** of gestation. (see next slide)

## Recommendation 17: Risk Factors for GDM (continued)

- Age  $\geq 35$  years
- Previous GDM
- Prediabetes
- High risk population
  - Aboriginal, Hispanic, South Asian, Asian, African
- BMI  $\geq 30$  kg/m<sup>2</sup>  
[Grade D, Consensus]
- Polycystic ovarian syndrome
- Acanthosis nigricans
- Corticosteroid use
- History of macrosomic infant
- Current fetal macrosomia or polyhydramnios



## Recommendation 18: Diagnosis of GDM

18. The **preferred approach** for the screening and diagnosis of GDM is the following [Grade D, Consensus]:

- a) Screening for GDM should be conducted using the **50 g glucose challenge test (GCT)** administered in the non-fasting state with plasma glucose measured one hour later [Grade D, Level 4]. A plasma glucose value  $\geq 7.8$  mmol/L at one hour will be considered a **positive screen** and will be an indication to proceed to the 75 gram OGTT [Grade C, Level 2]. A plasma glucose value  $\geq 11.1$  mmol/L can be considered to be **diagnostic** of gestational diabetes and does not require a 75 gram OGTT for confirmation [Grade C, Level 3].

2013

## Recommendation 18: Diagnosis of GDM (continued)

b) If the GCT screen is positive, a **75 gram OGTT** should be performed as the diagnostic test for GDM using the following criteria:  **$\geq 1$  of the following** values:

- Fasting  $\geq 5.3$  mmol/L,
- 1h  $\geq 10.6$  mmol/L,
- 2h  $\geq 9.0$  mmol/L

[Grade B, Level 1]

2013



## Recommendation 19: Diagnosis of GDM

19. An **alternative** approach that may be used to screen and diagnose GDM is the **one-step** approach [Grade D, Consensus]:

a) A **75 gram OGTT** should be performed (with no prior screening 50g GCT) as the diagnostic test for GDM using the following criteria [Grade D, Consensus]:

2013

**≥1 of the following** values:

- **Fasting  $\geq 5.1$  mmol/L,**
- **1h  $\geq 10.0$  mmol/L,**
- **2h  $\geq 8.5$  mmol/L**

[Grade B, Level 1 (4)]



# GDM: Glycemic Management During Pregnancy

- Perform SMBG, both fasting and postprandially
- **Glycemic Targets during pregnancy:**

Target glucose values
Fasting PG <5.3 mmol/L
1h postprandial PG <7.8 mmol/L
2h postprandial PG <6.7 mmol/L

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

# IOM Guidelines for Gestational Weight Gain

Pre-Pregnancy BMI	Recommended range of total weight gain (Kg)	Recommended range of total weight gain (lb)
BMI <18.5	12.5 – 18.0	28 – 40
BMI 18.5 - 24.9	11.5 – 16.0	25 – 35
BMI 25.0 - 29.9	7.0 – 11.5	15 – 23
BMI > or = 30	5.0 – 9.0	11 – 20

Recommended rate of weight gain and total weight gain for singleton Pregnancies according to pre-pregnancy BMI

# What About Insulin Analogues and Oral Agents Among Patients with GDM?

- May use rapid-acting analog insulin for postprandial glucose control – no difference in perinatal outcomes
- **May use glyburide or metformin** for women who are non-adherent to or who refuse insulin
  - Likely safe BUT it is **OFF-Label** → no long-term data, need discussion with patient



## GDM: Glycemic Management During Labour and Delivery

- Keep maternal blood glucose between **4.0 and 7.0** mmol/L → reduce risk of neonatal hypoglycemia
- Women should receive adequate glucose during labour in order to meet the high energy requirements



## Postpartum GDM Management Checklist

- ✓ 1. Encourage **Breastfeeding**
- ✓ 2. **75g OGTT** between **6 weeks - 6 months** postpartum to detect prediabetes or diabetes
- ✓ 3. **Discuss increased long-term risk of diabetes** – Importance of returning to pre-pregnancy weight



## Recommendation 20: Management During Pregnancy (GDM)

20. Women with GDM should:

a. Strive for **target glucose values**:

- **Fasting PG below 5.3 mmol/L** [Grade B, Level 2]
- **1h postprandial below 7.8 mmol/L** [Grade B, Level 2]
- **2h postprandial below 6.7 mmol/L** [Grade B, Level 2]

b. Perform **SMBG**, both fasting and postprandially to achieve glycemic targets and improve pregnancy outcomes [Grade B, Level 2]

c. **Avoid ketosis** during pregnancy [Grade C, Level 3]



## Recommendation 21: Management During Pregnancy (GDM)

21. Receive **nutrition counseling** from a registered dietitian during pregnancy [Grade C, Level 3] and postpartum [Grade D, Consensus]. Recommendations for weight gain during pregnancy should be based on pregravid BMI [Grade D, Consensus].

## Recommendation 22 and 24: Management During Pregnancy (GDM)

22. If women with GDM do not achieve glycemic targets within 2 weeks from nutritional therapy alone, **insulin therapy should be initiated** [Grade D, Consensus].

23. Insulin therapy in the form of **multiple injections** should be used [Grade A, Level 1].

24. **Rapid-acting bolus analog** insulin may be used over regular insulin for postprandial glucose control although perinatal outcomes are similar [Grade B, Level 2].



# Insulin Therapy

- Short acting insulin:
  - Insulin lispro (Humalog) or insulin aspart (NovoRapid) preferred
  - No data on insulin glulicine (Aphidra) in pregnancy yet
- Basal insulin
  - N or NPH currently recommended as first-line, especially for isolated fasting hyperglycemia
  - Insulin Detemir (Levemir) and insulin Glargine (Lantus) are presently being used.
  - No data in GDM



# Insulin

## Mealtime

- Improving glucose control in the mother reduces fetal insulin production
- Best postprandial control with aspart and lispro vs human insulin
- Insulin antibodies were not induced
- Lispro and aspart both approved for use in pregnancy

## Recommendation 25: Management During Pregnancy (GDM)

25. For women who are non-adherent to or who refuse insulin, **glyburide** [Grade B, Level 2] **or metformin** [Grade B, Level 2] may be used as alternative agents for glycemic control. Use of oral agents in pregnancy is **off-label** and this should be discussed with the patient [Grade D, Consensus].



# Insulin Vs Glyburide

In a study of 404 pregnant women receiving either insulin or Glyburide:

Glyburide:

- Does not cross the placenta
- No difference in glucose control

When comparing to insulin:

- No difference in fetal or maternal complications
- Not detected in cord blood
- Limited data on safety

**Meta-analysis** does not show increased risk for major malformations



# Glyburide

- Dosage up to 20 mg od
- Less maternal hypoglycemia
- Undetectable levels in cord blood
- Do not use for fasting hyperglycemia
- Switch to insulin if suboptimal control in 2 weeks
- Need larger RCTs to evaluate neonatal outcomes
- Does glyburide flog the maternal and/or fetal pancreas?

# Metformin

- Crosses the placenta
- Designed for pre-existing diabetes
- Does not appear to exhibit teratogenicity in humans

Patients treated for polycystic ovary syndrome:

- Discontinue metformin when conception is confirmed or at end of first trimester

# Metformin

- Not teratogenic
- No hyperinsulinemia
- No hypoglycemia
- 46.3% of metformin treated women required supplemental insulin
- No increase in adverse events in offspring



# Other Hypoglycaemic Agents

- Incretins
- New generation oral hypoglycaemic:  
(Acarbose, glimepiride, sitagliptin, TZDs, GLP-1s)
  - No data in pregnancy.
  - Lack of fetal safety data

## Recommendation 26: Intrapartum Management (GDM)

2013

26. Women should be closely monitored during **labour and delivery** and maternal blood glucose levels should be kept between **4.0 and 7.0 mmol/L** in order to minimize the risk of neonatal hypoglycemia.  
[Grade D, Consensus]

2013

26. Women should **receive adequate glucose** during labour in order to meet the high energy requirements  
[Grade D, Consensus].



## Recommendation 26: Intrapartum Management (GDM)

2013

26. Women should be closely monitored during **labour and delivery** and maternal blood glucose levels should be kept between **4.0 and 7.0 mmol/L** in order to minimize the risk of neonatal hypoglycemia.  
[Grade D, Consensus]

2013

26. Women should **receive adequate glucose** during labour in order to meet the high energy requirements  
[Grade D, Consensus].



## Recommendation 28: Postpartum (GDM)

2013

28. Women with GDM should be encouraged to **breastfeed** immediately after delivery in order to avoid neonatal hypoglycemia [Grade D, Level 4] and to **continue for at least three months postpartum** in order to prevent childhood obesity [Grade C, Level 3] and reduce risk of maternal hyperglycemia [Grade C, Level 3].
29. Women should be screened with a **75g OGTT** **between 6 weeks and 6 months postpartum** to detect prediabetes and diabetes [Grade D, Consensus].

# Postpartum GDM Follow-up

- 50% will develop type II diabetes mellitus within 15-20 years
- Advise women to exercise regularly, follow a healthy mealplan and maintain a healthy body weight
- Monitor the infant for hypoglycaemia, malformations and neurodevelopment



# Postpartum GDM Follow-Up

- Advise women of the increased risk of developing GDM in a future pregnancy
- Screen for diabetes mellitus prior to a future pregnancy
- Yearly screening for the development of type II diabetes mellitus
- ?Vitamin D3



# Vitamin D3

4000IU daily:

- Fewer infections
- Fewer pre-term labours
- Fewer pre-term deliveries

# Exercise

- Physical activity before and during pregnancy lowers the risk of GDM:
  - 30 minutes daily
- 56% risk reduction of developing gestational diabetes mellitus with exercise during pregnancy
- 69% risk reduction of developing GDM with exercise before and during pregnancy
- Potential for more than 70% of gestational diabetes mellitus prevented

# Gestational Diabetes

## Trends in Incidence of Diabetes in Pregnancy and Serious Perinatal Outcomes: A Large, Population- Based Study in Ontario, Canada, 1996–2010

Denice S. Feig, Jeremiah Hwee, Giliian L. Booth, Baiju R. Shah, Arlene S. Bierman, and Lorraine L. Lipscombe

*\*\*Diabetes Care 2014;37:1590–1596 | DOI: 10.2337/dc13-2717*



# Gestational Diabetes

## OBJECTIVE

Women with diabetes in pregnancy have high rates of pregnancy complications.

To explore trends in the incidence of diabetes in pregnancy and examine whether the risk of serious perinatal outcomes has changed.

# Gestational Diabetes

A population-based cohort study of 1,109,605 women who delivered in Ontario, Canada, between 1 April 1996 and 31 March 2010.

Women were categorized as gestational diabetes (GDM) (n = 45,384), pregestational diabetes (pre-GDM) (n = 13,278), or no diabetes (n = 1,050,943).

The annual age-adjusted rates of diabetes in pregnancy were calculated, and rates of serious perinatal outcomes were compared between groups and by year using Poisson regression.



# Gestational Diabetes

## RESULTS

The age-adjusted rate of both GDM (2.7–5.6%,  $P < 0.001$ ) and pre-GDM (0.7–1.5%,  $P < 0.001$ ) doubled from 1996 to 2010.

The rate of congenital anomalies declined by 23%, whereas the rate of perinatal mortality did not change significantly.

However, compared with women with no diabetes, women with pre-GDM and GDM faced an increased risk of congenital anomalies (relative risk 1.86 [95% CI 1.49–2.33] and 1.26 [1.09–1.45], respectively), and perinatal mortality remained elevated in women with pre-GDM (2.33 [1.59–3.43]).



# Gestational Diabetes

## CONCLUSIONS

The incidence of both GDM and pre-GDM in pregnancy has doubled over the last 14 years

The overall burden of diabetes in pregnancy on society is growing.

Although congenital anomaly rates have declined in women with diabetes, peri-natal mortality rates remain unchanged, and the risk of both remains significantly elevated compared with nondiabetic women.

Increased efforts are needed to reduce these adverse outcomes.

# Conclusions

- Therapy for GDM may improve fetal outcome
- Need for early, aggressive therapy with intensification in a timely fashion
- Decrease in infant morbidity and mortality
- With treatment, IUFD is uncommon.



# Conclusions

- 10% of women with gestational diabetes mellitus are undiagnosed type II diabetics.
- 2-3% of woman remain diabetic post-partum.
- 50% chance of progression to type 2 diabetes in 15-20 years.
- 90% chance of progression to type 2 diabetes mellitus within their lifetime.



# Recommendations for health

- Reduction of both maternal and paternal obesity
- Optimize glucose control during pregnancy
- Timing is everything
- Pre-conception nutrition and lifestyle
- Early postnatal nutrition of low birth weight infants
- Reduce early exposure to pollutants, drugs, plastics, etc
- Prioritize breastfeeding
- Avoid overfeeding low birth weight babies

# Reassessment

True or False:

1. Gestational diabetes is a time-limited disorder of pregnancy which resolves postpartum.
2. A diagnosis of gestational diabetes is secured when there are 2 or more abnormal glucose values on a 75g 2-hr gestational screen.
3. Women with gestational diabetes have an increased risk for the development of Type I diabetes.



## **Gestational diabetes: Take-Home Messages**

- CDA Guidelines has been instituted in Canada but they are confusing!!!
- Women at high risk should be screened for diabetes mellitus prior to her pregnancy or in her first trimester (South Asian population).
- Gestational diabetes mellitus is type 2 diabetes mellitus of pregnancy and is often associated with the metabolic syndrome.



# **The Future Risk of Diabetes**

## **The Mother**



Questions....



Thank You...



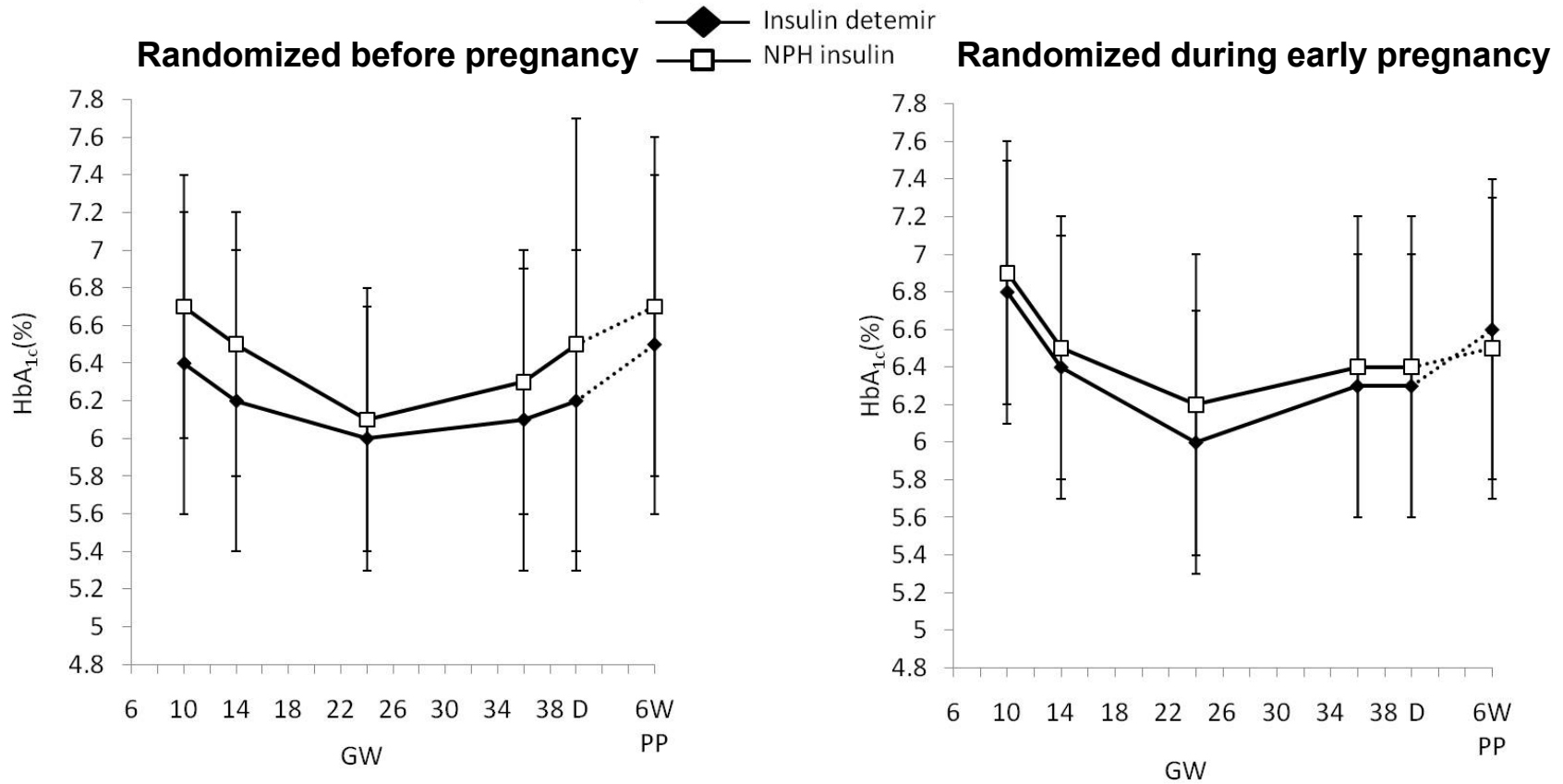


# Additional Slides

# **Insulin in Pregnant Patients with Type 1 Diabetes**

- **Perinatal Outcomes in a Randomized Trial Comparing Insulin Detemir with NPH Insulin in 310 Pregnant Women with Type 1 Diabetes**
- A prospective, randomized, controlled, parallel-group, open-label trial was to compare the efficacy and safety of insulin detemir (IDet) vs. NPH insulin (both with mealtime insulin aspart) in type 1 diabetic pregnancy.

# Insulin Detemir vs. NPH Insulin in Pregnant Patients with Type 1 Diabetes





## Perinatal Outcomes in Pregnancy: Insulin Detemir vs. NPH insulin in Women with Type I Diabetes

Outcome	Insulin Detemir	NPH Insulin
Pregnancy outcomes within the trial	142	145
Live births, n	128	136
Mean birth weight (g)	3504	3571
Mean birth length (cm)	51.2	51.7
Mean gestational age at delivery (weeks)	38.2	37.8
Preterm delivery (< 37 weeks), %	20.3%	26.5%
Small for gestational age (< 10 <sup>th</sup> percentile), %	2%	1%
Large for gestational age (> 90 <sup>th</sup> percentile), %	46%	54%
Macrosomia > 4000 g, %	19%	26%
<b>Incidence of composite endpoint*</b>	<b>62.7%</b>	<b>66.2%</b>

Live born infants with birth weight <10<sup>th</sup> or >90<sup>th</sup> percentile for gestational age (GA) and sex; preterm delivery (<37 gestational weeks); early fetal demise (<22 GWs); perinatal mortality; neonatal mortality; or presence of major congenital malformations.



## **Insulin in Pregnant Patients with Type 1 Diabetes**

When administered to pregnant women with type 1 diabetes, insulin Detemir is as well-tolerated as NPH with respect to perinatal morbidity and mortality.



# **Insulin in Pregnant Patients with Type 1 Diabetes**

Maternal Efficacy and Safety Outcomes in a Randomized Trial Comparing Insulin Detemir with NPH Insulin in 310 Pregnant Women with Type 1 Diabetes




## Maternal Efficacy and Safety Outcomes

Outcome	Insulin Detemir	NPH Insulin
N=	152	158
Estimated mean FPG (mmol/L): GW 24	5.38	6.32
Estimated mean FPG (mmol/L): GW 36	4.76	5.41
Hypoglycemia Rates (episodes per year)		
Overall Major	1.1	1.2
Overall minor	104.4	101.0
Nocturnal Major	0.3	0.2
Nocturnal Minor	15.6	17.4

## **Maternal Efficacy and Safety Outcomes**

- In summary, lower FPG, but comparable HbA1c in late pregnancy were obtained using insulin detemir in comparison to NPH insulin in women with type 1 diabetes.
- Not powered for congenital abnormalities
- No studies in GDM.



# Insulin Glargine: Maternal Outcomes in Pregnant Women Using Insulin Glargine compared with NPH Insulin: A Meta-analysis



Outcome	Studies / women	Mean difference (glargine - NPH)	Odds Ratio	95% CI
Weight at delivery (kg)	4 / 546	-0.82	-	-6.79 to 5.15
Weight gain (kg)	5 / 495	0.16	-	-1.03 to 1.35
A1C - 1 <sup>st</sup> trimester (%)	4 / 301	-0.08	-	-0.64 to 0.49
A1C - 3 <sup>rd</sup> trimester (%)	6 / 538	-0.01	-	-0.07 to 0.05
Maternal hypoglycemia - severe	5 / 472	-	0.84	0.18 to 3.79
Pre-eclampsia	8 / 702	-	0.55	0.23 to 1.32
Caesarean section	6 / 608	-	1.04	0.72 to 1.52
Gestational / new-onset hypertension	4 / 360	-	0.49	0.20 to 1.20