MAYO CLINIC

University of Nebraska Medical Center
Nebraska Medicine

# DIABETES & PREGNANCY

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2024 Diabetes Update

 

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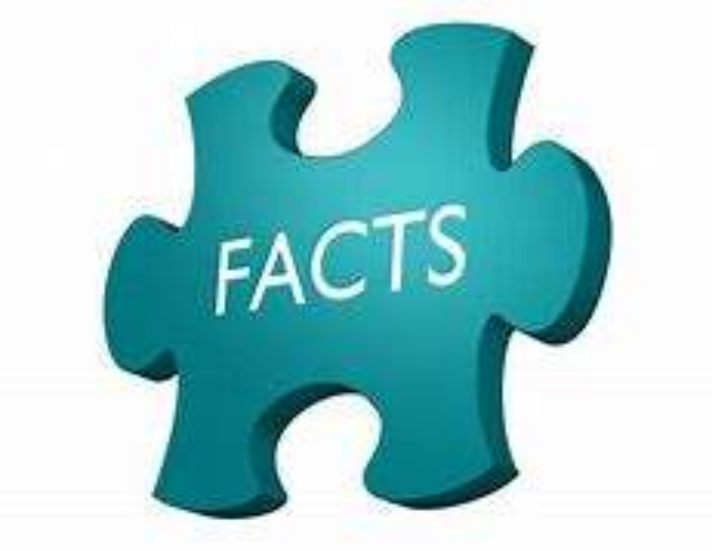
# NO RELEVANT DISCLOSURES

# RATIONALE: DIABETES AS A WOMEN'S HEALTH ISSUE

- ✓ Estimated that 11% of Americans have diabetes
- ✓ >50% of persons with diabetes are women
- ✓ Prevalence is 2-4 times higher among black, Hispanic, American Indian and Asian/Pacific Islander women compared to white women
- ✓ Women with diabetes lose their premenopausal protection from ischemic heart disease
- ✓ Women with diabetes who develop IHD have worse survival and QOL measures
- ✓ Women are at greater risk for blindness due to diabetes than men




*ADA https://diabetes.org/about-diabetes/statistics/about-diabetes*
*Diabetes & Women's Health Across the Life Stages: A Public Health Perspective. CDC.*

# DIABETES IN PREGNANCY

**Pregestational**

1-2% pregnancies in USA

Type 1, Type 2 etc.

**Gestational Diabetes Mellitus (GDM)**

8-12% pregnancies in USA

| GDM Diagnostic Criteria @ 24-28 weeks | Number abnormal values | Oral Glucose Load | Glucose cut-offs, mg/dL (mmol/L) |
|---|---|---|---|
| Two-step strategy<br>Non-fasting CGT | 1 | 50 | ≥130,135, or 140 (7.2,7.5, or 7.8) |
| Followed by either:<br>1. Carpenter and Coustan | ≥2 | 100 | Fasting ≥95 (5.3)<br>1-h ≥180 (10.0)<br>2-h ≥155 (8.6)<br>3-h ≥140 (7.8) |
| 2. NDDG | ≥2 | 100 | Fasting ≥105 (5.8)<br>1-h ≥190 (10.6)<br>2-h ≥165 (9.2)<br>3-h ≥145 (8.0) |
| One-step strategy:<br>2010 IADPSG / 2013 WHO | ≥1 | 75 | Fasting ≥92 (5.1)<br>1-h ≥180 (10.0)<br>2-h ≥153 (8.5) |

If OGTT not suitable (Eg. Post roux-en-Y) - monitor for 2 weeks and assume GDM if not meeting >80% glucose targets

# SHOULD WE SCREEN FOR DIABETES IN PREGNANCY BEFORE THE USUAL 24-28 WEEK GDM SCREEN?

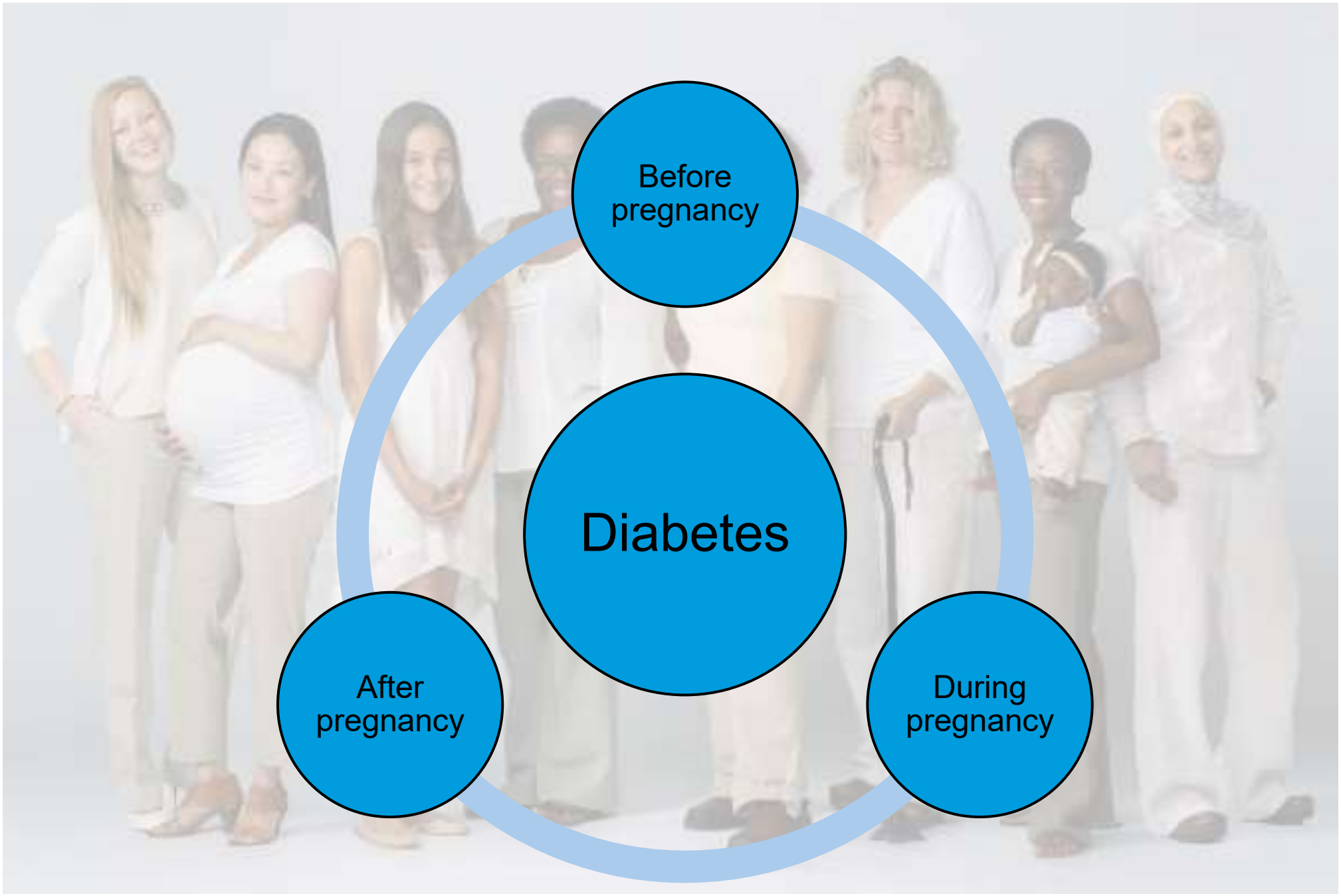
Reasonable to rule out T2DM with HbA1c +/- fasting glucose at initial OB visit

If no evidence of T2DM can screen for GDM at usual time of 24-28 weeks gestation

If A1c 5.9 – 6.4% or fasting glucose 110-125mg/dL: ↑ risk for GDM, nutrition counseling and block testing *(ADA Standards of Care 2024)*

Practice point: No strong evidence to continue metformin for PCOS after 1st trimester in absence of hyperglycemia



# BEFORE PREGNANCY

# PREGNANCY PLANNING
## & DIABETES

*Caroline (24y), was diagnosed with T1D aged 7. She is using a Tandem T Slim X2 pump in automode with a Dexcom G6 CGM.*

*HbA1c is 7.3% with minimal hypoglycemia*

*No known diabetes-related complications, last retinal screen 19 months prior*

*An intrauterine contraceptive device is in place, but Caroline expresses a desire to have it removed and become pregnant.*

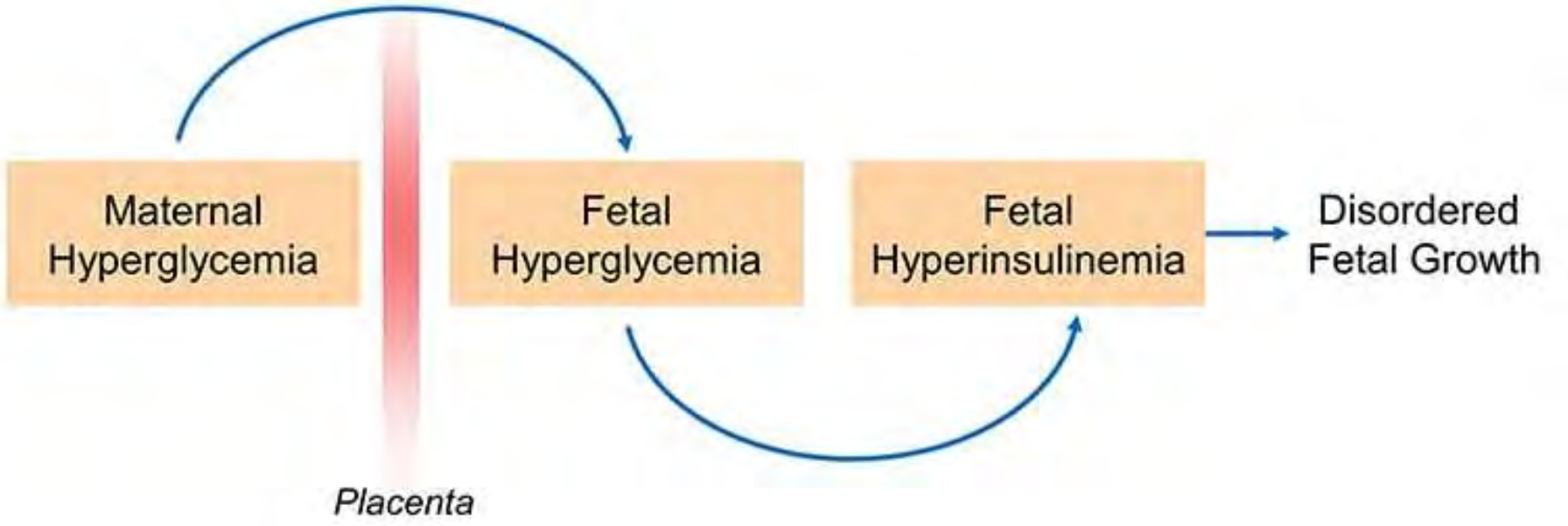
*She has had no prior pregnancies.*

*Issues to consider……..?*

# DIABETES & PREGNANCY

## THE PEDERSEN HYPOTHESIS



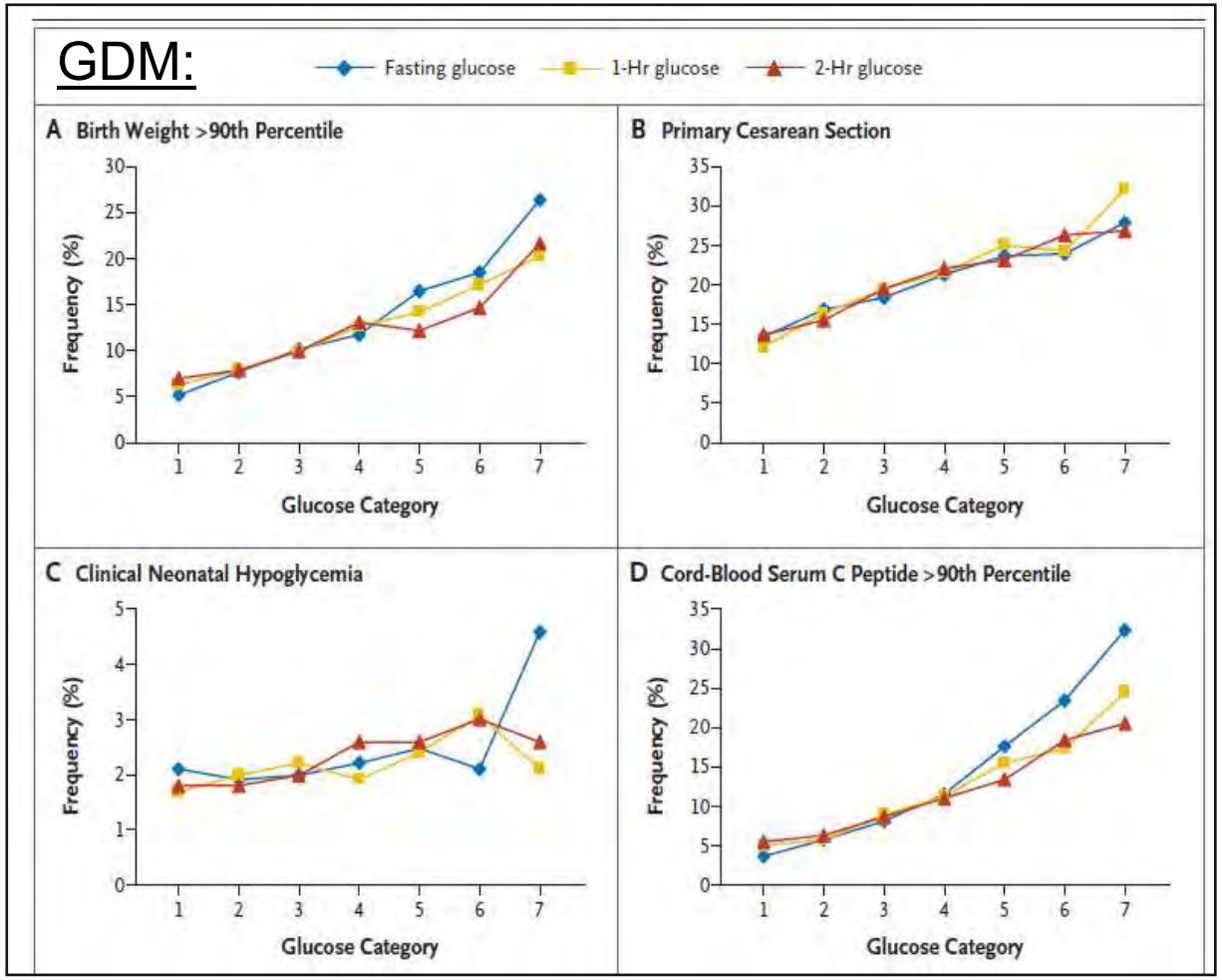

*Pedersen PhD thesis, 1952*

# ASSOCIATED ADVERSE OUTCOMES

Type 1 and Type 2 (odds ratio):

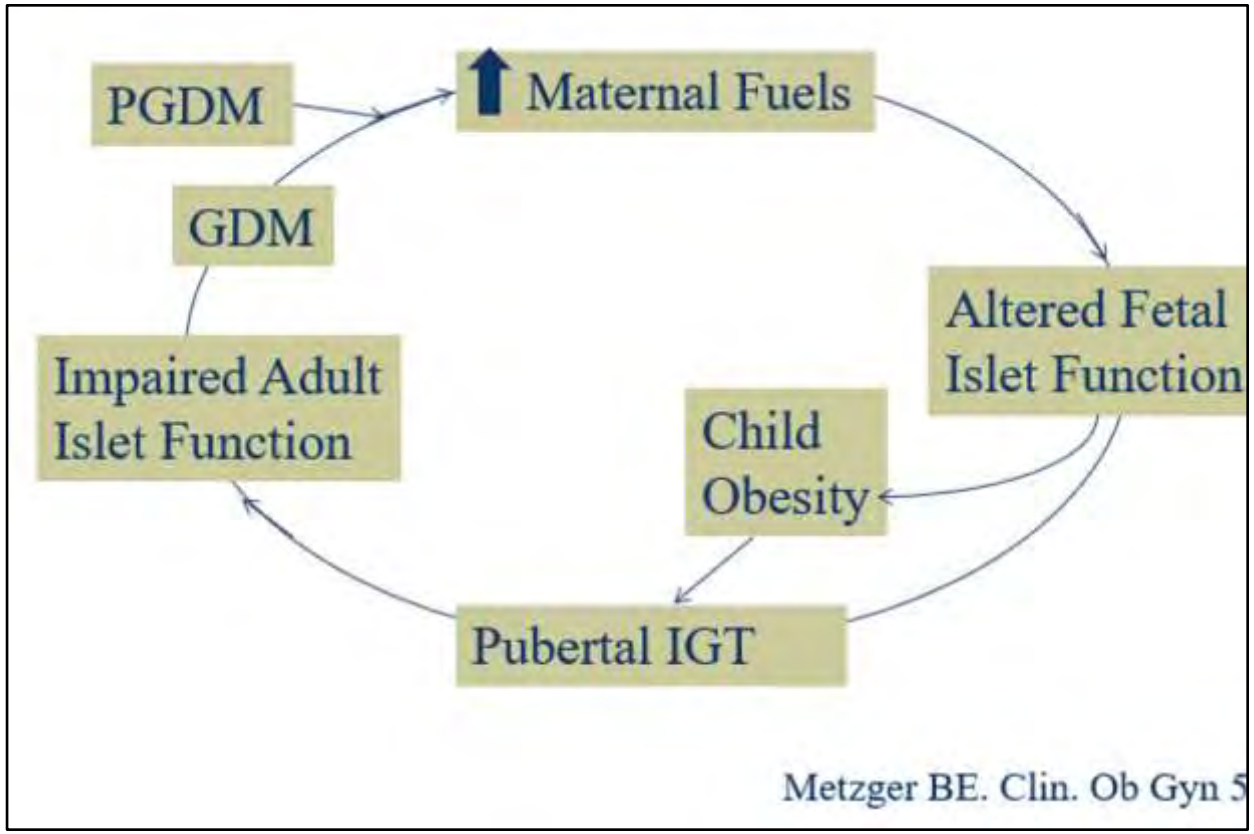
| | |
|---|---|
| Preeclampsia: | 3.48 (3.01-4.02) |
| Cesarean: | 3.52 (2.91-4.25) |
| Stillbirth: | 3.52 (3.19-3.88) |
| Anomalies: | 6.98 (5.93-11.32) |
| Macrosomia: | 1.91(1.74-2.10) |
| Neonatal Hypo: | 26.6 (15.37-46.11) |




*Yu et al, Oncotarget 2017*
*Correa et al, Am J Obstet Gynecol. 2008*
*The HAPO Study. N Engl J Med 2008;358:1991-2002.*

# LONG TERM EFFECT




# BEGIN INTERVENTIONS BEFORE PREGNANCY

Preconception counseling: inform of risks and avoid unplanned pregnancy

*AND*

Prepregnancy/Preconception care: targeted support and additional clinical care offered to women with diabetes planning pregnancy

Average 6 months duration

Delivered by a multidisciplinary team

*Murphy et al. Diabetes Care 2010*
*Egan et al. JCEM 2016*

# PPC COMPONENTS

## Preconception Education:

- ✓Nutrition
- ✓Lifestyle
- ✓Diabetes self-management – goal A1c <6.5%
- ✓Expectations during pregnancy
- ✓Supplementation

## Medical Assessment & Plan:

- ✓Overall health, review of medications (note: statins, GLP-1, SGLT-2I, ACR/ARB, adjust therapies)
- ✓Screening and treatment of diabetes complications
- ✓Ob/Gyn History +/- Specialty Involvement

*ADA Standards of Care, 2024; Egan et al. Mayo Clinic Proceedings 2020*

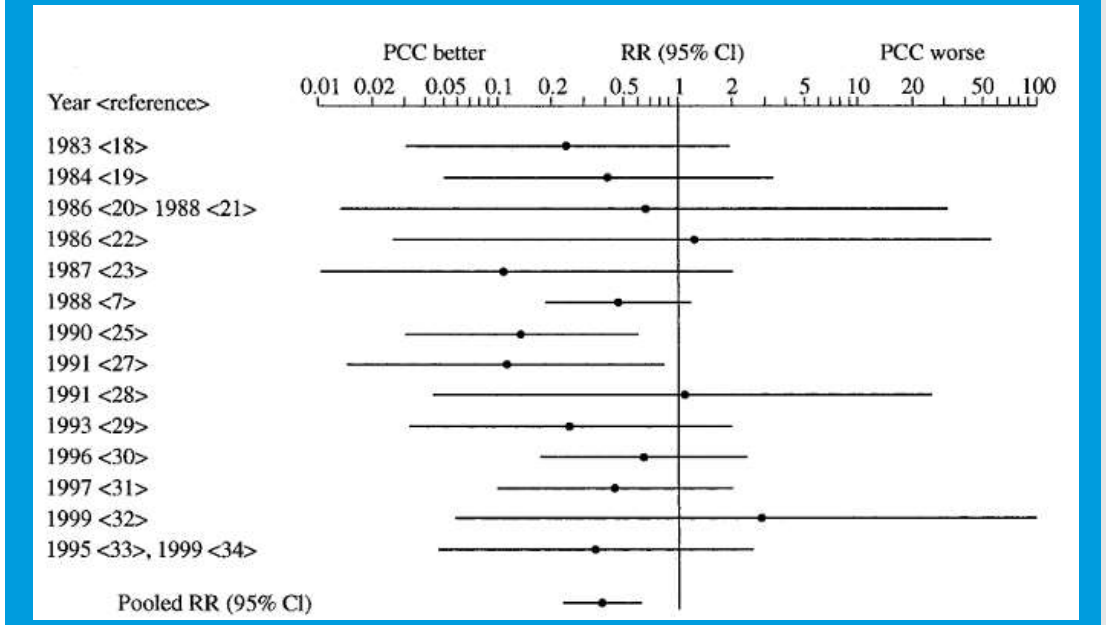
 

# PPC

Meta-analysis

- 14 cohort studies; 1970 – 2000; pre-gestational diabetes
- 1,192 offspring with PPC and 1,479 without PPC

- 9 studies, pooled difference in mean HbA1c -2.3% (95% CI -2.1 to -2.4%) for PPC




Congenital anomalies with PPC 2.1% vs 6.5% without

RR 0.36, 95% CI 0.22-0.59

*Ray, O'Brien, Chan, QJM 2001*

# PREGNANCY PLANNING
## & DIABETES

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*She has had no prior pregnancies.*

 

# PREGNANCY PLANNING
## & DIABETES

- ✓Define a timeline
- ✓Provide a supportive, educational environment
- ✓Safe lowering of A1c <6.5%
- ✓Up to date screening
- ✓Start folic acid supplementation
- ✓Routine labs and thyroid function

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# DURING PREGNANCY

# DETERMINING THE PLAN FOR PREGNANCY

*Tamika (36y) has type 2 diabetes and is 8W4D gestation. This is her 3rd pregnancy, and had GDM in her most recent pregnancy.*
*Her HbA1c is 8.2% on metformin 1000mg bid*
*Her sugars are 120-140mg/dL fasting in the morning, and 140-180mg/dL 2-hours after meals*

*She wonders about continuous glucose monitoring, and highlights that she wishes to avoid insulin if possible*

*What to recommend……..?*

# NON-PHARMACOLOGIC

## Dietary modifications

Dietician review (DRI) – complex high fiber carbs 40% total cal (min 175g), 20% protein, 40% fat (saturated fat <7% total cal)

Promote fetal/maternal health, achieve glycemic & GWG goals

| Pre-pregnancy BMI ($kg/m^2$) | Recommended total weight gain range (kg) |
|---|---|
| Underweight (<18.5) | 12.5 - 18.0 |
| Normal weight (18.5 - 24.9) | 11.5 - 16.0 |
| Overweight (25.0 - 29.9) | 7.0 - 11.5 |
| Obese (≥30.0) | 5.0 - 9.0 |

## Regular exercise

30 minutes moderate intensity aerobic exercise, 5 days/week

Walk for 10-15 mins after each meal.

*ACOG Feb 2018*
*Egan et al, JCEM 2014*
*IOM 2009*

# GLYCEMIC GOALS & MONITORING

Fasting glucose <95mg/dL

*and*

1-hr postprandial <140mg/dL

*or*

2-hr postprandial <120mg/dL

HbA1c <6.0-6.5%

Educate on DKA risk (17% fetal loss) and risk of hyperglycemia with steroids

Hypoglycemia treatment (<63mg/dL)

*Dhanasekaran….Egan JCEM 2022*

# CONTINUOUS GLUCOSE MONITORING

CONCEPTT

Pregnant Users using CGM

- ✓ HbA1c -0.19%, p=0.02
- ✓ Time in target 68% (versus 61%, p=0.28
- ✓ Comparable hypoglycemia
- ✓ LGA (OR 0.51, p=0.02)
- ✓ NICU >24 hours (OR 0.48, p=0.02)
- ✓ Neonatal hypoglycemia (OR 0.45, p=0.03)
- ✓ 1-day shorter hospital stay (0.01)

*Feig et al. Lancet 2017*

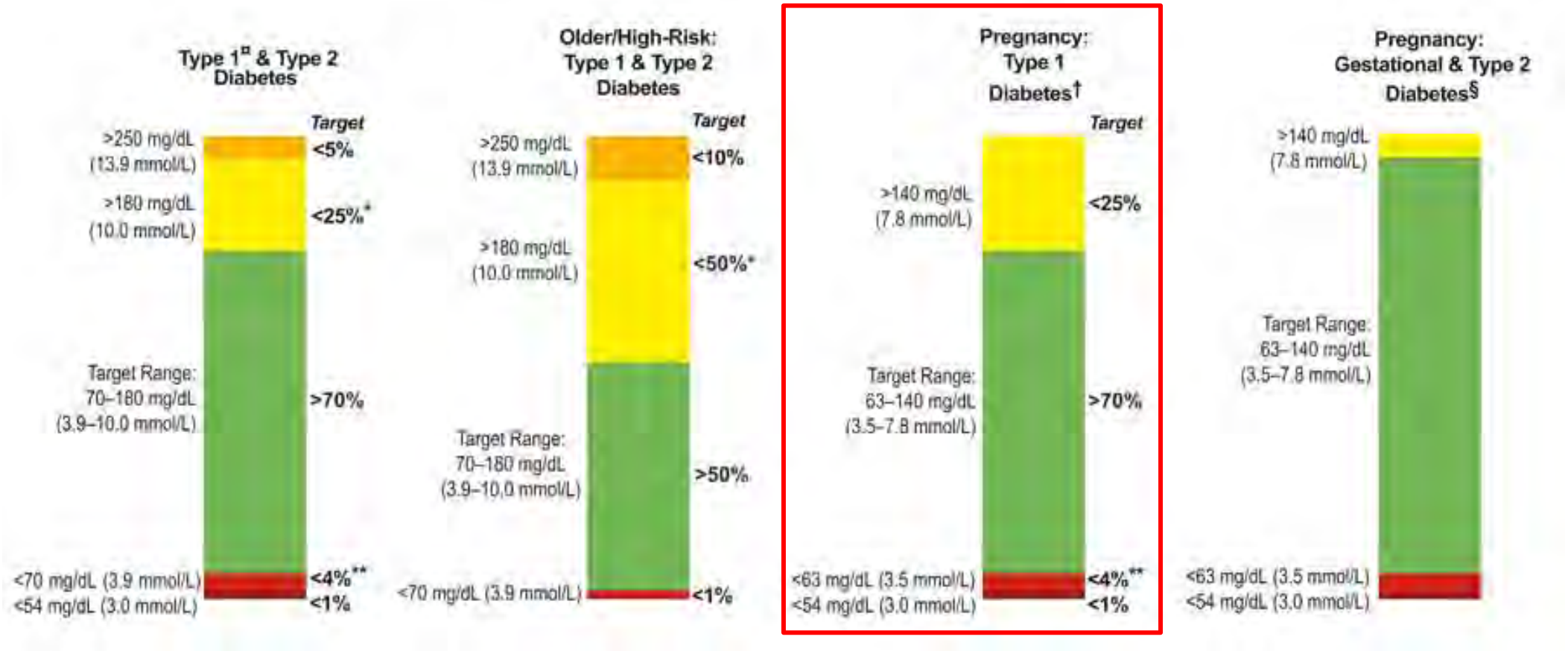
Increasing use of CGM systems (Freestyle Libre 2,3, Dexcom G7 approved)

ADA

- CGM is recommended for type 1 diabetes in pregnancy
- CGM metrics may be used as an adjunct but should not be used as a substitute for pre and post meal monitoring of blood glucose to achieve optimal pre- and postprandial glycemic targets in Type 1 diabetes

# GLYCEMIC TARGETS – TIME IN RANGE




*Note: Although frequently used in clinical practice, there is no high-quality evidence to support CGM in women with GDM or T2DM*

*Battelino et al. Diabetes Care 2019*

# PHARMACOLOGY: WHAT TO CHOOSE?

## Type 1

Multiple daily injection regimen or insulin pump

Long and rapid acting insulin analogues

## Type 2 / GDM

Insulin preferred (needed in Type 2)

Long and rapid acting insulin analogues/NPH

Oral Agents:

Metformin

Glyburide

# PREGNANCY SAFE PHARMACOTHERAPY

| Insulin | Time to Onset | Peak Effect | Effect Duration |
|---|---|---|---|
| ***Rapid*** | | | |
| Aspart (Novolog) (B) *[Fiasp]* | 10-15 mins | 1-2 hours | 3-4 hours |
| Lispro U-100/200 (Humalog) (B) | 10-15 mins | 1-2 hours | 3-4 hours |
| Glulisine (Apidra) (C) | 10-15 mins | 1-2 hours | 3-4 hours |
| ***Intermediate*** | | | |
| NPH (B) | 2-4 hours | 4-6 hours | 8-12 hours |
| ***Long*** | | | |
| Detemir (Levemir) (B) | 1-2 hours | None | 6-24 hours |
| Glargine (Lantus) U-100 (C) | 1-2 hours | None | 22-24 hours |
| Glargine (Lantus) U-300 (C) | >6 hours | None | 22-24 hours |
| Degludec (Tresiba) U-100/300 (C) | 1 hour | None | 42 hours |

Metformin (B) and Glyburide (C) are options in GDM and T2DM

# IF STARTING INSULIN DE NOVO

Look at glucose patterns

If predominantly fasting hyperglycemia, start 8-10 units of basal insulin at night

If predominantly post meal hyperglycemia, start 4 units of insulin before meals

May need to start both at the same time

Insulin absorption is delayed after 20 weeks gestation

- Up to 20 weeks: bolus 15 +/- 10 mins pre meals
- After 20 weeks: bolus 45 +/- 15 mins pre meals

Frequent adjustments is the key

# INSULIN THERAPY TYPE 1 DIABETES

MDI & Pump are both effective, typically don't start pump during pregnancy

*Hybrid closed-loop systems are not approved for use in pregnancy (except for CamAPS Fx)*

*Can switch off once pregnancy confirmed but if using consider:*

*1. Using lowest glucose target possible*

*2.Frequent corrections ( "fake carbs") but not more than 2 hourly*

*3. Utilizing low glucose suspend features*

*4. Consider "super-bolus"*

*5. Update presets regularly*

# APPROACH TO DOSING

## Basal rate adjustment:

At least 1-2 hours before the inflection point on a CGM trace.

Aim for no more than six basal time blocks per 24 hours and avoid short (less than 1-2 hour) blocks

## Basal:bolus ratio:

Up to 20 weeks of gestation: 50:50 to 35:65

Beyond 20 weeks of gestation: 35:65 to 25:75

## Insulin:carbohydrate (I:C) ratio:

Usually adjust by 20%

Up to 20 weeks of gestation: breakfast 300/TDD, other meals 400/TDD

Beyond 20 weeks of gestation: breakfast 200/TDD, other meals 300/TDD

# ORAL AGENTS IN T2DM

Typically, not capable of overcoming the insulin resistance of pregnancy in T2DM

Metformin and sulfonylureas cross the placenta

One major metformin trial no major glyburide trial in type 2 diabetes

# Metformin in women with type 2 diabetes in pregnancy (MiTy): a multicentre, international, randomised, placebo-controlled trial

*Denice S Feig, Lois E Donovan, Bernard Zinman, J J Sanchez, Elizabeth Asztalos, Edmond A Ryan, I G Fantus, Eileen Hutton, Anthony B Armson, Lorraine L Lipscombe, David Simmons, Jon F R Barrett, Paul J Karanicolas, Siobhan Tobin, H David McIntyre, Simon Yu Tian, George Tomlinson, and Kellie E Murphy, on behalf of the MiTy Collaborative Group**

Women with Type 2 diabetes on insulin, 6-22 weeks gestation
Metformin 1000mg bid or placebo, added to insulin

253 participants assigned to metformin, 249 to placebo: 2 wk dose titration

Metformin treated:

- ✓ Better HbA1c at 34 weeks' gestation (5·90% *vs* 6·10%; p=0·015)
- ✓ Required less insulin (1·1 units/kg/day *vs* 1·5 units/kg/day, p<0·0001),
- ✓ gained less weight (7·2 kg *vs* 9·0 kg, p<0·0001)
- ✓ fewer caesarean births (53% vs 63%, p=0·031)

# MITY TRIAL

30 (13%) infants in the metformin group and 15 (7%) in the placebo group were small for gestational age

(RR 1·96 [1·10 to 3·64]; p=0·026)

? Direct effect of metformin

GI side effects similar between groups

….Clinical practice effects??

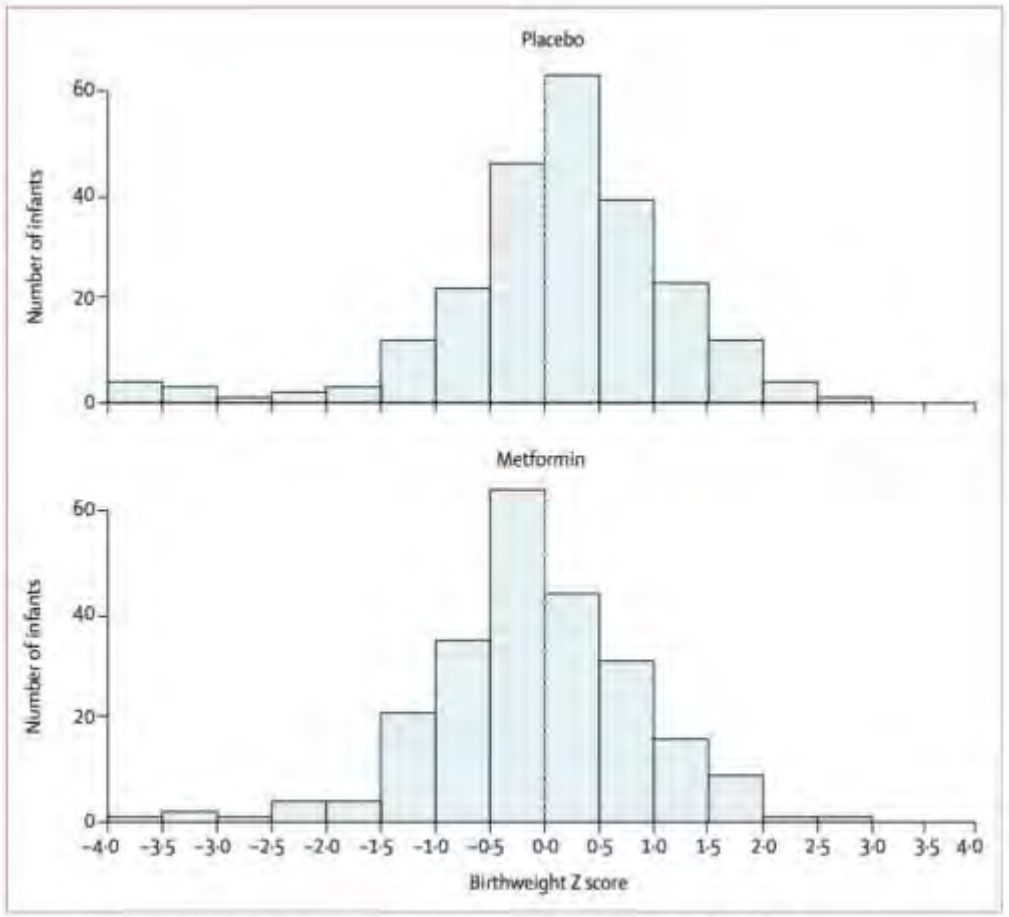



*Figure 2:* **Birthweight distributions in infants of women in the metformin and placebo groups**

# ORAL AGENTS IN TYPE 2 DIABETES

## Guidelines:

*ACOG: "For those women with type 2 diabetes who decline insulin, those who their obstetricians or obstetric care providers believe will be unable to safely administer insulin, or those who cannot afford insulin, metformin (and rarely glyburide) is a reasonable alternative choice in the context of discussing with the patient the limitations of the safety data and a high rate of treatment failure, which requires insulin supplementation"*

*ADA: "Insulin is the preferred treatment for type 2 diabetes in pregnancy"*

*ACOG practice bulletin no 201*
*ADA Standards of Care 2024*

# ORAL AGENTS IN GDM

Metformin and glyburide cross the placenta

Trials reveal reasonable safety and efficacy in GDM, but insulin is preferred as first line

# META-ANALYSIS

## Metformin v Insulin:

No difference in neonatal outcomes

↑ preterm birth (RR 1.5) but ↓

gestational hypertension (RR 0.53) and maternal weight gain (1.3kg)

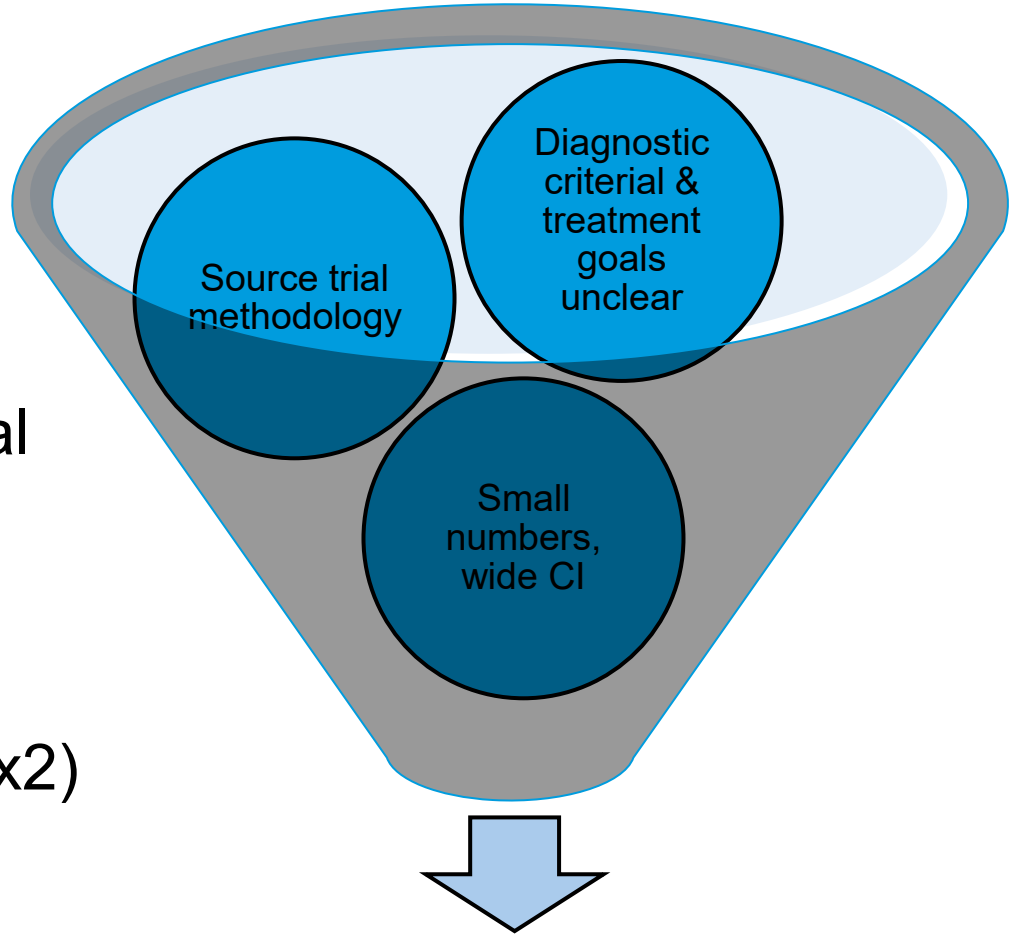
## Glyburide v Insulin:

↑ birthweight (100g), ↑ neonatal hypoglycemia (x2)

## Glyburide v Metformin:

↑ birthweight with glyburide (200g)

No difference in neonatal hypoglycemia




? Robust Results

*Balsells et al BMJ 2015*

# GUIDELINES ON ORAL GLUCOSE-LOWERING AGENTS FOR GDM

| Professional Organization | Preferred | Alternative |
|---|---|---|
| ACOG | Insulin | Metformin |
| ADA | Insulin | Metformin / Glyburide |
| SMFM | Insulin / Metformin | Glyburide |

# DETERMINING THE PLAN FOR PREGNANCY

*Tamika (36y) has type 2 diabetes and is 8W4D gestation. This is her 3rd pregnancy, and had GDM in her most recent pregnancy.*
*Her HbA1c is 8.2% on metformin 1000mg bid*
*Her sugars are 120-140mg/dL fasting in the morning, and 140-180mg/dL 2-hours after meals*

*She wonders about continuous glucose monitoring, and highlights that she wishes to avoid insulin if possible*

*What to recommend……..?*

# DETERMINING THE PLAN FOR PREGNANCY

Reasonable to start CGM, but don't loose focus on pre- and post- meal targets

Insulin will be needed for optimal control

Renew focus on diet (↓ variability post meals)
Exercise

MDT support

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# Nephropathy

May result in:

1. Development of severe hypertension with deterioration in renal function
2. Preterm delivery due to ↑ BP or PE
3. IUGR due to placental dysfunction

Treatment:

1. Prepregnancy stabilization e.g. transplant
2. Glycemic control
3. Low-dose aspirin (continue/initiate at 12 wk)
4. BP: Methyldopa, labetalol, nifedipine (thiazides/loop diuretics with caution)

Watch for rise in BP (>135/90) and urinary albumin (>300mg/24hours)

*Mathiesen et al. CJASN 2012*

# Retinopathy

Risk factors for progression:

| | OR | CI | *P* value |
|---|---|---|---|
| Duration of diabetes | 1.04 | 0.99–1.10 | 0.12 |
| Diabetes type | 0.47 | 0.15–1.54 | 0.21 |
| 1st trimester HbA1c | 0.83 | 0.53–1.30 | 0.42 |
| HbA1c reduction between 1st & 3rd trimester | 2.05 | 1.09–3.87 | 0.03 |
| Systolic BP at booking | 1.03 | 1.01–1.06 | 0.02 |

Aim to stabilize pre-pregnancy

Follow each trimester or per ophthalmology

*Egan et al. J Diabetes Res. 2015*

 

# LABOR & DELIVERY

Hourly glucose testing & IV insulin if required

Glucose target 70-100mg/dL

Can continue pump (dependent on available expertise and protocol)

Neonatology review of infant after delivery

Exclude neonatal hypoglycemia with capillary glucose 2-4 hours post delivery

Tube feeding / IV dextrose if <36mg/dL despite feeding

*Egan et al. MCP 2020*

 

# POST-PARTUM

# POSTPARTUM
## TYPE 1 & 2 DIABETES

Glucose:

<140mg/dL fasting / before meals

<180mg/dL random

NB: Hypoglycemia avoidance

Postpartum regimen in the medical record pre delivery

Endocrine Consult during admission

Support breastfeeding

Close follow up, contraception

Insulin:

70% of pre-pregnancy doses or

Stop insulin & use correction scale to assess requirements if not on pre-pregnancy insulin

Resume hybrid closed loop systems on dismissal – hard resets may be necessary if continued throughout pregnancy

Metformin:

Can be restarted if not used during pregnancy

Other non-insulin agents C/I

 

# QUESTION

Camila, a 44-year-old woman had gestational diabetes during her last pregnancy 5 years ago which resolved on postpartum testing. She had routine labs completed and her HbA1c is now 7% with a fasting glucose of 142mg/dL. She is not on any glucose-lowering medication. Camila identifies as Hispanic.

Which of the following are true:

1. As Camila is female, her risk of diabetes-related blindness is lower than her male counterparts
2. Camila's ethnicity placed her at 2-4 times higher risk of diabetes compared to White women
3. Camila should have received metformin therapy following pregnancy to reduce her risk of progression to type 2 diabetes
4. As Camila is female, she experiences cardiovascular protection in the context of diabetes



 

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# POSTPARTUM
## GDM

Resolves following delivery

GDM recurrence is 50%

T2DM Risk >60% lifelong

75g OGTT 4-12 weeks postpartum

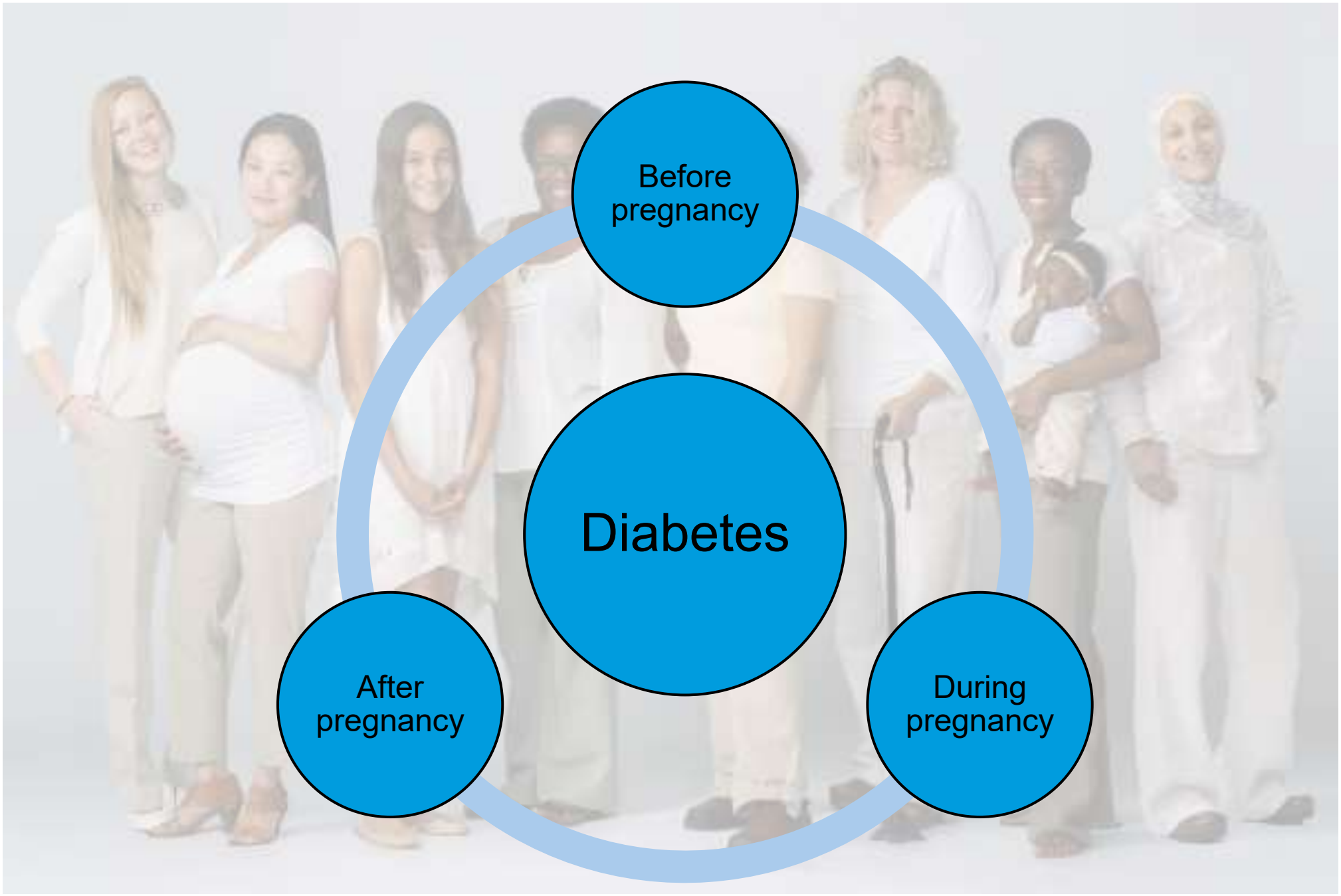
Annual testing thereafter

*Egan et al J Clin Med 2021*

## ACTION AREAS

- ✓Support breastfeeding
- ✓Contraception
- ✓Metformin if prediabetes
- ✓Weight management
- ✓Early pregnancy screening for diabetes




# QUESTIONS & ANSWERS

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