Pregnancy Complicated by Pregestational Diabetes

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Disclosures

- Consultant for: Abbott, NovoNordisk, Sanofi
- Advisor to: Bayer, Eli Lilly, Madrigal

Objectives

- Discuss the prevalence of pregestational diabetes
- Review family planning for those with diabetes
- Explore treatment options for those with pregestational diabetes
- Discuss treatment options in delivery and postpartum
- Discuss treatment in reproductive-age women who have T2DM and complications

Epidemiology

- Approximately 9% of women in the US have T2DM
  - 35% of newly diagnosed are of reproductive age
- Pregestational diabetes affects 1-2% of all pregnancies
- Diabetes increases maternal and fetal risks
  - Fetal anomalies
  - Spontaneous abortion
  - Preeclampsia
  - Fetal demise
  - Macrosomnia
  - Neonatal hypoglycemia
  - Child obesity and T2 diabetes mellitus

Case Study

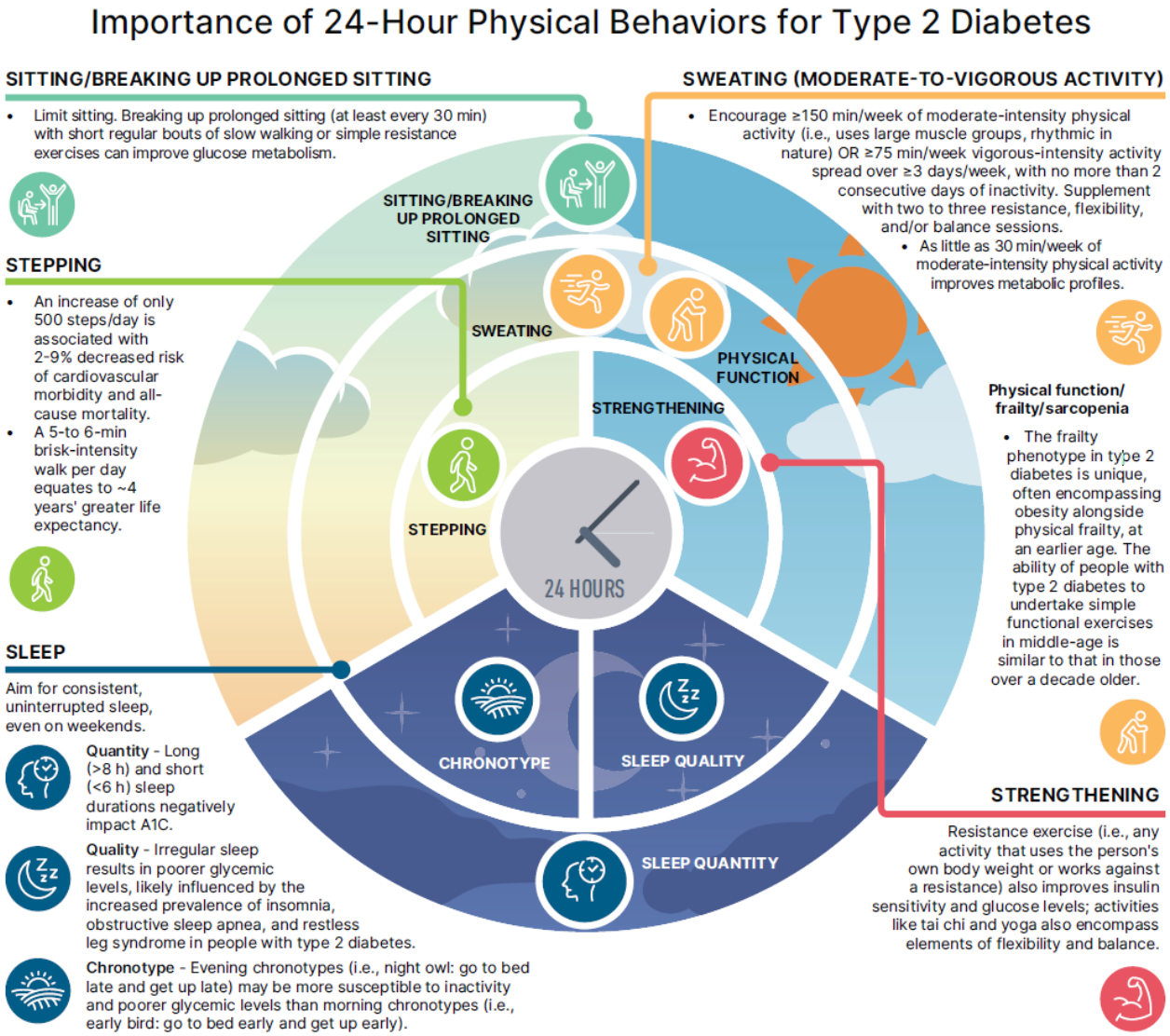
- A 28-year-old female presents to you for type 2 diabetes management. She reports that she had GDM before (2 years ago), but it never went away. She has had gaps in her care, so she presents as a new patient to you. She was advised to get her diabetes under control before she conceives again.
- Past Med Hx: GDM, Type 2 DM, MASLD, dyslipidemia, obesity, P4G2
- Medications: metformin 1000mg bid
- No vitamins, herbs or supplements
- Allergies: no medication, latex, or food allergies

Case Study continued

- She is checking 1-2 times per day
  - Fasting 140-180
  - Postprandial 150-220
  - No hypoglycemia
- The only other medication tried was insulin during pregnancy
- Physical Exam
  - BMI 35, BP 130/78
  - Trace edema lower extremities
  - Exam otherwise normal
- A1c: 8.9% with a glucose of 249 mg/dl pp in the office

Case Study Questions

- Are there any questions you want to ask this patient?
- How would you start treatment?
- What is your HbA1c goal?
- What are the pharmacologic choices?



	Glucose/ insulin	Blood pressure A1C	A1C	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

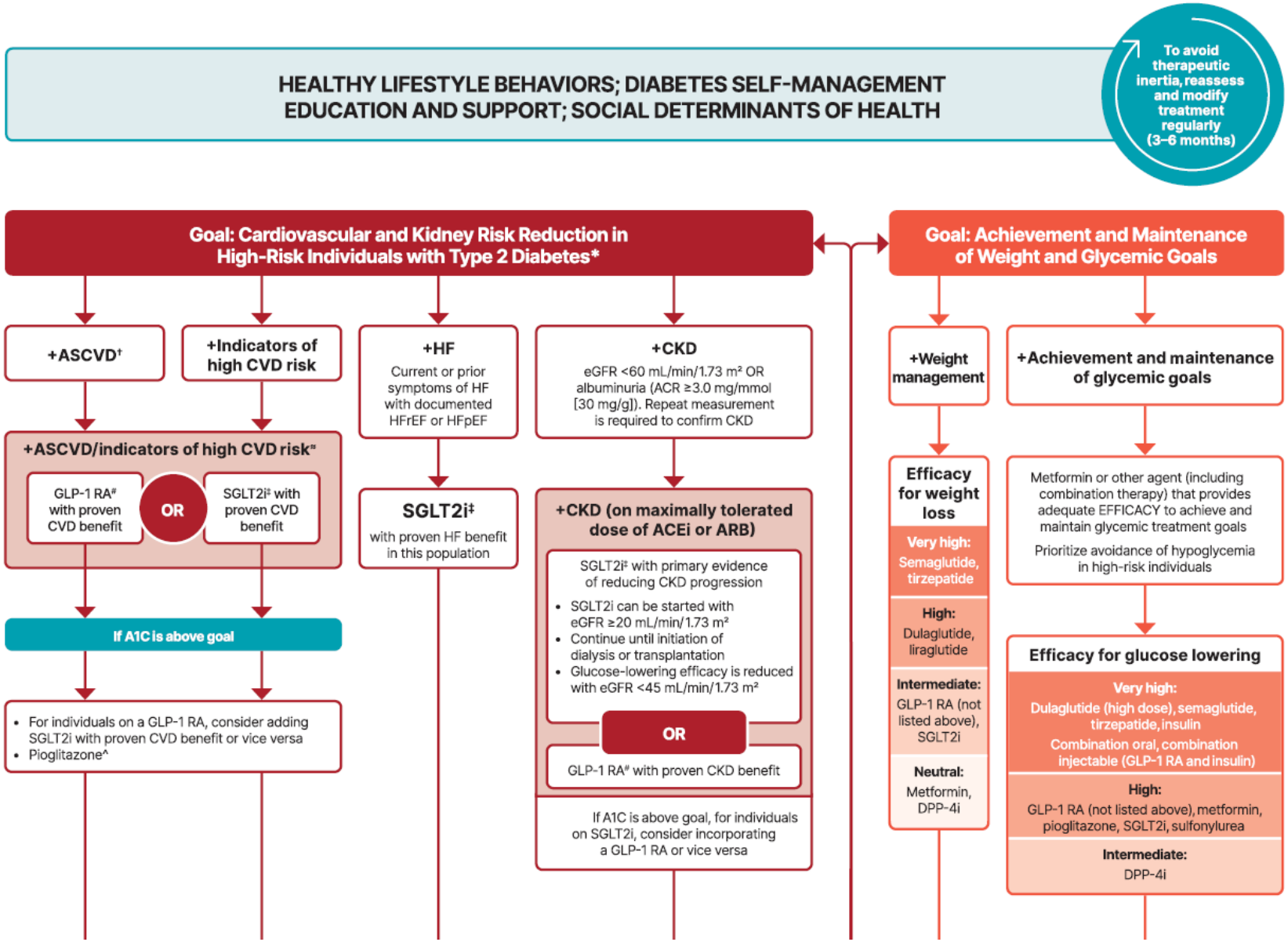
IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ Higher levels of improvement (physical function, quality of life) ↓ Lower levels of improvement (glucose/insulin, blood pressure, A1C, lipids, depression)
? No data available
↑ Green arrows = strong evidence ↑ Yellow arrows = medium-strength evidence ↑ Red arrows = limited evidence

Figure 5.2—Importance of 24-h physical behaviors for type 2 diabetes. Adapted from Davies et al. (75).

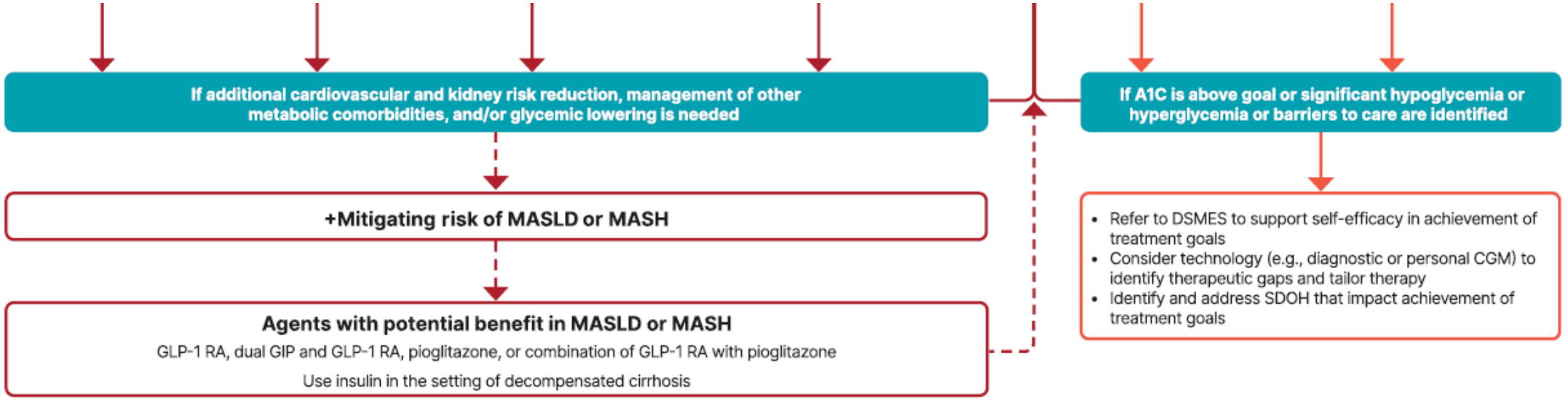
Facilitating Positive Heath Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes - 2025*. *Diabetes Care* 2025;48(Suppl. 1):S86-S127

Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



Pharmacologic Approaches to Glycemic Treatment:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S181-S206

Figure 9.3 (continued)



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of background use of metformin or A1C.

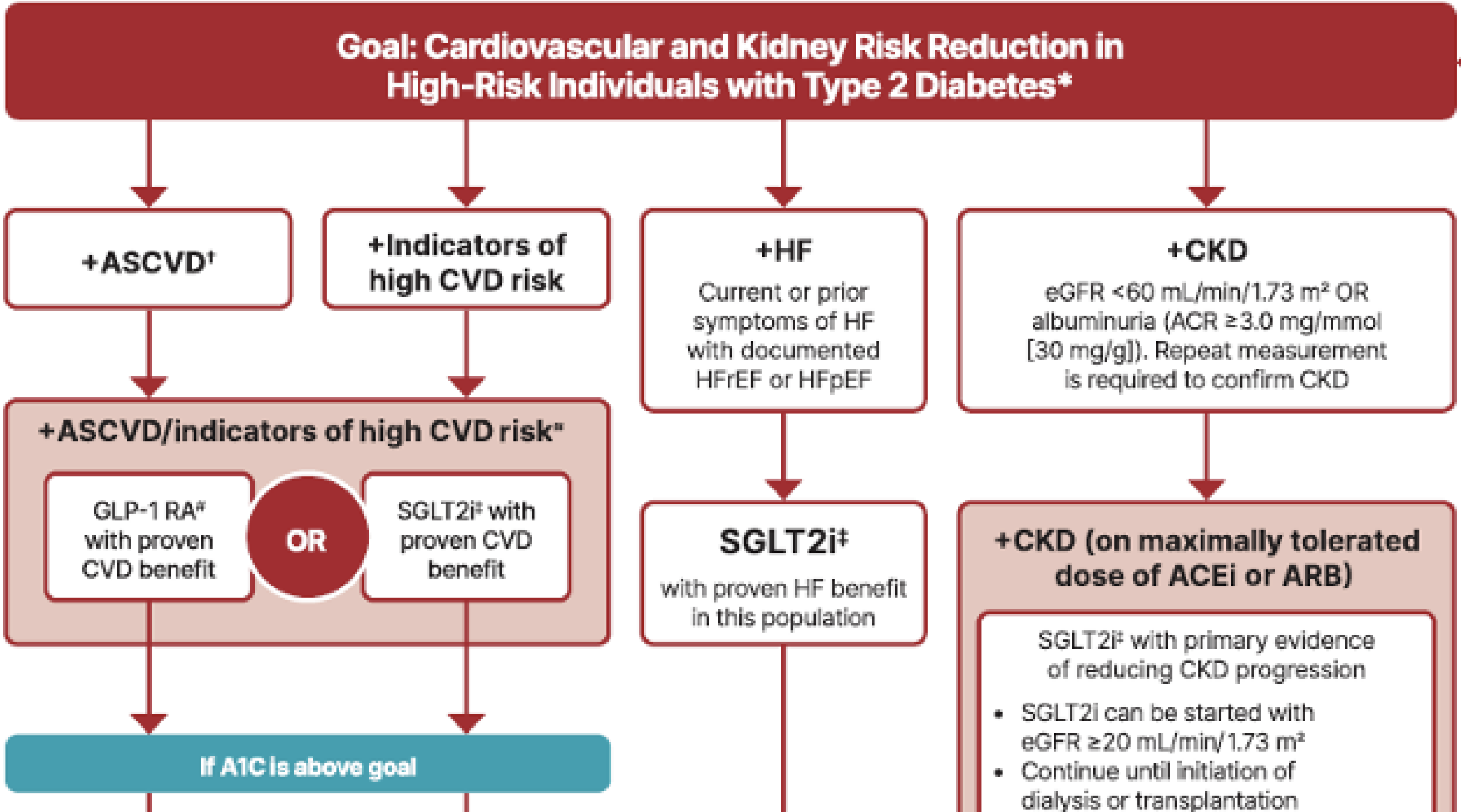
† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

≈ A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high-risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

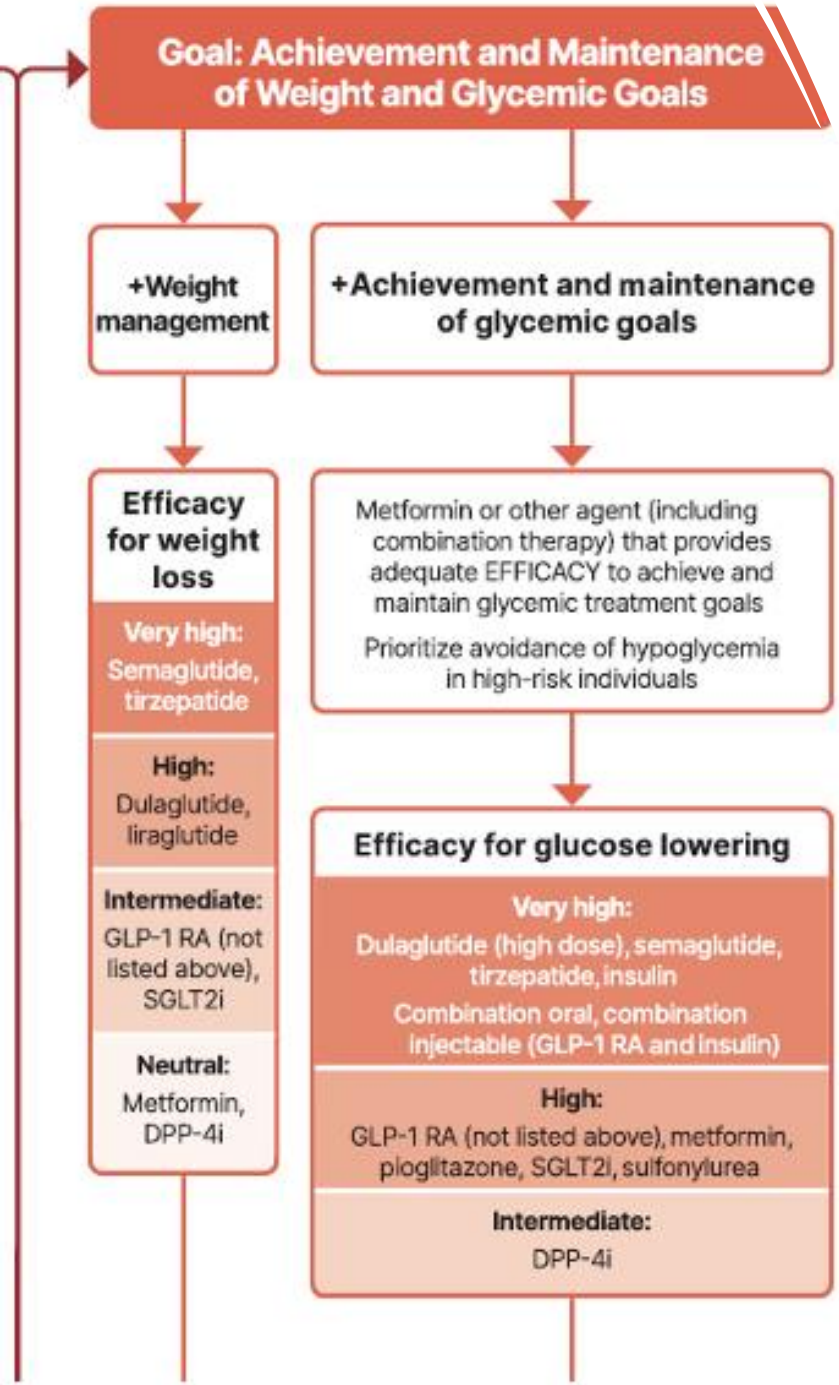
For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

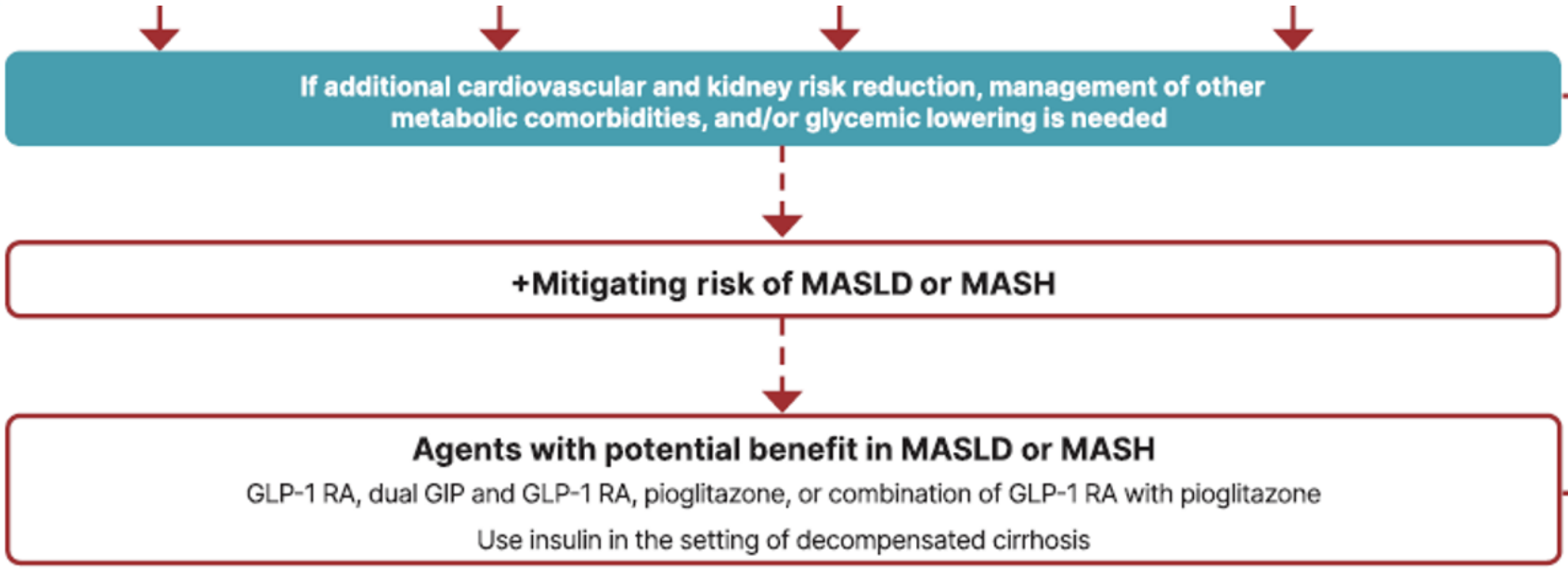
‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HHF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.


Goal: Cardiovascular and Kidney Risk Reduction in High-Risk Individuals with Type 2 Diabetes*
+ASCVD†
+Indicators of high CVD risk
+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF
+CKD
eGFR <60 mL/min/1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). Repeat measurement is required to confirm CKD
+ASCVD/indicators of high CVD risk"
GLP-1 RA# with proven CVD benefit
OR
SGLT2i‡ with proven CVD benefit
SGLT2i‡
with proven HF benefit in this population
+CKD (on maximally tolerated dose of ACEi or ARB)
SGLT2i‡ with primary evidence of reducing CKD progression
SGLT2i can be started with eGFR ≥20 mL/min/1.73 m²
Continue until initiation of dialysis or transplantation
If A1C is above goal

ADA SOC 2025


Goal: Achievement and Maintenance of Weight and Glycemic Goals
+Weight management
+Achievement and maintenance of glycemic goals
Efficacy for weight loss
Very high:
Semaglutide, tirzepatide
High:
Dulaglutide, liraglutide
Intermediate:
GLP-1 RA (not listed above), SGLT2i
Neutral:
Metformin, DPP-4i
Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals
Prioritize avoidance of hypoglycemia in high-risk individuals
Efficacy for glucose lowering
Very high:
Dulaglutide (high dose), semaglutide, tirzepatide, insulin
Combination oral, combination injectable (GLP-1 RA and insulin)
High:
GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea
Intermediate:
DPP-4i


If additional cardiovascular and kidney risk reduction, management of other metabolic comorbidities, and/or glycemic lowering is needed
+Mitigating risk of MASLD or MASH
Agents with potential benefit in MASLD or MASH
GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or combination of GLP-1 RA with pioglitazone
Use insulin in the setting of decompensated cirrhosis

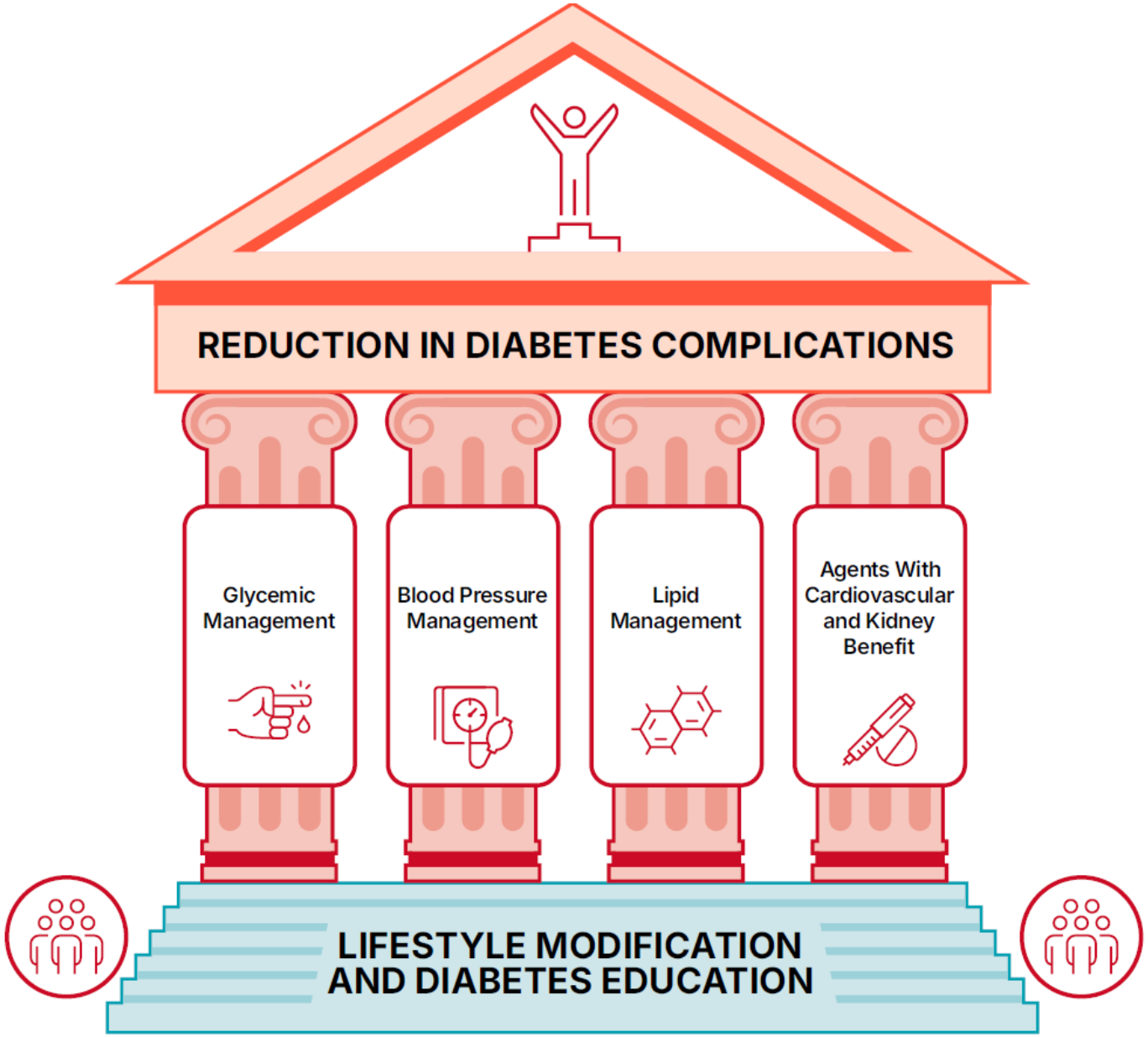
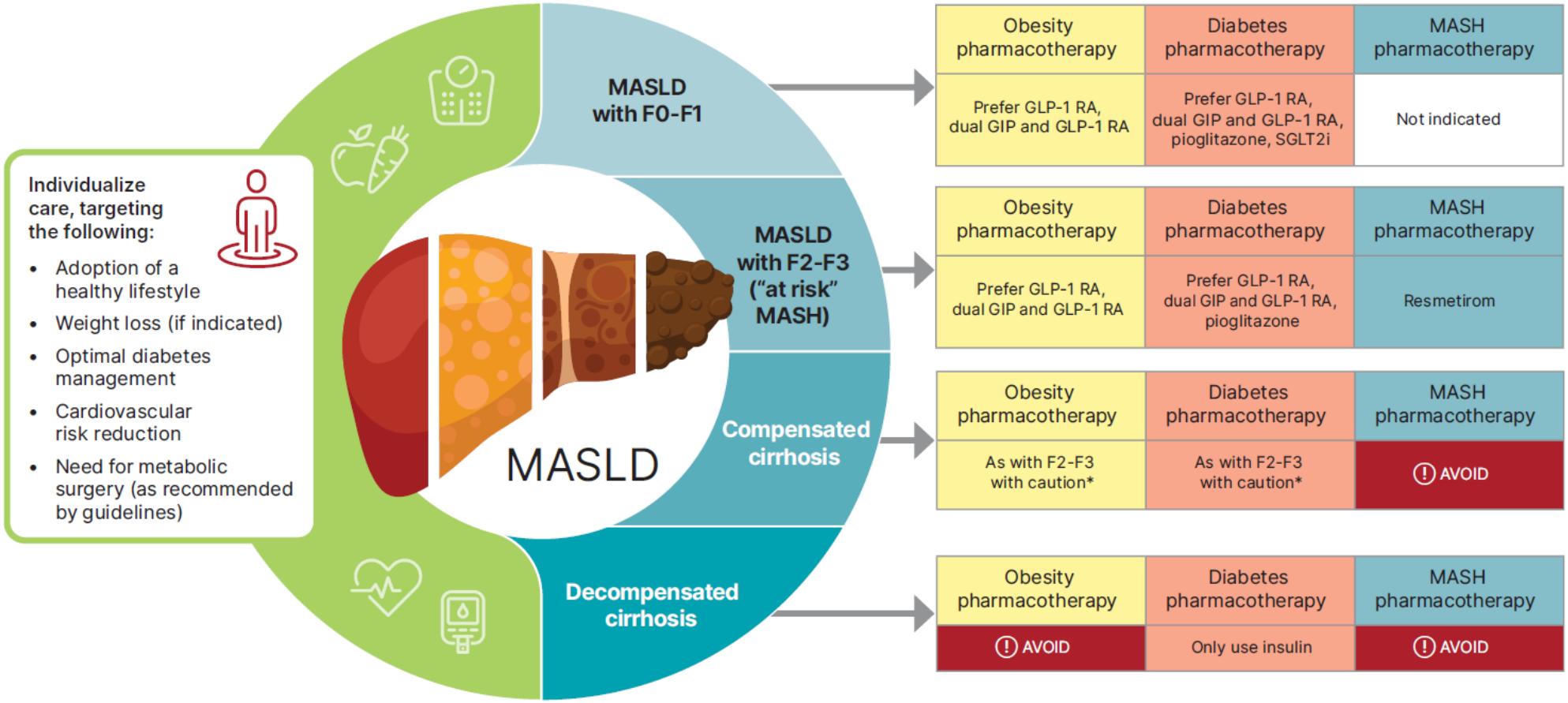


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications.

Cardiovascular Disease and Risk Management:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S206-S238

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) Treatment Algorithm



*Individualized care and close monitoring needed in compensated cirrhosis given limited safety data available.

Figure 4.3—Metabolic dysfunction–associated steatotic liver disease (MASLD) treatment algorithm. F0-F1, no to minimal fibrosis; F2-F3, moderate fibrosis; F4, cirrhosis; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; MASH, metabolic dysfunction–associated steatohepatitis; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Care in Diabetes - 2025. *Diabetes Care* 2025;48(Suppl. 1):S59-S85

Case Study (continued)

- She went back to DM education
- Started a walking program
- She started a GLP-1RA (semaglutide SQ) + ongoing metformin
  - A1c at 3 months is now 6.5%
  - She feels great and is happy with progress, no side effects

- What advice do you have for her?
- She has lost about 18lbs (BMI 32.5)
- Any changes in the treatment program?

Case Study

- 6 weeks later she reports that she is pregnant per 2 home tests

- What do you recommend in terms of treatment?

GLP-1 RA in pregnancy

- There is no long-term data to suggest safe in pregnancy
- A recent poster at the Society for Maternal - Fetal Medicine (2/1/25)
  - 4 .6 million pregnancies 2021-4/2024
  - Mean age 29.5- 30.3 years
  - 0.2% were on semaglutide (about 9200)
- Outcomes
  - 26% less likely to deliver preterm (OR 0.74 CI 0.67-0.81, p<0.001)
  - Higher rates of
    - preeclampsia (OR 1.16, CI 1.11-1.23, p< 0.001)
    - HEELP (OR 1.88, CI 1.38-2.56, p< 0.001)
    - Eclampsia (OR 2.74, CI 2.17-3.47, p< 0.001)

Adams E, et al "Pregnancy outcomes in patients with type-2 diabetes treated with Semaglutide: A multi-center observational cohort study" SMFM 2025.

Type 2 diabetes treatments in early pregnancy

- International Pregnancy Safety Study (InPreSS) consortium
- Finland, Sweden, Iceland, Norway, Isreal, US
- Looked at periconception exposure of medication
- Based on at least 1 fill of a SU, DPP-4, GLP-1RA, or SGLT-2I
- 3,514,865 pregnancies
  - 51,826 has pregestational diabetes (1.5%)
    - 15,148 (29%) were on noninsulin meds
    - 7,440 (50%) metformin
    - 1352 (9%) on SU
    - 687 (4.5%) on DPP-4 I
    - 325 (2.2%) on SGLT-2 I
    - 938 (6.2%) on GLP-1RA

Cesta CE, et al. Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy. *JAMA Intern Med.* 2024;184(2):144–152.

JAMA Network™

From: **Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy**

JAMA Intern Med. 2024;184(2):144-152. doi:10.1001/jamainternmed.2023.6663

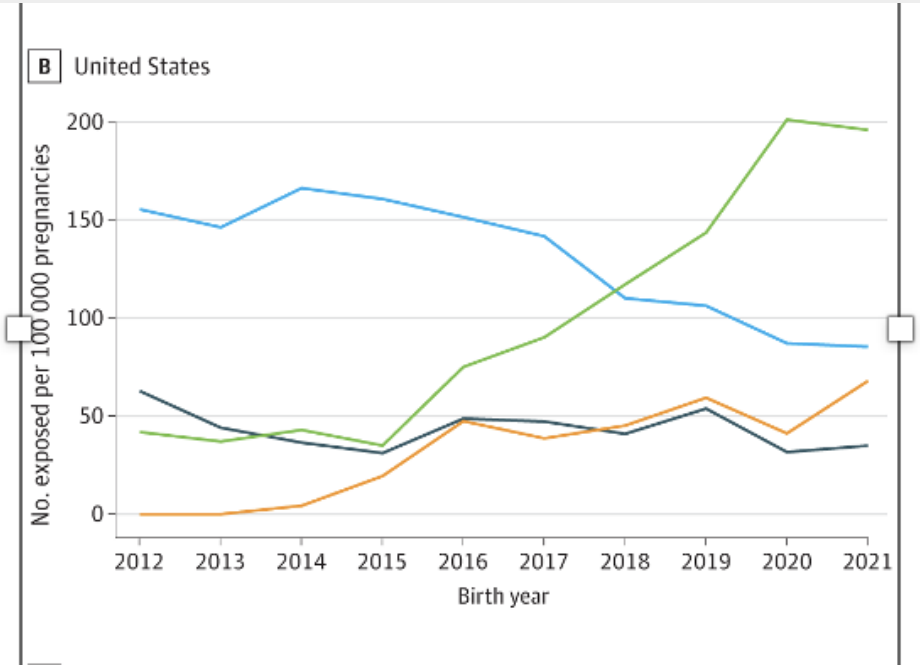
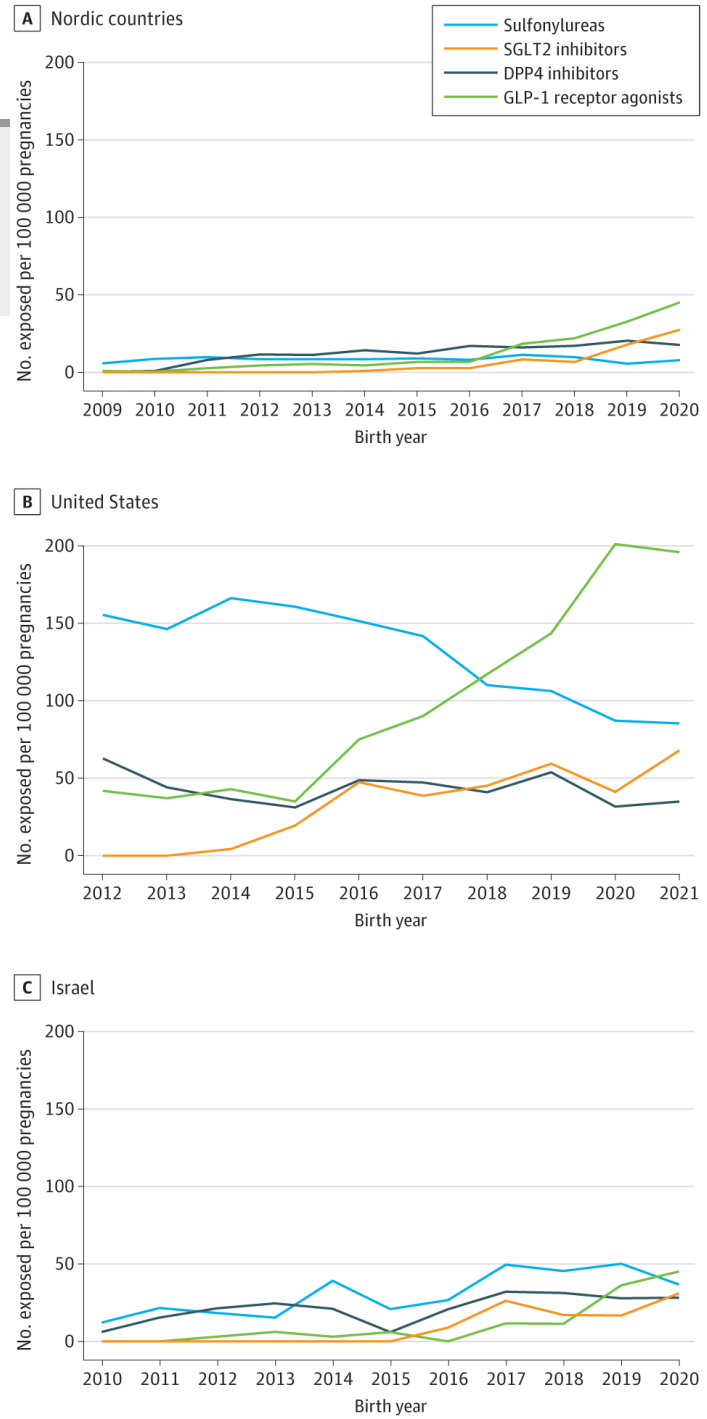


Figure Legend:

Prevalence of Periconceptional Second-Line Noninsulin Antidiabetic Medication Exposure Over Time in the Nordics, US, and IsraelThe denominator contains all live-born infants per year per database. Nordic results are based on pooled data from national health registers in Finland, Iceland, Norway, and Sweden. US results based on data from the MarketScan database. Israel results based on data from Maccabi Health Service database. DPP-4 indicates dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose cotransporter 2.



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From: **Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy**

JAMA Intern Med. 2024;184(2):144-152. doi:10.1001/jamainternmed.2023.6663

Table 2. Risk for Any and Cardiac Major Congenital Malformations in Infants Born to Women With Type 2 Diabetes and Periconceptional Use of Second-Line Noninsulin Antidiabetic Medications Compared With Insulin[a]

Treatment	No. of exposed cases/No. of exposed (%)[b]	Crude relative risk (95% CI)	Adjusted relative risk (95% CI)[c]
Any major congenital malformation			
Insulin	400/5078 (7.8)	1 [Reference]	1 [Reference]
Sulfonylureas	121/1362 (9.7)	1.14 (0.91-1.42)	1.18 (0.94-1.48)
DPP-4 inhibitors	50/687 (6.1)	0.91 (0.67-1.24)	0.83 (0.64-1.06)
GLP-1 receptor agonists	75/938 (8.2)	1.02 (0.78-1.33)	0.95 (0.72-1.26)
SGLT2 inhibitors	30/335 (7.0)	1.13 (0.76-1.67)	0.98 (0.65-1.46)[d]
Cardiac malformations			
Insulin	212/5078 (4.2)	1 [Reference]	1 [Reference]
Sulfonylureas	50/1362 (4.8)	1.05 (0.75-1.47)	1.05 (0.75-1.48)
DPP-4 inhibitors	24/687 (3.3)	0.91 (0.59-1.41)	0.90 (0.58-1.39)
GLP-1 receptor agonists	23/938 (3.2)	0.67 (0.42-1.06)	0.68 (0.42-1.12)
SGLT2 inhibitors	15/335 (3.9)	1.22 (0.70-2.13)	1.10 (0.63-1.92)[d]

Abbreviations: DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose cotransporter 2.

[a] Individual study cohort estimates are reported in eTable 8 in Supplement 1.

[b] Standardized prevalence.

[c] Adjusted for birth year, maternal age, obesity, and specific Nordic country (in the pooled Nordic cohort only; Finland, Iceland, Norway, Sweden).

[d] US model only adjusted for birth year and obesity.

Risk for Any and Cardiac Major Congenital Malformations in Infants Born to Women With Type 2 Diabetes and Periconceptional Use of Second-Line Noninsulin Antidiabetic Medications Compared With Insulin[a]Abbreviations: DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose cotransporter 2.

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[d] US model only adjusted for birth year and obesity.

Section 15

Management of Diabetes in Pregnancy

(https://doi.org/10.2337/dc25-S015)

Preconception Counseling

15.1 Starting at puberty and continuing in all people with diabetes and childbearing potential, preconception counseling should be incorporated into routine diabetes care. **A**

15.2 Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until an individual's treatment plan and A1C are optimized for pregnancy. **A**

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

15.4 Individuals with a history of gestational diabetes mellitus (GDM) should seek preconception screening for diabetes and preconception care to identify and treat hyperglycemia and prevent congenital malformations. **E**

Preconception Care

15.5 Individuals with preexisting diabetes who are planning a pregnancy should ideally begin receiving interprofessional care for preconception, which includes an endocrinology health care professional, maternal-fetal medicine specialist, registered dietitian nutritionist, and diabetes care and education specialist, when available. **B**

15.6 In addition to focused attention on achieving glycemic goals, **A** standard preconception care should be augmented with extra focus on nutrition, physical activity, diabetes self-care education, and screening for diabetes comorbidities and complications. **B**

15.7 Individuals with preexisting diabetes who are planning a pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy as well as in the first trimester, and then pregnant individuals should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care health care professional. **B**

Table 15.1—Checklist for preconception care for people with prediabetes, diabetes, or a history of gestational diabetes mellitus

Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
  - Overweight and obesity or underweight
  - Meal planning
  - Correction of dietary nutritional deficiencies
  - Caffeine intake
  - Safe food preparation technique
- ☐ Lifestyle recommendations for:
  - Regular moderate exercise
  - Avoidance of hyperthermia (hot tubs)
  - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- ☐ Counseling on diabetes in pregnancy per current standards, including natural history of insulin resistance in pregnancy and postpartum; preconception glycemic goals; avoidance of DKA and severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy in individuals with preexisting diabetes; PCOS (if applicable); fertility in people with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, stillbirth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy
- ☐ Supplementation
  - Folic acid supplement (400–800 μg/day routine)
  - Appropriate use of over-the-counter medications and supplements

Health assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including DKA and severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, MASLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease in individuals with preexisting diabetes, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric or gynecologic history, including a history of cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- ☐ Review of current medications and appropriateness during pregnancy

Screening should include:

- ☐ Diabetes complications and comorbidities in individuals with preexisting diabetes, including comprehensive foot exam; comprehensive ophthalmologic exam; ECG in individuals starting at age 35 years who have cardiac signs or symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine albumin-to-creatinine ratio
- ☐ Anemia
- ☐ Genetic carrier status (based on history):
  - Cystic fibrosis
  - Sickle cell anemia
  - Tay-Sachs disease
  - Thalassemia
  - Others if indicated
- ☐ Infectious disease (per ACOG guidelines)

Preconception plan should include:

- ☐ Immunizations (per ACOG guidelines) (165–167)
- ☐ Nutrition and medication plan to achieve glycemic goals prior to conception, including appropriate implementation of blood glucose monitoring, continuous glucose monitoring (if indicated and appropriate), and pump technology (if indicated and appropriate)
- ☐ Contraceptive plan to prevent pregnancy until glycemic goals are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction

Created using information from American College of Obstetricians and Gynecologists (ACOG) (5) and others (20,22). DKA, diabetic ketoacidosis; DVT/PE, deep vein thrombosis/pulmonary embolism; ECG, electrocardiogram; MASLD, metabolic dysfunction-associated steatotic liver disease; PCOS, polycystic ovary syndrome; TSH, thyroid-stimulating hormone.

Glycemic Goals in Pregnancy

15.8 Fasting, preprandial, and postprandial blood glucose monitoring are recommended in individuals with diabetes in pregnancy to achieve optimal glucose levels. Glucose goals are fasting plasma glucose <95 mg/dL (<5.3 mmol/L) and either 1-h postprandial glucose <140 mg/dL (<7.8 mmol/L) or 2-h postprandial glucose <120 mg/dL (<6.7 mmol/L). **B**

15.9 Due to increased red blood cell turnover, A1C is slightly lower during pregnancy in people with and without diabetes. Ideally, the A1C goal in pregnancy is <6% (<42 mmol/mol) if this can be achieved without significant hypoglycemia, but the goal may be relaxed to <7% (<53 mmol/mol) if necessary to prevent hypoglycemia. **B**

15.10 Continuous glucose monitoring (CGM) can help to achieve glycemic goals (e.g., time in range, time above range) **A** and A1C goal **B** in type 1 diabetes and pregnancy, and may be beneficial for other types of diabetes in pregnancy. **E**

Glycemic Goals in Pregnancy

15.11 Recommend CGM to pregnant individuals with type 1 diabetes. **A** In conjunction with aims to achieve traditional pre- and postprandial glycemic goals, real-time CGM can reduce the risk for large-for-gestational-age infants and neonatal hypoglycemia in pregnancy complicated by type 1 diabetes. **A**

15.12 CGM metrics may be used in combination with blood glucose monitoring to achieve optimal pre- and postprandial glycemic goals. **E**

15.13 Commonly used estimated A1C and glucose management indicator calculations should not be used in pregnancy as estimates of A1C. **C**

Table 15.2—Blood glucose goals in pregnancies associated with diabetes

	Blood glucose goal		
Glucose measurement	Type 1 diabetes or type 2 diabetes^	GDM treated with insulin	GDM not treated with insulin
Fasting glucose	70–95 mg/dL (3.9–5.3 mmol/L)	70–95 mg/dL (3.9–5.3 mmol/L)	<95 mg/dL (<5.3 mmol/L)
1-h postprandial glucose	110–140 mg/dL* (6.1–7.8 mmol/L)	110–140 mg/dL* (6.1–7.8 mmol/L)	<140 mg/dL* (<7.8 mmol/L)
2-h postprandial glucose	100–120 mg/dL (5.6–6.7 mmol/L)	100–120 mg/dL (5.6–6.7 mmol/L)	<120 mg/dL (<6.7 mmol/L)

Gestational diabetes mellitus (GDM) blood glucose goals shown are recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (42). ^Lower glucose limits do not apply to individuals with type 2 diabetes treated with nutrition alone. Aim for less stringent goals if these cannot be achieved without significant hypoglycemia, based on clinical experience and individualization of care. *Optimal goal includes either a 1-h postprandial glucose level or 2-h postprandial glucose level within column of type of diabetes.

Management of Diabetes in Pregnancy

15.14 Nutrition counseling before and during pregnancy should promote an eating pattern including fruits, vegetables, legumes, whole grains, nuts, seeds, fish, and other lean protein, which will provide a balance of macronutrients and healthy n-3 fatty acids. **C**

15.15 Lifestyle behavior change is an essential component of management of GDM and may suffice as treatment for many individuals. Insulin should be added if needed to achieve glycemic goals. **A**

15.16 Telehealth visits used in combination with in-person visits for pregnant people with GDM can improve outcomes compared with standard in-person care alone. **A**

15.17 Insulin should be used to manage type 1 diabetes in pregnancy **A** and is the preferred agent for the management of GDM **A** and type 2 diabetes **B** in pregnancy.

15.18 Either multiple daily injections or insulin pump technology can be used in pregnancy complicated by type 1 diabetes. **C**

Management of Diabetes in Pregnancy (continued)

15.19 Automated insulin delivery (AID) systems with pregnancy-specific glucose targets are recommended for pregnant individuals with type 1 diabetes. **A**

15.20 AID systems without pregnancy-specific glucose targets or a pregnancy-specific algorithm may be considered for select pregnant individuals with type 1 diabetes when used with assistive techniques and working with experienced health care teams. **B**

15.21 Metformin and glyburide, individually or in combination, should not be used as first-line agents for management of diabetes in pregnancy, as both cross the placenta to the fetus **A** and may not be sufficient to achieve glycemic goals. **B** Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data and are not recommended. **E**

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

Preeclampsia and Aspirin

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

Pregnancy and Drug Considerations

15.24 In pregnant individuals with diabetes and chronic hypertension, a blood pressure threshold of 140/90 mmHg for initiation or titration of therapy is associated with better pregnancy outcomes than reserving treatment for severe hypertension, with no increase in risk of small-for-gestational-age birth weight. **A** There are limited data on the optimal lower limit, but therapy should be deintensified for blood pressure <90/60 mmHg. **E** A blood pressure goal of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension. **A**

15.25a Potentially harmful medications in pregnancy (e.g., ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists) should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception. **B**

15.25b In most circumstances, lipid-lowering medications should be stopped prior to conception and avoided in sexually active individuals of childbearing potential with diabetes who are not using reliable contraception. **B** In some circumstances (familial hypercholesterolemia, prior atherosclerotic cardiovascular disease event), statin therapy may be continued when the benefits outweigh risks. **E**

Postpartum Care

15.26 Insulin requirements need to be evaluated and adjusted for individuals requiring insulin after delivery because insulin resistance decreases dramatically immediately postpartum. **C**

15.27 A contraceptive plan should be discussed and implemented with all people with diabetes of childbearing potential. **A**

15.28 Breastfeeding efforts are recommended for all individuals with diabetes. **A** Breastfeeding is recommended for individuals with a history of GDM for multiple benefits, **A** including a reduced risk for type 2 diabetes later in life. **B**

15.29 Postpartum care should include psychosocial assessment and support for self-care. **E**

15.30 Screen individuals with a recent history of GDM at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. **B**

15.31 Individuals with a history of GDM should have lifelong screening for the development of type 2 diabetes or prediabetes every 1–3 years. **B**

15.32 Individuals with overweight or obesity and a history of GDM found to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent diabetes. **A**

Treatment for pregestational diabetes

- Type 1: Insulin
- Type 2: Insulin
- GDM: Insulin
- Why: Metformin and Glyburide cross the placenta. Others have insufficient data to advise.
- Insulin needs may decrease in 1st trimester, but insulin resistance increases in 2nd and 3rd trimester until delivery of placenta.
- We use CGMs whenever possible in women on insulin

Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S306-S320

CGM goals in pregnancy

- Goal glucose sensor range: 63-140 mg/dl
- Time below range: < 63 mg/dl **(4%)**
- Time below range < 54 mg/dl. **(<1%)**
- Time above range >140 mg/dl **(<25%)**
- Time in range **(>70%)**

- Challenges: alarm fatigue, higher risk of hypoglycemia, inconsistency between FSG, patient, and clinician “getting to know the CGM”

Management of Diabetes in Pregnancy:
Standards of Care in Diabetes - 2025 Diabetes Care 2025;48(Suppl. 1):S306-S320

Case Study cont'd

- We stopped semaglutide
- Recommend keeping metformin through the end of the first trimester
- Started NPH insulin bid, titrated to target
- Started CGM
- MNT with a dietitian (appt q 2 weeks)
- Eye exam, care with diabetes team (monthly appt), and MFM
- A1c was 6% by the end of the first trimester, 5.7% at delivery
- Delivered vaginally at 39 weeks

Treatment in the peripartum period

- Primarily determined by the setting in the clinician involved
- Great time to have a peer-to-peer conversation
- For those on insulin pumps/AID systems– the best practice is to keep it on (this means keeping the pump and sensor on)
- Those on insulin injections- hold short-acting- cut long-acting 50% labor day or if surgical- after surgery.
- Often, patients can return to pre-pregnancy treatment after delivery

Case Study 2

- Pregestational T2DM is currently 3 months postpartum with ongoing breastfeeding with no current date to stop
- Taking NPH 7 units in the am and 20 units in the pm
- Delivery info:
- Current problems: Type 2 DM, G2A3 (CKD)- measured postpartum
  - eGFR 78 ml/min
  - UACr: 238 mg/g
- BMI 32, BP 138/82
- Exam normal

Case Study 2

- What questions do you have for this patient?
- What do you advise for immediate treatment?
- What is you short, intermediate and long term plan for her T2DM?

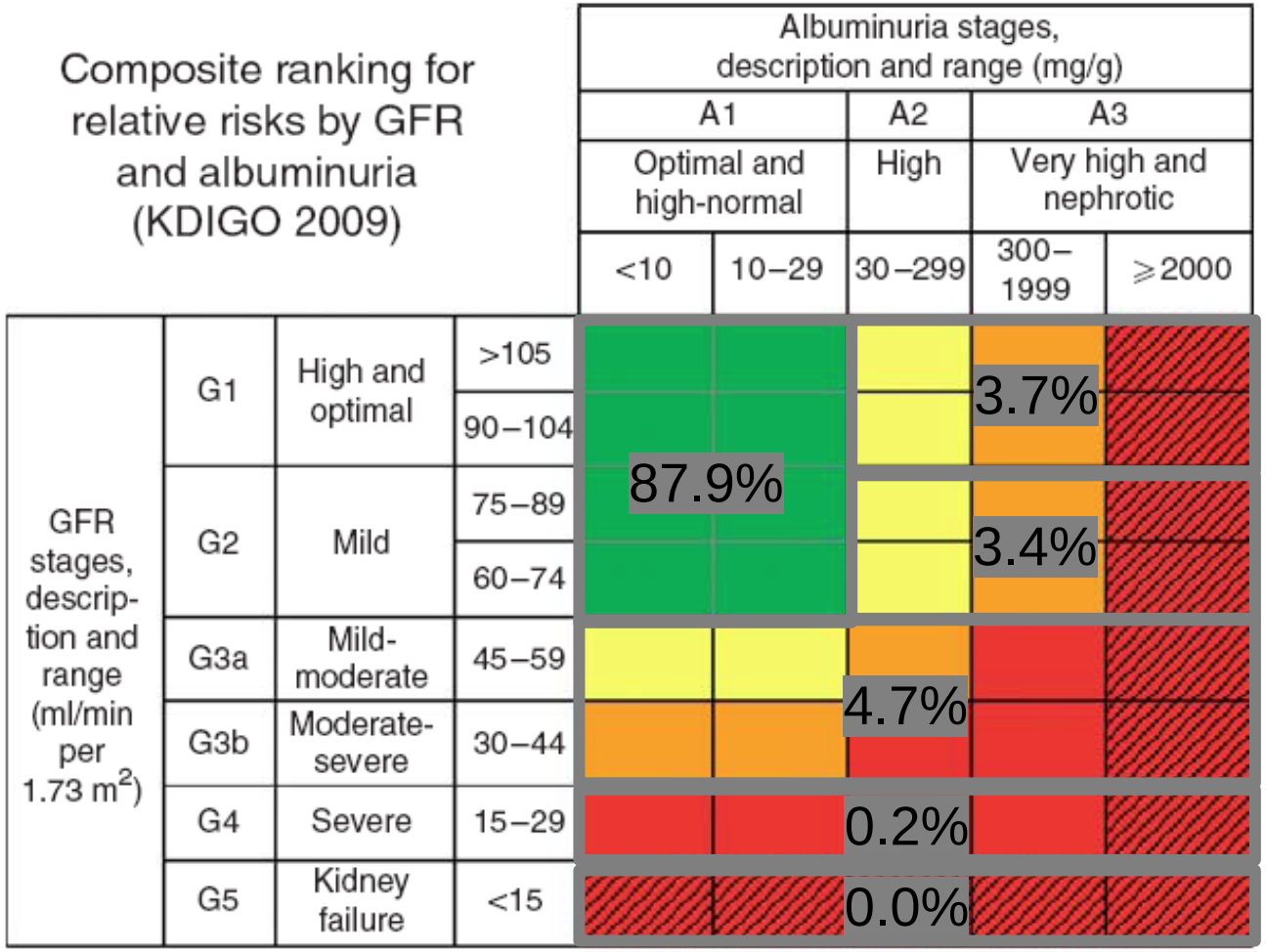
Case Study 2 CGM

Burden of complications in those diagnosed with T2DM at younger age

- The younger you are diagnosed with type 2 diabetes
  - The more progressive the disease is
  - Treatments are less effective and durable
  - Complications develop earlier in the disease process

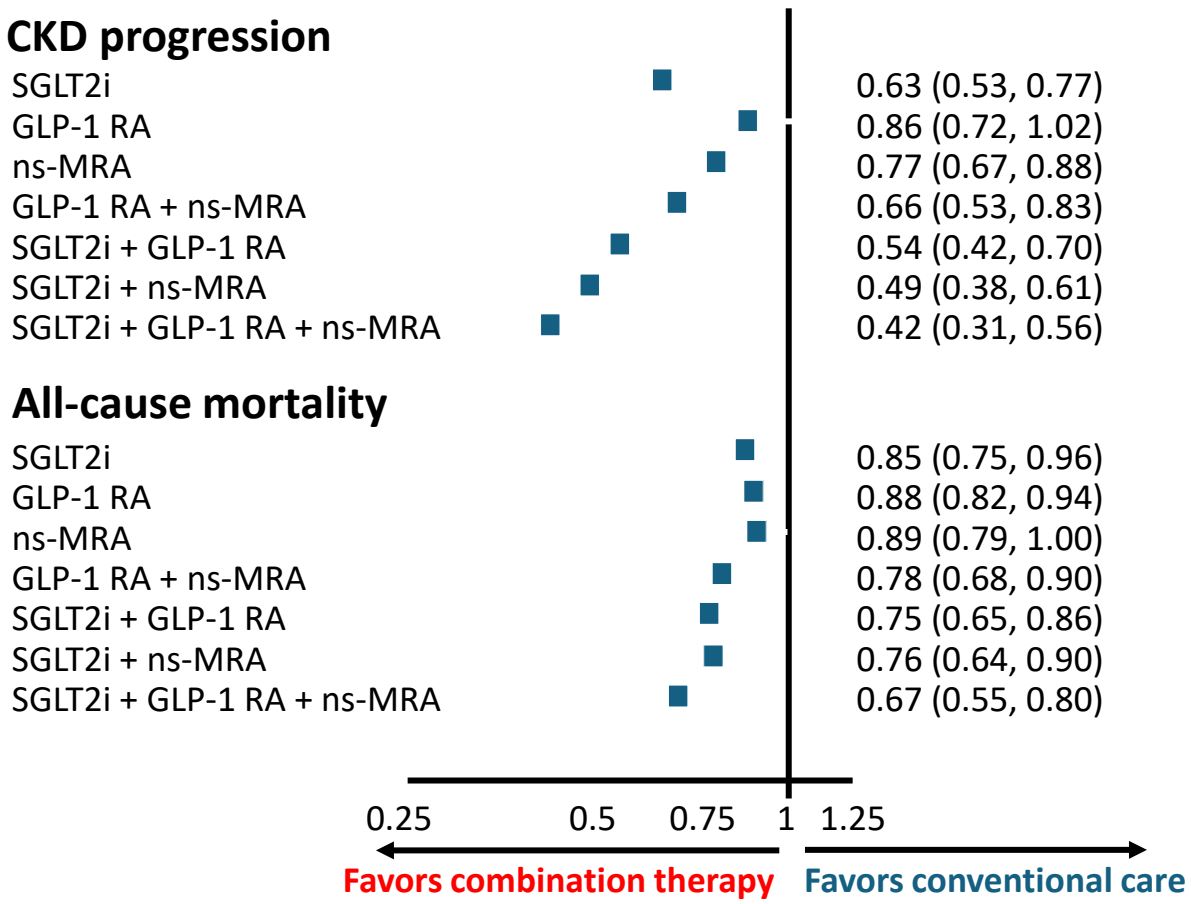
- As more young people get diagnosed with type 2 diabetes mellitus, we will have more complicated patients who are of reproductive age and become pregnant

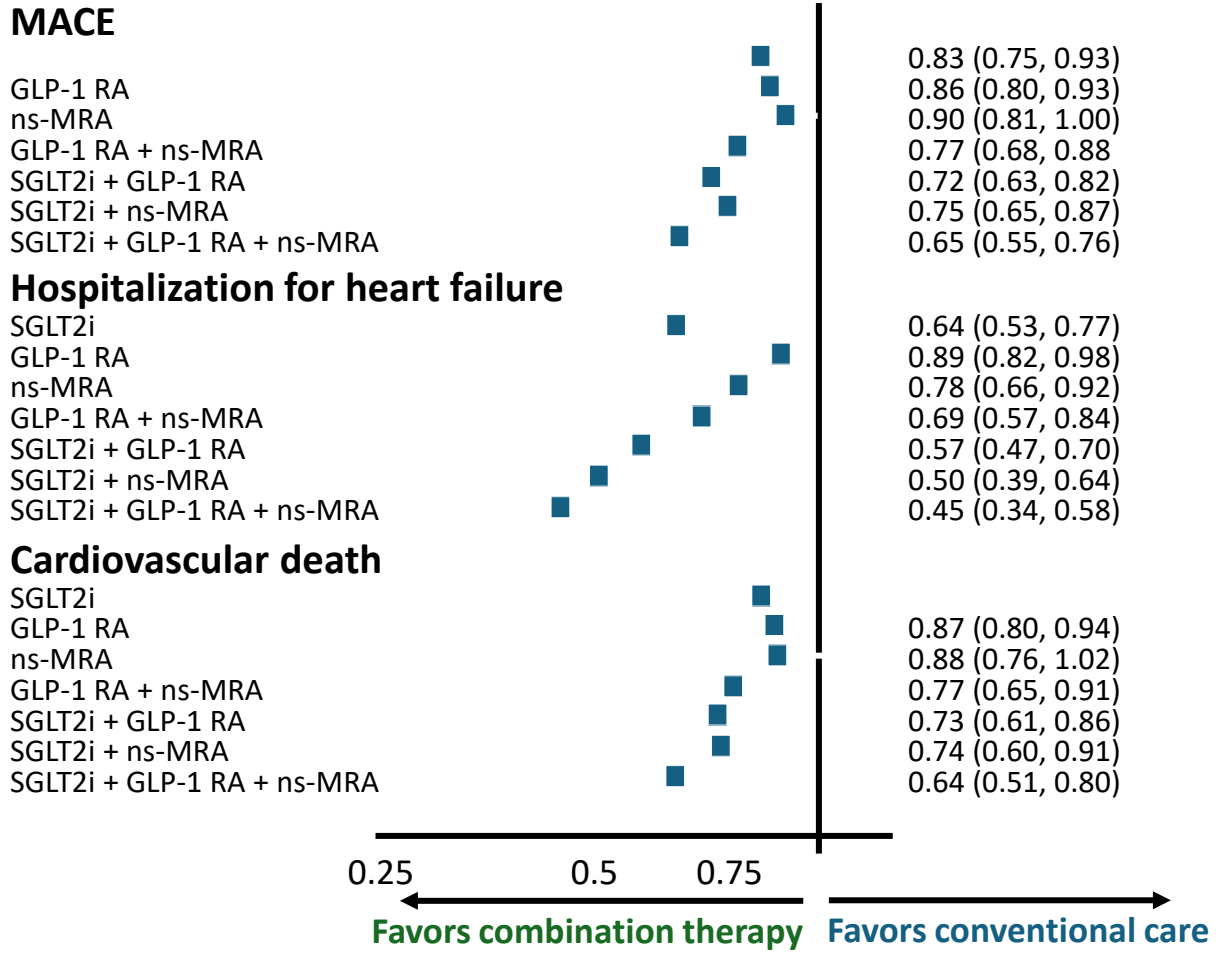
Percentage of US Population by Estimated Glomerular Filtration Rate (eGFR) and Albuminuria Category



Levey, AS Kidney Int. 2011 Jul;80(1):17-28.

Estimated Lifetime CV, Kidney, and Mortality Benefits of Combination Treatment in Patients With T2D and Albuminuria





Neuen. Circulation. 2023;0.. Slide from clinicaloptions

Extraglycemic Effects of GLP-1RA/Twincretins

Drug	3 pt MACE	Stroke	CKD	MASLD/MASH	Cognition
Exenatide weekly			↓		Parkinson
Liraglutide	↓		↓	↓	
Dulaglutide	↓	↓	↓		Dementia
Semaglutide SQ	↓	↓	↓	↓	Dementia
Semaglutide oral	↓				
Trrzepatide				↓	

↓ = FDA indication
↓ = Studies/ Recommended
* = Exploratory

Extraglycemic Effects of GLP-1 RA

Nørgaard CH, et al. *Alzheimers Dement (NY)*. 2022;8(1):e12268.
Armstrong MJ, et al. *Lancet (London England).* 2016;387(10019):679-90.
Newsome PN, et al. *N Engl J Med.* 2021;384:1113-1124.
Vijiaratnam N, et al. *BMJ Open.* 2021;11(5):e047993.
Chang YF, et al. *J Clin Neurosci.* 2020;81:234-239.
Yaffe T, et al. *Lancet Neurology.* 2020;4422(20):30173.

GLP-1 RA Meta-analysis of CVOTs

Outcome	3-point MACE	CV mortality	All cause mortality	Renal composite
Risk reduction	12%	16%	12%	17%
Hazard Ratio	0.88	0.84	0.88	0.83
Confidence interval	0.82-0.94	0.76-0.93	0.83-0.95	0.78-0.89
P value	P < 0.001	P < 0.001	P < 0.001	P < 0.001
NNT	75		113	62

Safety Outcome	Thyroid cancer	Pancreatitis	Pancreatic Cancer	Retinopathy
Risk		2%	-1%	7%
Hazard Ratio		1.02	0.99	1.07
Confidence interval		0.77-.136	0.56-1.70	0.92-1.25
P value	NS	NS p = 0.88	NS p = 0.93	NS
	Event too few to analyze			

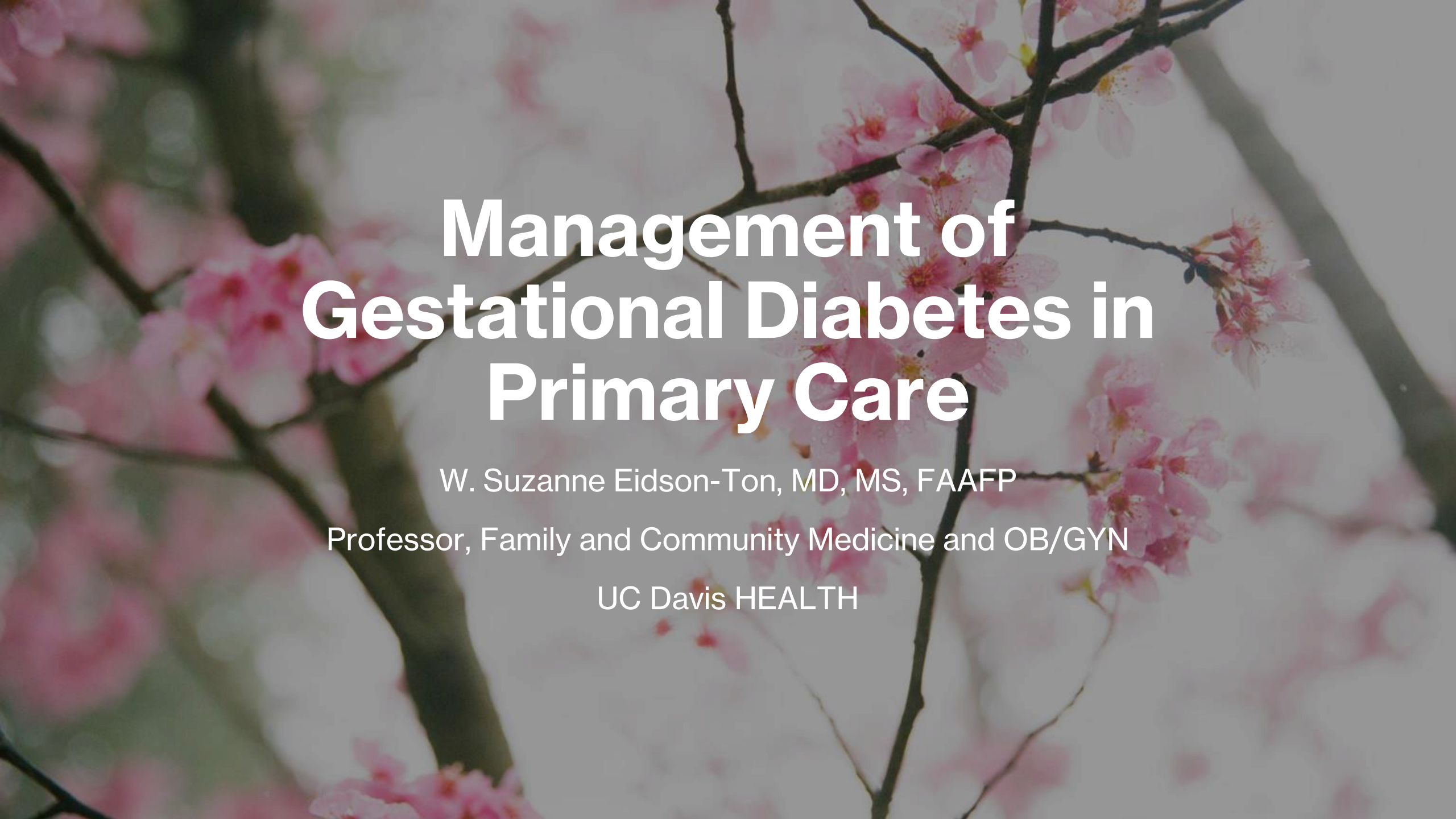
Includes 7 trials: ELIXA, LEADER, SUSTAIN-6, EXSCEL, Harmony Outcomes, REWIND, PIONEER 6

Kristensen SL, et al [published correction appears in *Lancet Diabetes Endocrinol*. 2020 Mar;8(3):e2]. *Lancet Diabetes Endocrinol*. 2019;7(10):776-785.

Summary

- Today we discussed
  - the prevalence of pregestational diabetes
  - family planning for those with diabetes
  - treatment options for those with pregestational diabetes
  - treatment options in delivery and postpartum
  - treatment in reproductive-age women who have T2DM and complications

- What questions do you have?
  - jshubroo@touro.edu



Management of Gestational Diabetes in Primary Care

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UC Davis HEALTH

I have no conflicts of interest to disclose.

Learning Objectives

1. Describe the epidemiology of gestational diabetes.
2. Explain screening options for gestational diabetes.
3. Implement appropriate care for pregnant patients with gestational diabetes.
4. Describe intra- and post-partum care for patients with gestational diabetes.

CASE

- MT is a 34 yo G2P0010 woman, who identifies as native Hawaiian, here for her first prenatal visit at 8 2/7 weeks based on her LMP. Of note, her BMI is 45, and her mother has Type 2 DM. She has no personal history of diabetes and her last Hgb A1C was 5.2 two years ago.

When to screen for PRE-gestational diabetes

- Not all pregnant people who may have pregestational diabetes are aware of their diagnosis.
- ACOG recommends screening pregnant people with BMI over 25 (or 23 in Asian people) as early in their pregnancy as possible if they have any of the following risk factors:

•First-degree relative with diabetes
•Black, Hispanic, Native American, Asian American, and Pacific Islander individuals
•History of cardiovascular disease
•Hypertension (ie, greater than or equal to 140/90 mmHg or on therapy for hypertension)
•Prior history of hyperlipidemia (ie, high-density lipoprotein cholesterol level less than 35 mg/dL (0.90 mmol/L), a triglyceride level greater than 250 mg/dL (2.82 mmol/L))
•Women with polycystic ovary syndrome
•Physical inactivity
•Other clinical conditions associated with insulin resistance (eg, severe obesity, acanthosis nigricans)
•Prediabetes (ie, A1c greater than or equal to 5.7% [39 mmol/mol], impaired glucose tolerance, or impaired fasting glucose)
•Previous gestational diabetes diagnosis
•Age 35 years or greater
•HIV
•Or other factors suggestive of an increased risk for pregestational diabetes

Modified from: Classification and diagnosis of diabetes: standards of medical Care in diabetes—2022. American Diabetes Association Professional Practice Committee. Diabetes Care 2022;45:S17–38. doi: 10.2337/dc22-S002.

Source: ACOG Clinical Practice Update: Screening for Gestational and Pregestational Diabetes in Pregnancy and Postpartum. Obstetrics & Gynecology 144(1):p e20-e23, July 2024. | DOI: 10.1097/AOG.0000000000005612

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Which of these risk factors does the patient in our case have?

Diagnosis of pregestational diabetes in Pregnancy

Tests for type-2 DM have not been validated in pregnancy but can be considered to diagnose pregestational diabetes in pregnancy:

--A_{1c} value 6.5 or higher,

--Fasting plasma glucose value 126 mg/dL or higher,

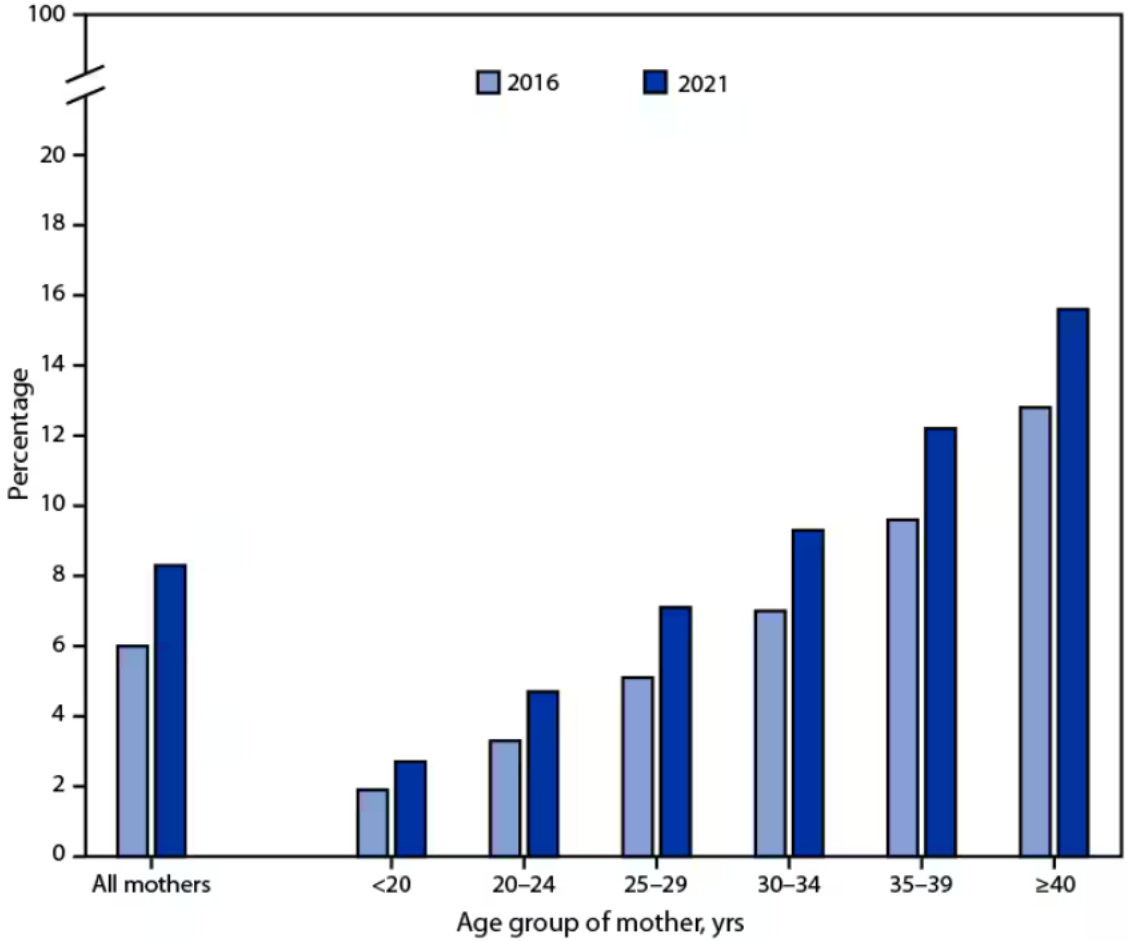
--2-hour plasma glucose value 200 mg/dL or higher during a 75-g OGTT,

--Random plasma glucose value 200 mg/dL or higher in patients with classic hyperglycemia symptoms

All pregnant patients diagnosed with pregestational diabetes should be prescribed aspirin prophylaxis prior to 26 weeks to prevent development of pre-eclampsia. (Start as early as possible after 12 weeks.)

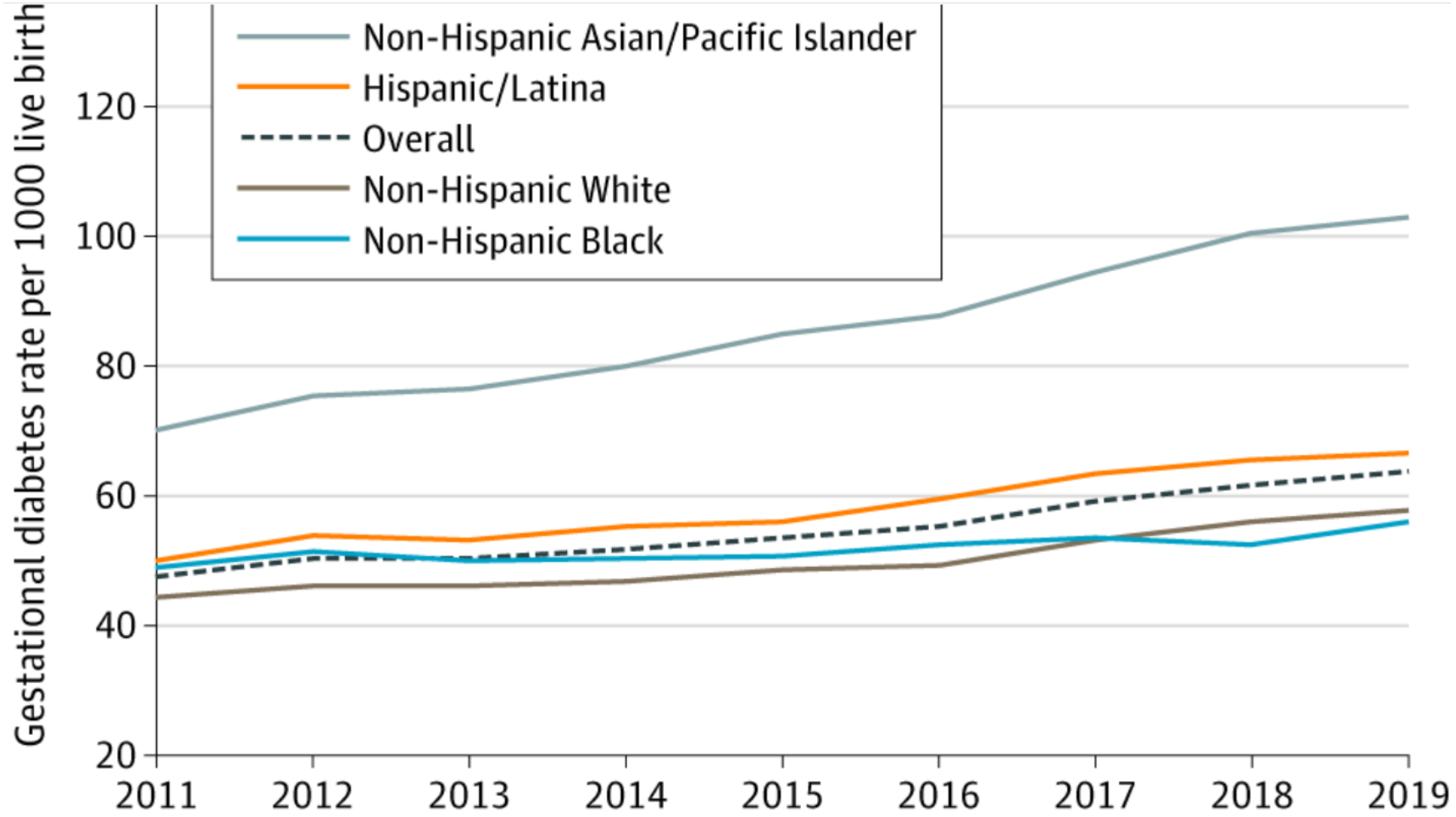
Increasing Prevalence of Gestational Diabetes

- Overall, increased from 6% of births in 2016 to 8.3% of births in 2021.

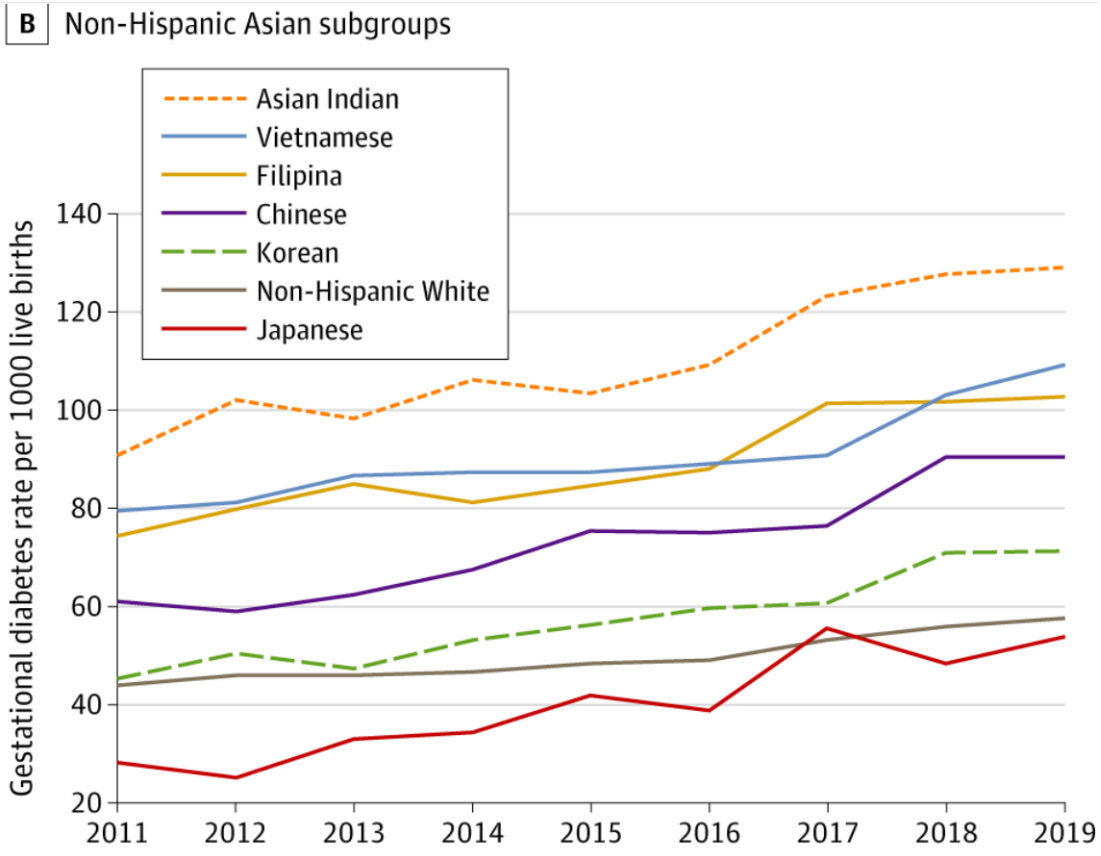


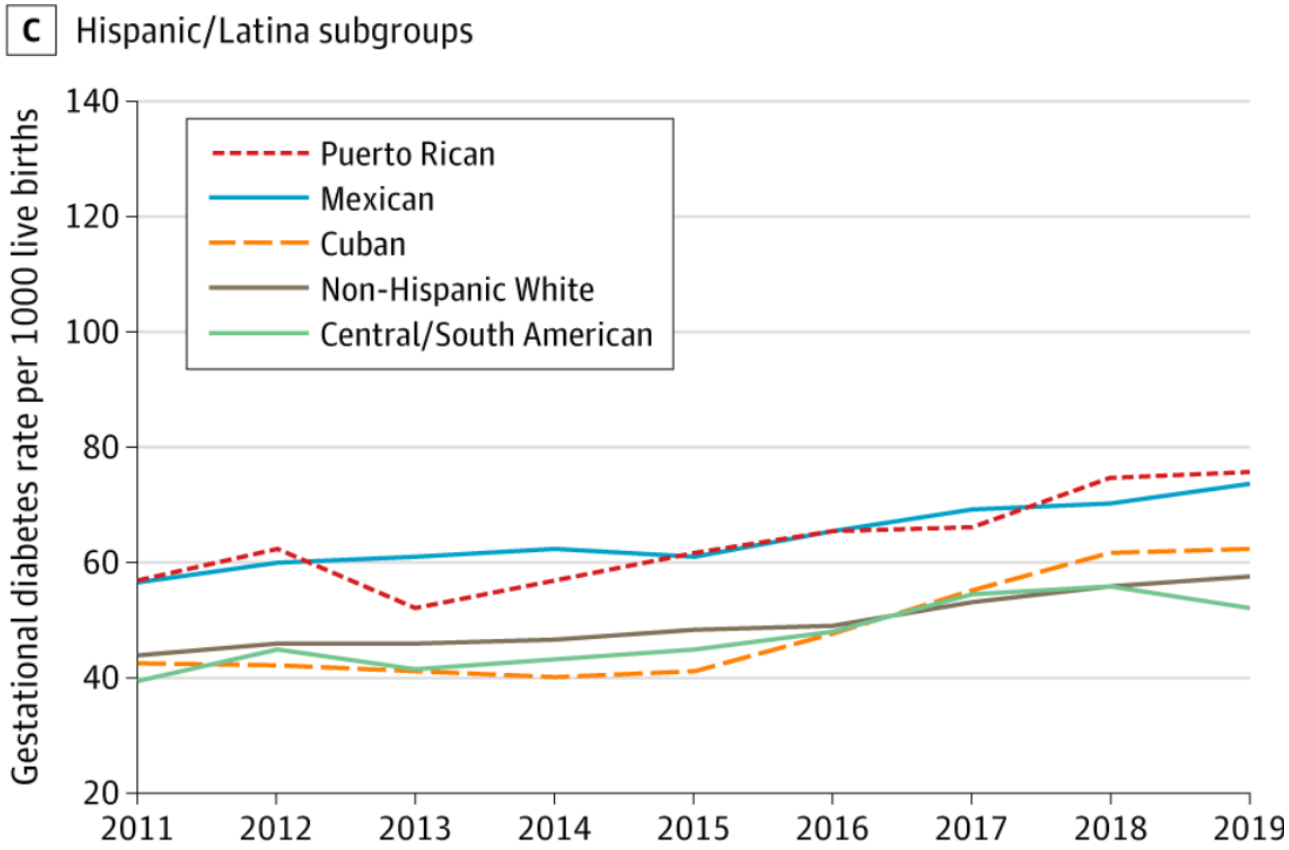
QuickStats: Percentage of Mothers with Gestational Diabetes, by Maternal Age — National Vital Statistics System, United States, 2016 and 2021. MMWR Morb Mortal Wkly Rep 2023;72:16. DOI: http://dx.doi.org/10.15585/mmwr.mm7201a4

Increasing Prevalence of Gestational Diabetes by Race/Ethnicity



Increasing Prevalence of Gestational Diabetes by Race/Ethnicity Subgroups





Shah NS, Wang MC, Freaney PM, et al. Trends in Gestational Diabetes at First Live Birth by Race and Ethnicity in the US, 2011-2019. *JAMA*. 2021;326(7):660–669. doi:10.1001/jama.2021.7217

Complications of Gestational Diabetes

Maternal:

- Increased risk of type-2 DM later in life (approx. 50% of those with GDM)
- Associated with increased risk of pre-eclampsia (almost double the risk)
- Increased risk of cesarean delivery

Fetal:

- Macrosomia
- Operative delivery, shoulder dystocia, birth trauma (compared to same-weight fetuses)
- Neonatal hypoglycemia and hyperbilirubinemia
- Later development of obesity and DM-2

Screening for Gestational Diabetes

- Should occur between 24-28 weeks
- ACOG continues to recommend a two-step approach:
  - Nonfasting 50-g 1 hour screen (cut off between 130-140, ACOG rec is 140)
  - 100-g OGTT (ACOG rec cut offs: 95, 180, 155, 140), positive if 2 or more are at threshold
- Some practices may choose a one-step approach:
  - 75-g OGTT (ACOG rec cut offs: 92, 180, 153), positive if 1 value at threshold
- Several studies have demonstrated that the one-step approach significantly increases the number of people diagnosed with GDM *without* a significant improvement in neonatal outcomes.

Case Continued

- MT's first trimester Hgb A1C is 5.5.
- At 26 2/7 weeks her 1-hour GCT is 154.
- At 28 weeks her 3-hour GTT is: 96, 179, 152, 144.

What is her diagnosis?

Gestational Diabetes

Initial Management of Gestational Diabetes

Glucose Monitoring

- Pregnant patients with GDM should ideally measure their blood sugar 4 times daily:
  - Fasting– Goal of <95
  - 1-(or 2-) hours after breakfast– Goal of <140
  - 1-(or 2-) hours after lunch-- Goal of <140
  - 1-(or 2-) hours after dinner-- Goal of <140

Dietary Modifications

- Goal is achieving normal blood glucose levels while maintaining adequate fetal growth and development and avoiding ketosis.
- All pregnant people with GDM should be seen by a registered dietician who can aid in developing a personalized nutrition plan.

Exercise

Case Continued

- MT receives glucose monitoring supplies and is referred for nutrition counseling. She returns to see you 2 weeks later at 30 4/7 weeks with the following blood glucose ranges:
  - Fasting: average of 92, range of 89-98, with 5/14 values above range
  - PP Breakfast: average of 111, range of 105-135
  - PP Lunch: average of 108, range of 100-143, with 3/14 values out of range with dietary explanations
  - PP Dinner: average of 125, range of 115-152, with 2/14 values our of range with dietary explanations

What should be next in the care of MT?

- Continue lifestyle management, consider adding a walk after lunch and dinner.
- Given BMI, order ultrasound for interval fetal growth.
- RTC in 2 weeks

Case continued

- MT returns in two weeks at 32 4/7 weeks. She has been trying to incorporate a walk after lunch and after dinner, but she isn't always able to. She has been following the diet much more closely as well. Fetal growth ultrasound shows good growth with the fetal weight at the 64%ile, and the AC:HC ratio slightly above 1. Her blood sugar log shows the following:
  - Fasting: average of 98, range of 94-105, with 12/14 values above range
  - PP Breakfast: average of 110, range of 103-132
  - PP Lunch: average of 105, range of 98-136, with 0/14 values out of range
  - PP Dinner: average of 120, range of 112-138, with 0/14 values our of range

What now?

Treating GDM with Insulin

- Total daily dose of insulin = units/kg
  - 1 unit/kg at 36+ weeks gestation
  - 0.9 unit/kg at 26-35 6/7 weeks
  - 0.8 unit/kg at 18-25 6/7 weeks
  - 0.7 unit/kg at 4-17 6/7 weeks
- Evening NPH (to treat high fasting BS) = 1/6 of TDD or 17%
- Short-acting pre-meal insulin = 5/6 (83%) of TDD divided into 3 meals per day
- Only use the doses needed based on the BS data

Case continued

MT weighs 100 kg at this visit.

Only her fasting BS are elevated, so we will start with only an evening NPH dose.

Calculated dose would be 100 X 0.9 X 1/6(17%) = 15 units

Start 10-15 units NPH qhs and follow-up in 1 week.

Case continued

- The following week at 33 4/7 weeks gestation, all of MT's blood sugars are controlled.
- Given that patient is now using insulin to control her GDM, will need to start ante-natal testing with weekly modified biophysical profile (NST + DVP) at 34 weeks.
- Continue to see patient every 1-2 weeks and modify insulin as needed.
- Given BMI, growth scan every 3-4 weeks, and at 38-39 weeks for EFW.
- Delivery is recommended in the 39th week of pregnancy, or after 37 weeks if poor glycemic control.
- Discuss risks/benefits of planned cesarean delivery if EFW at 38-39 weeks is >4500 g.

Intrapartum care for Patients with GDM

Check BS every 1 hour in active labor for patients using insulin in pregnancy or every 2 hours if lifestyle controlled GDM.

Goal of BS 80-110 mg/dL in active labor.

Use an insulin gtt for patients with BS > 110-120 in active labor.

Neonatal and Postpartum Care

Neonates should be monitored for hypoglycemia and hyperbilirubinemia. Check BS routines Q1 hour for the first 4 hours of life.

Provide immediate skin-to-skin care and early breastfeeding support.

Test birthing parent for Type 2 DM at 6-8 weeks postpartum, ideally with a 75-gram 2 hour GTT.

BREAST/CHEST FEEDING AS A CRITICAL INTERVENTION FOR DYADS WITH GDM

The Benefits of Breastfeeding for Infants

Condition	RR with ANY BF	Reduced Risk with Exclusive BF	Notes
Acute Otitis Media	23 %	50 %	> 3 months BF
Atopic Dermatitis		42 %	>= 3 months
GI Infections	64 %		current
Lower Resp. Disease		72 % (hospitalization)	>= 4 months
Childhood Asthma		27 % (no FH); 40% (+FH)	>= 3 months
Cognition			Increased verbal IQ*
Childhood Obesity		22 – 79 %	Ever vs 1 yr
Diabetes Mellitus		33 - 56 % (Type 2); 57 % (T1)	Ever vs 1 yr (T2) 6 months (T1)
Leukemia (Childhood)		19 % (ALL); 15% (AML)	> 6 months
NEC (Necrotizing Enterocolitis)		ARR 5 %, p=0.04	High case-fatality with NEC
SIDS	36%		

AAP Breastfeeding Policy Statement 2022: Metanalyses review & 2007 AHRQ Review

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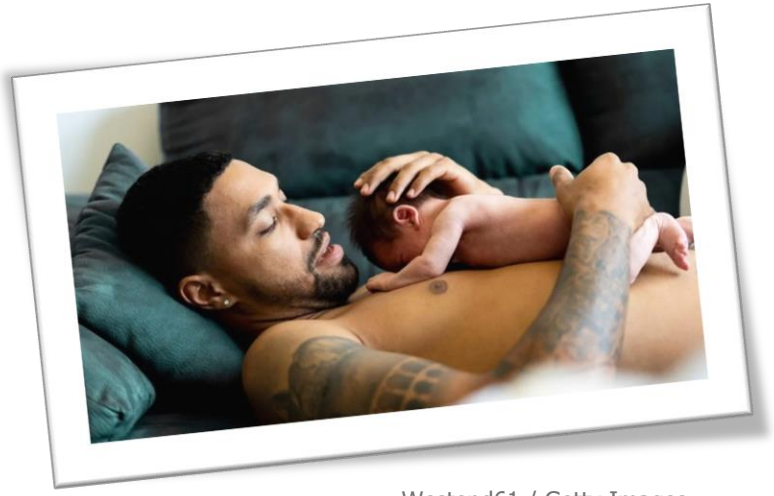
AAP Breastfeeding Policy Statement 2022: Metanalyses review & 2007 AHRQ Review

The Benefits of Breastfeeding for Society

- If 90% of US infants were exclusively breastfed to the age of 6 months, **we would save**
  - $13 billion per year
  - 911 infant lives
  - FUTURE costs of caring for populations with excess rates of obesity and diabetes

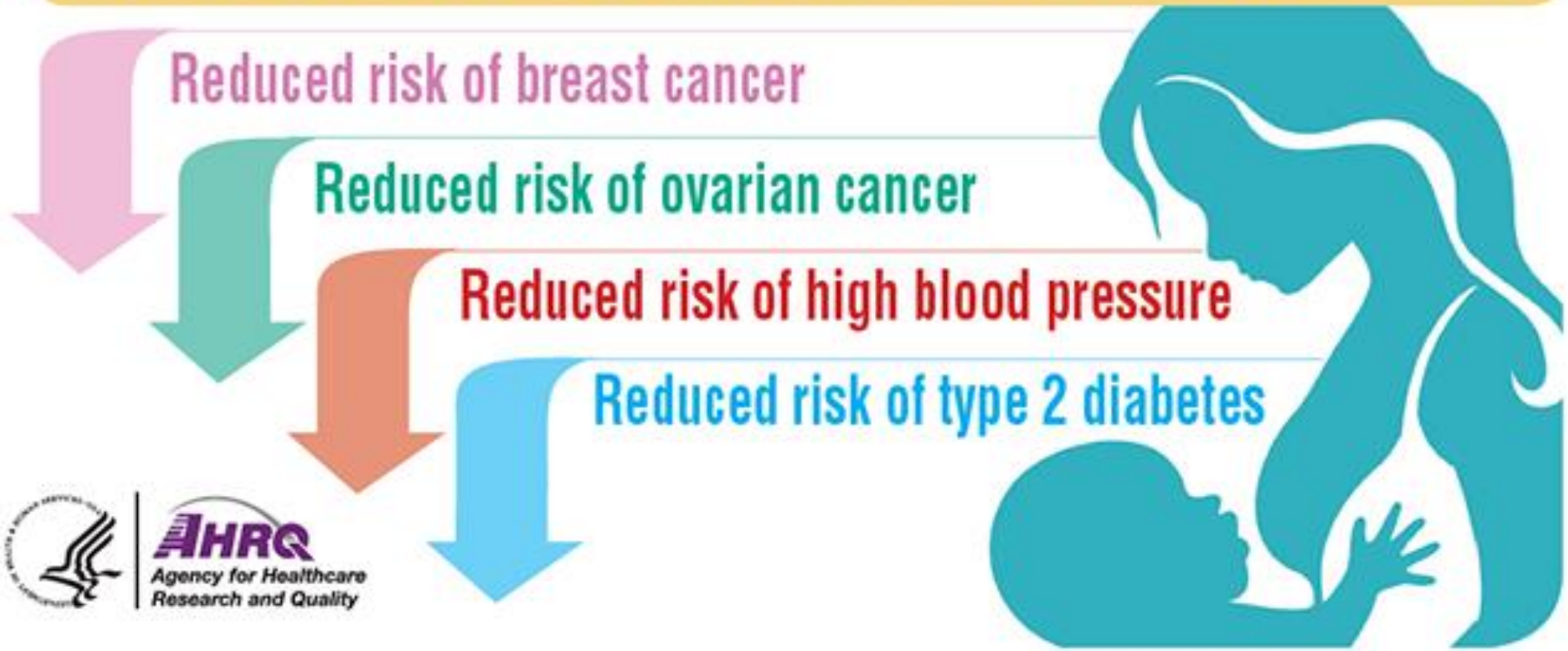


Westend61 / Getty Images

Benefits to Environment

- For one million breastfed babies, **we save**
  - 150 million formula containers from the landfill
  - Economic and environmental costs of production (including the maintenance of millions of lactating cows)
  - Costs of transportation

Benefits Associated with Moms Who Breastfeed



Breastfeeding Programs and Policies, Breastfeeding Uptake, and Maternal Health Outcomes in Developed Countries. Comparative Effectiveness Review No. 210. AHRQ Publication No. 18-EHC014-EF. July 2018

Data from AHRQ 2007 Review & JAMA 2019 Meta-analysis

Condition	Risk Reduction	Notes
Breast Cancer	4.3 %/ year of BF	
Hypertension	13%	>1 year
Obesity		Conflicting results
Osteoporosis	No increased risk	
Ovarian Cancer	21%	Compared to never BF
Postpartum Depression	Associated with lower risk	Unclear causation relationship
Type 2 DM	4-12% / year	30% after >1 yr in some studies

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https://www.yahoo.com/entertainment/transgender-man-navigates-chest-feeding-174739013.html

Lactation may be *necessary* to reset the postpartum Person's metabolism

Breastfeeding and Glucose Metabolism

- In pregnant rodents, beta-cell proliferation is suppressed during pregnancy by a protein called menin, which leads to relative glucose intolerance.
- Prolactin down regulates the production of menin, thus increasing the production of beta-cells during lactation in rats.
- Observational studies in humans have shown:
  - People with a history of gestational diabetes have improved glucose tolerance and fasting glucose levels in the postpartum period if they are breastfeeding.
  - Insulin levels and insulin:glucose ratios are lower in lactating women in the 3-6 month postpartum period.
  - Adiposity does not seem to affect the results.
- Duration of breastfeeding is associated with decreasing likelihood of Type 2 Diabetes, regardless of BMI.

QUESTIONS

???

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