

GESTATIONAL DIABETES: AN EARLY MANIFESTATION OF CARDIOMETABOLIC DISEASE?

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Disclosures

- Nothing to Disclose
- No Conflicts of Interest

Introduction - Avin Pothuloori, MD, EMBA

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Endocrine Society

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Agenda

Review

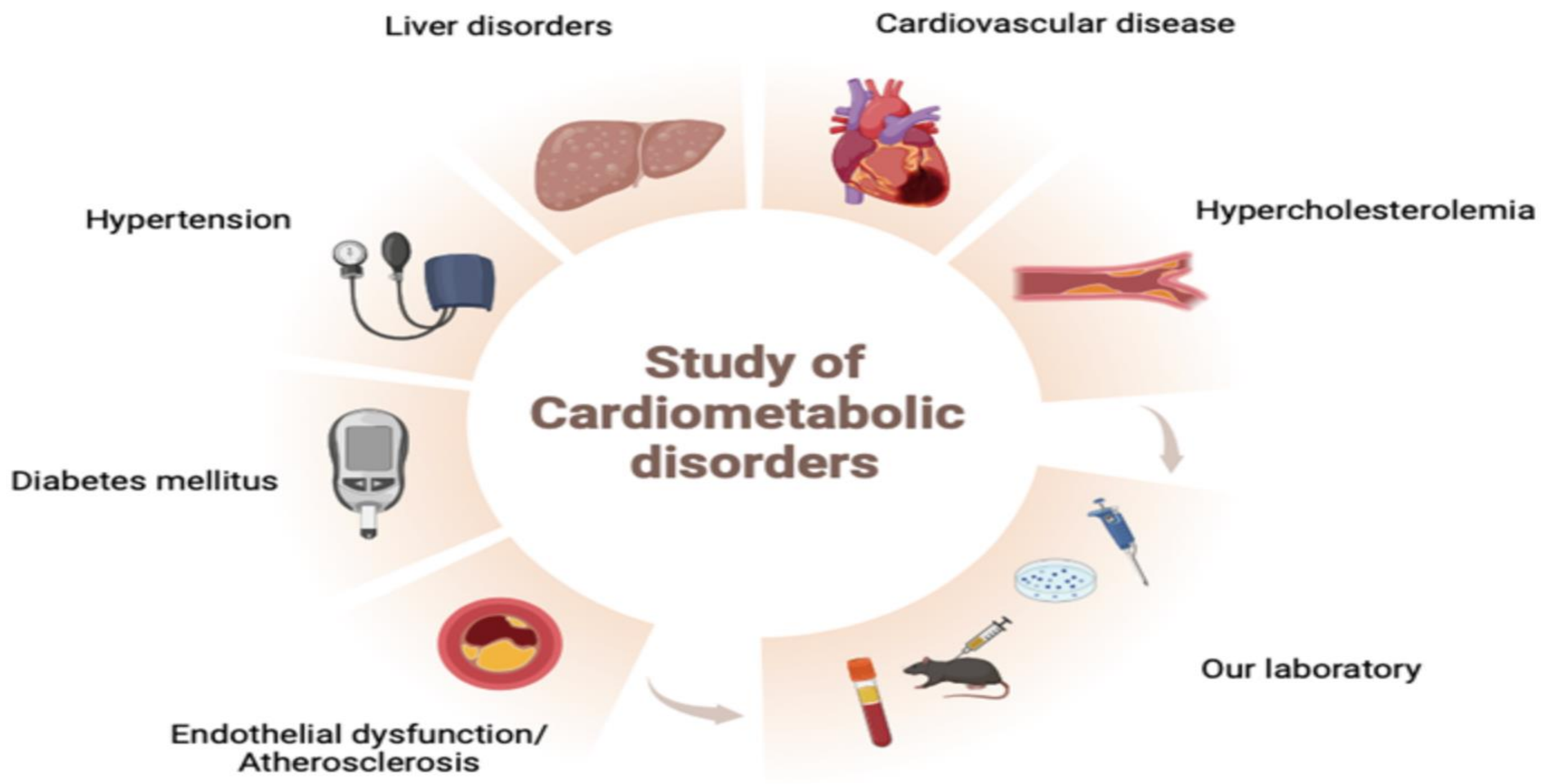
Review Cardiometabolic Disorders

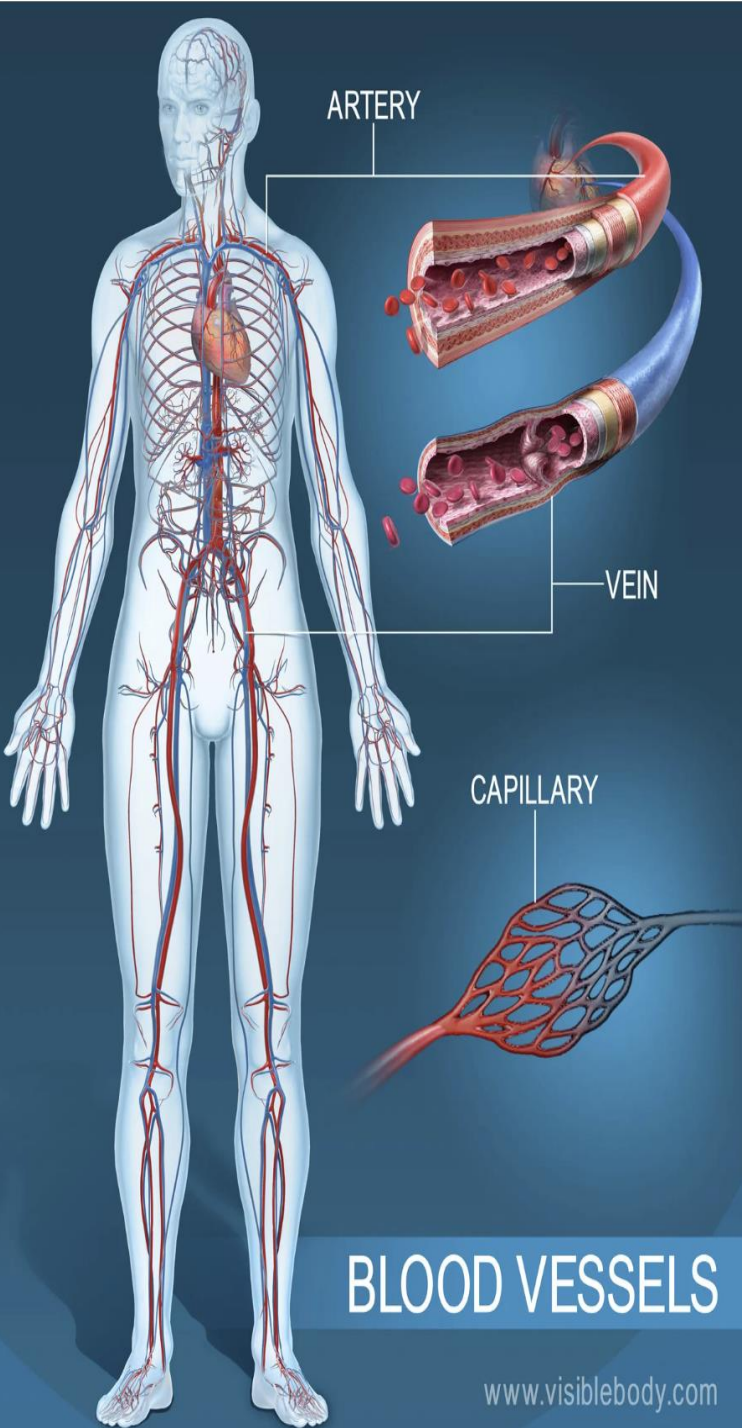
Review

Review Current Research on Gestational Diabetes and Cardiometabolic Disease

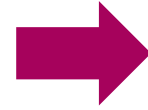
Review

Review Workup, Management of Cardiometabolic Disorders





Carbs



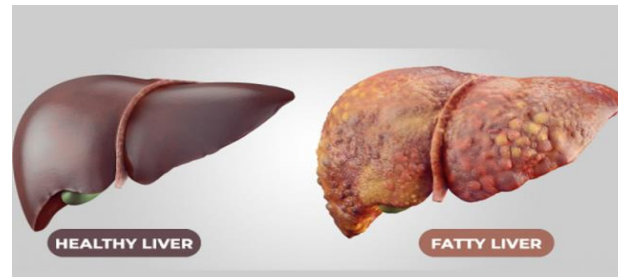
(Key = Insulin)



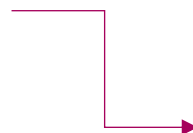
MUSCLE



Energy



FAT



Inflammation, blood vessel damage



Metabolic Syndrome Diagnostic Criteria

Diagnosis of Metabolic Syndrome	
Adult Criteria 3+ criteria	Pediatric Criteria 2+ criteria
WC > 102 cm (men) or 88 cm (women)	WC $\geq$ 90 th percentile for age and gender
Triglycerides $\geq$ 150 mg/dL	Triglycerides $\geq$ 150 mg/dL
HDL-C < 40 (men) or < 50 (women)	HDL-C < 40 mg/dL
Systolic BP > 130 mmHg or > 85 mmHg diastolic	Systolic BP $\geq$ 130 or diastolic $\geq$ 85 mmHg
Fasting glucose $\geq$ 100 mg/dL Or known T2DM	Fasting glucose $\geq$ 100 mg/dL Or known T2DM

Definition of Cardiometabolic Disorders

The American Heart Association recently came out with a new set of guidelines

A cluster of conditions that significantly increase your risk of developing cardiovascular disease and Type 2 diabetes.

- Excess visceral fat
- Insulin resistance or high blood sugar
- Hypertension
- Dyslipidemia
- Metabolic Associated Fatty Liver Disease

GESTATIONAL DIABETES RISK FACTORS



Obesity



**Older maternal age
(above 35 years old)**



**Family
history of diabetes**



PCOS



**History
of delivering a baby
weighing 4000 g or more**



Persistent glucosuria

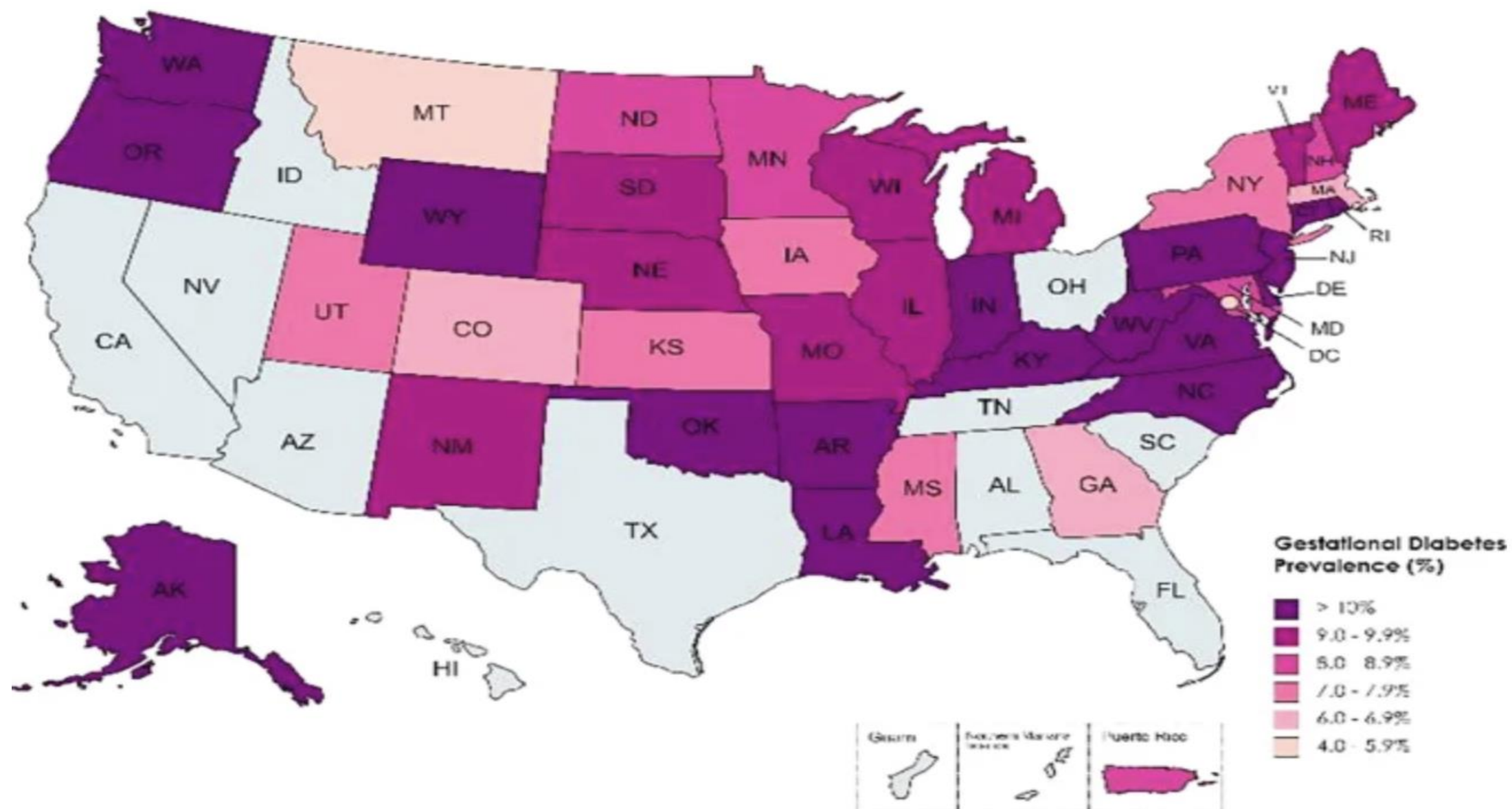
Metabolic Syndrome During Pregnancy

- **2025 Systematic Review and Meta-analysis**
 - Overall Prevalence – 17% in United States, 11% in Nebraska
 - Before 16 weeks gestation – 9.9%
 - After 20 weeks gestation – 24.1%
- **Cardiometabolic Risk Factors affect >30% of pregnancies in USA**

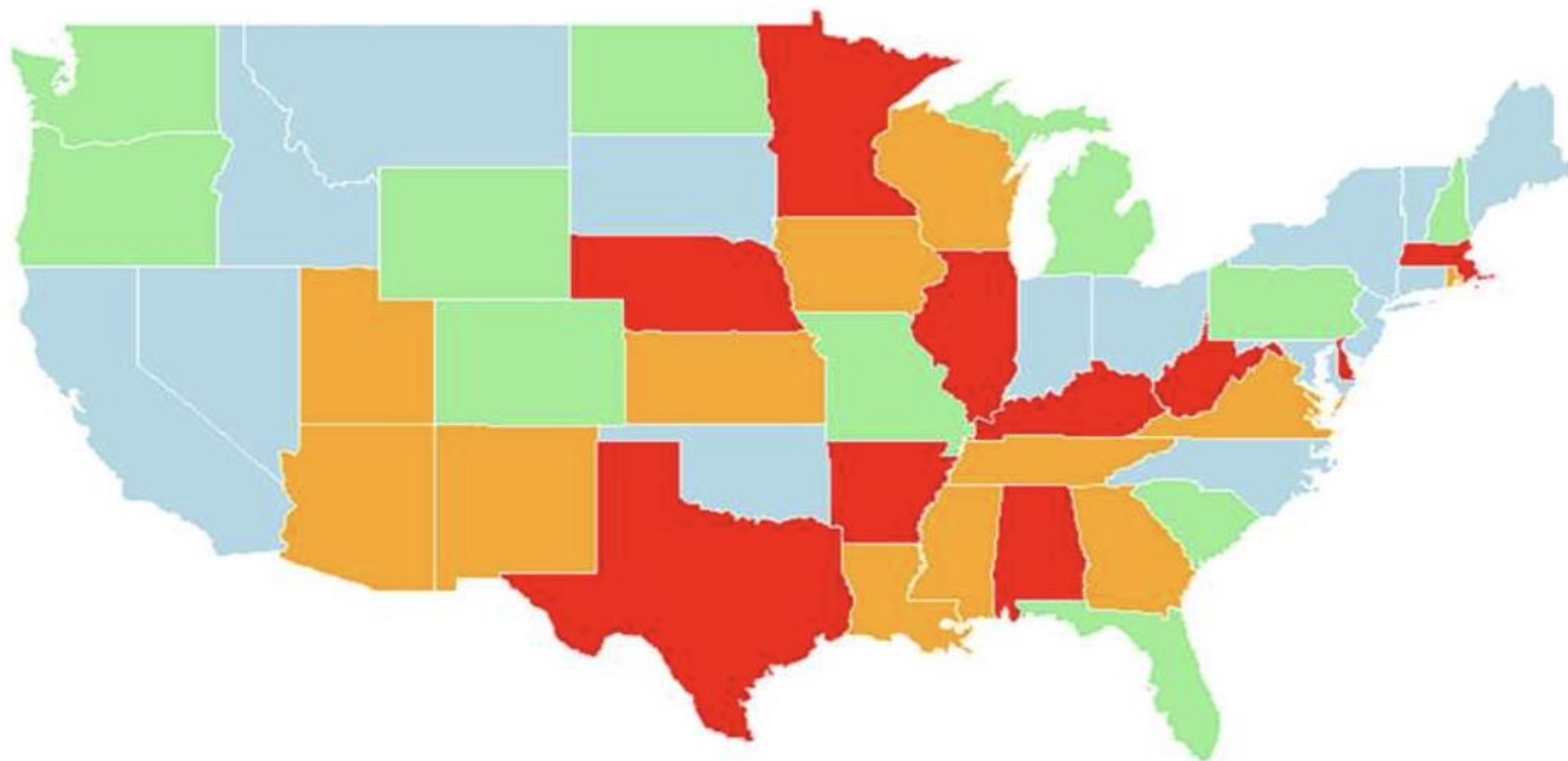
The background is a composite image. At the top, a portion of the periodic table is visible, showing elements like Nb, Mo, Tc, Ru, Rh, Pt, Au, Hg, Re, Os, Ir, and Pt. Below the periodic table, there are several glass test tubes in a rack. One test tube in the foreground is filled with a bright orange liquid. Above this test tube, a glass dropper is shown dispensing a drop of the same orange liquid. To the right of the test tubes, there are faint, stylized chemical structures, including a hexagon with a double bond and the label $=H^3O$, and another structure with the label $OH^2=$ and O^3 .

POPULATION HEALTH EVIDENCE

THE DATA EXISTS!



Percentage Change in Diabetes Prevalence by US States, 2012-2022



Incidence of gestational diabetes continues to rise

A recent U.S. analysis of **12.6 million births** found:

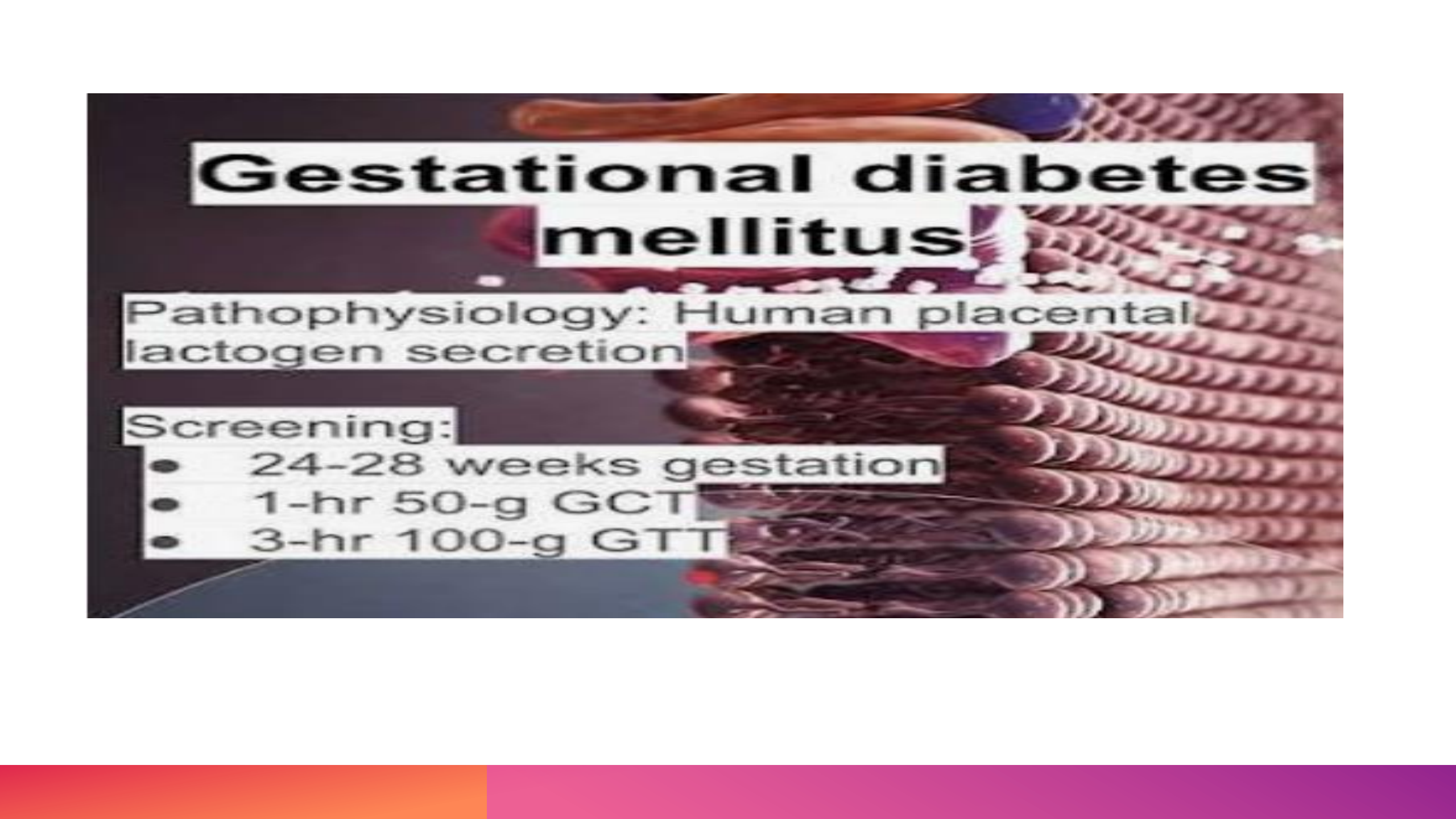
- Gestational diabetes increased **36%** from **2016 to 2024**
- Higher prevalence among:
 - American Indian
 - Alaska Native
 - Asian
 - Native Hawaiian
 - Pacific Islander populations

This trend parallels increasing obesity and metabolic disease in women of reproductive age.



Is Gestational Diabetes an Isolated Complication of Pregnancy?





Gestational diabetes mellitus

Pathophysiology: Human placental lactogen secretion

Screening:

- 24-28 weeks gestation
- 1-hr 50-g GCT
- 3-hr 100-g GTT

Genetic and
epigenetic factors

Lifestyle

Dyslipidemia

Gestational
diabetes
Insulin resistance

Inflammation

Obesity
Metabolic
syndrome

Hypertensive
disorders
Endothelial
dysfunction

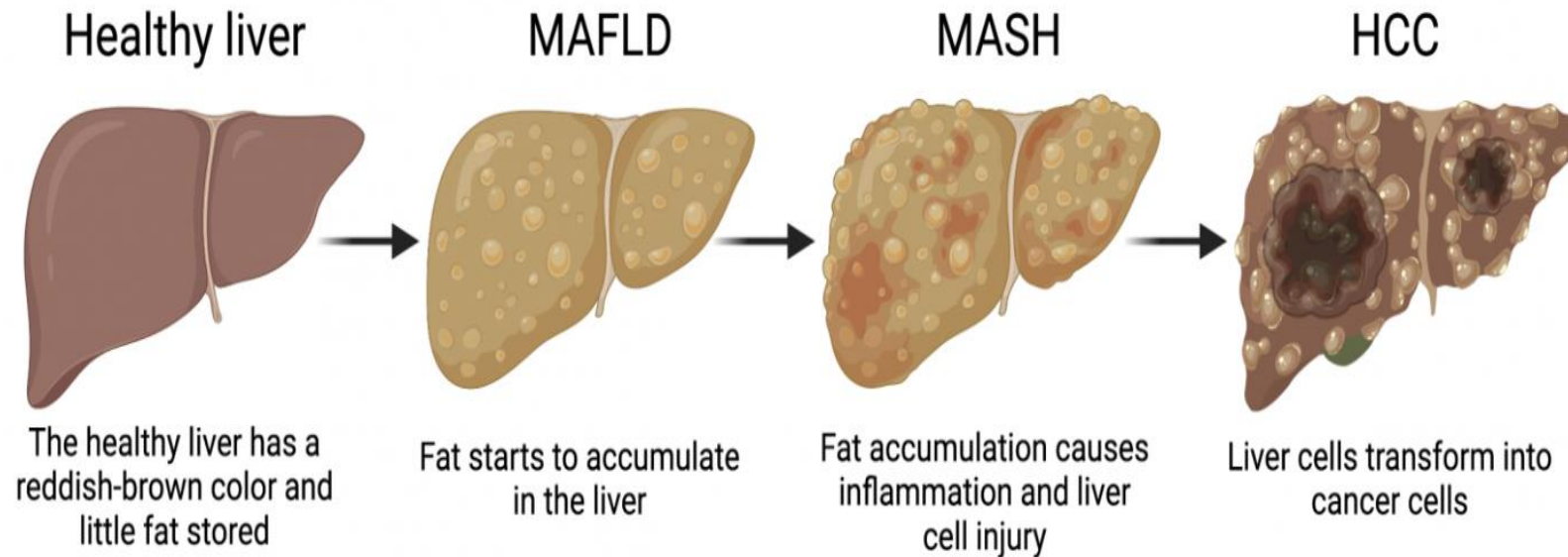
Type 2 diabetes
Cardiovascular
disease

Gestational Diabetes - A Part of Evolving Cardiometabolic Disease

- Gestational Diabetes is a clue of underlying cardiometabolic disease

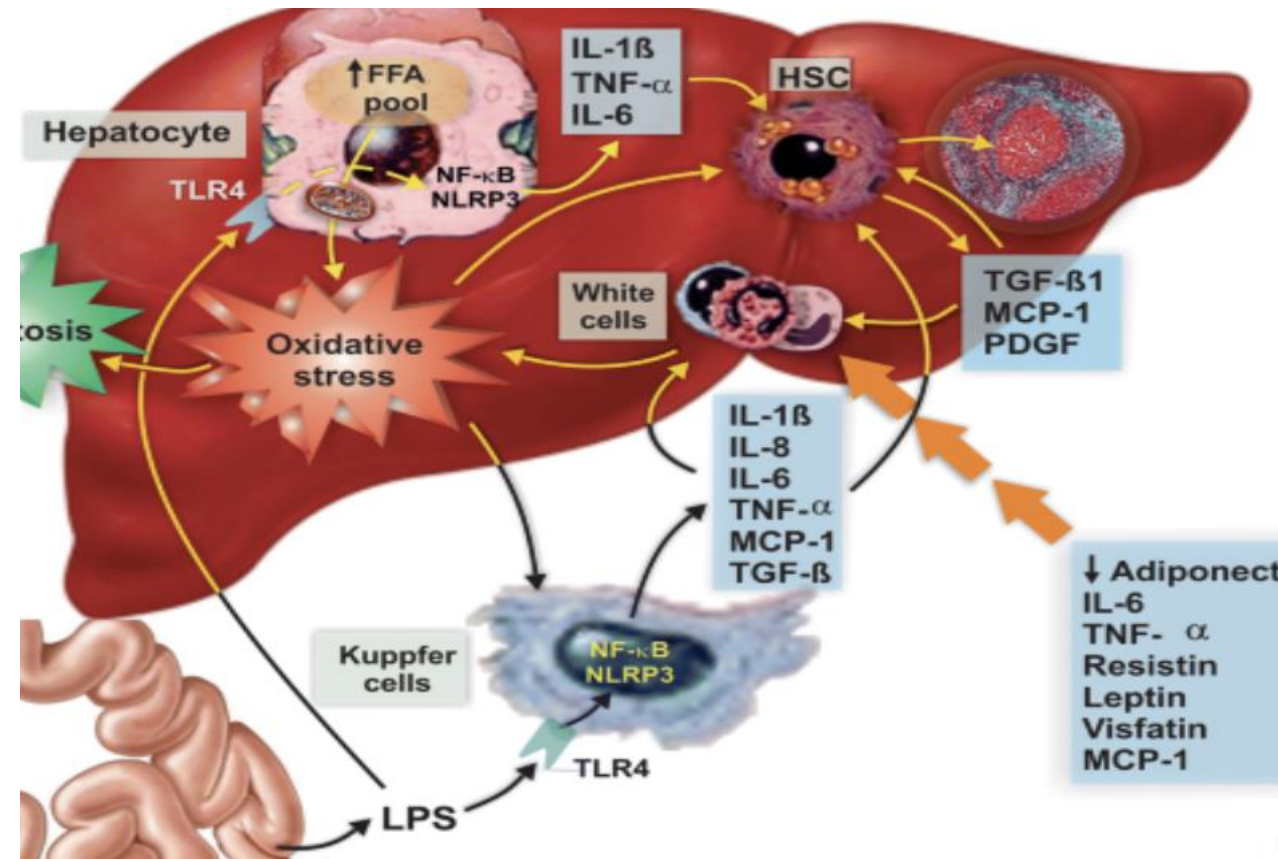
Metabolic Associated Fatty Liver Disease

- By 2035:
 - Becoming the #1 cause of Chronic Liver Disease in the US
 - 100+ million Americans with the disease, >90% not diagnosed properly



MAFLD and Inflammatory Cytokines

- Visceral Fat Production in the liver is hormonally and immunologically active
- Production of inflammatory cytokines that damage vasculature, insulin receptors



Metabolic dysfunction–associated steatotic liver disease and pregnancy

Monika Sarkar¹ and Tatyana Kushner²

Published May 15, 2025 - [More info](#)

- **Underdiagnosis:**

- One of the most striking findings is how MAFLD goes unrecognized before pregnancy
- In the above-mentioned USA ultrasound study, 17-20% of women met criteria for MAFLD
- Less than 3% had documented diagnosis before pregnancy

MAFLD Relationship to Cardiometabolic Disease in Pregnancy

- **Pregnant women with MAFLD have a substantially increased risk of:**
 - Gestational Diabetes - 26% and approximately 2.9x higher odds in women with MAFLD to develop gestational diabetes
 - Hypertensive disorders of pregnancy, including preeclampsia
 - Preterm birth
 - Cesarean delivery
 - Large-for-gestational age infants
 - Future maternal Type 2 Diabetes and Cardiovascular Disease



PHYSIOLOGIC STRESS TEST



Cardiometabolic Stress Test

Pregnancy is a physiologic stress test

During a normal pregnancy, women experience:

- 40–50% increase in blood volume
- 30–50% increase in cardiac output
- Progressive insulin resistance beginning in the second trimester
- Increased hepatic triglyceride synthesis
- Hyperlipidemia (physiologic rise in triglycerides and LDL cholesterol)
- Low-grade systemic inflammation
- Endothelial activation and oxidative stress

Most women adapt successfully. Those with limited metabolic reserve develop complications such as gestational diabetes, preeclampsia, or fetal growth abnormalities, revealing an underlying cardiometabolic vulnerability. This concept is endorsed by the American Heart Association and American College of Cardiology.

Consequences of GD and Cardiometabolic Disease in Pregnancy

- Women with gestational diabetes and underlying cardiometabolic disorders during pregnancy if left untreated:

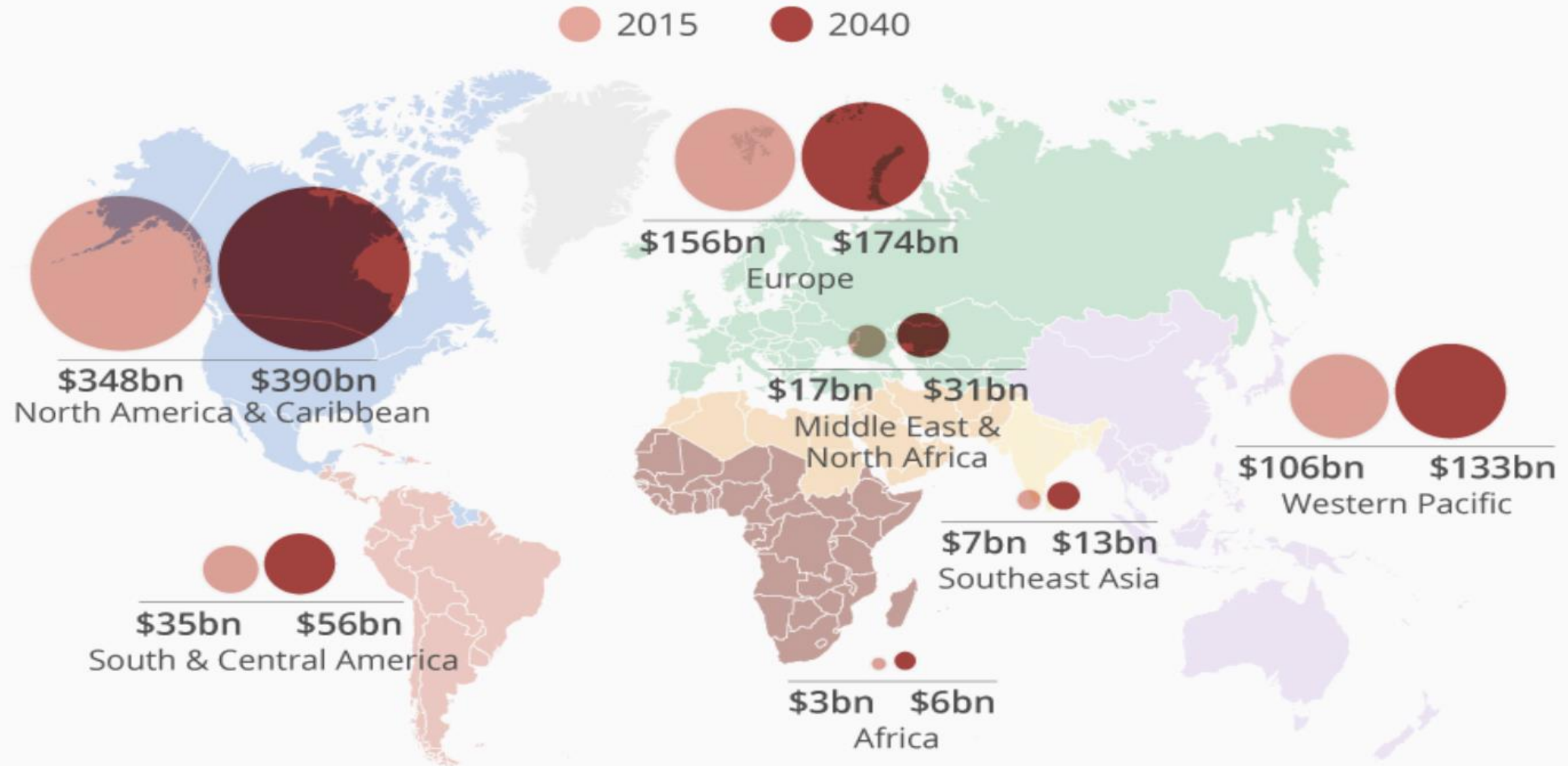
Outcome	Approximate Increased Risk
Coronary artery disease	1.5-2-fold
Myocardial infarction	60%
Heart Failure	70-75%
Ischemic Stroke	70%
Cardiovascular Mortality	30-50%

Longterm Consequences for Children

- Cardiometabolic disease during pregnancy affects offspring through fetal metabolic programming.
- Increased risk of the following;
 - Childhood obesity
 - Insulin resistance
 - Prediabetes
 - Type 2 Diabetes
 - Hypertension
 - Dyslipidemia
 - Metabolic Associated Fatty Liver Disease
 - Premature Coronary Artery Disease

The Global Cost Of Diabetes

Worldwide healthcare expenditure due to diabetes in 2015 and 2040, by region*



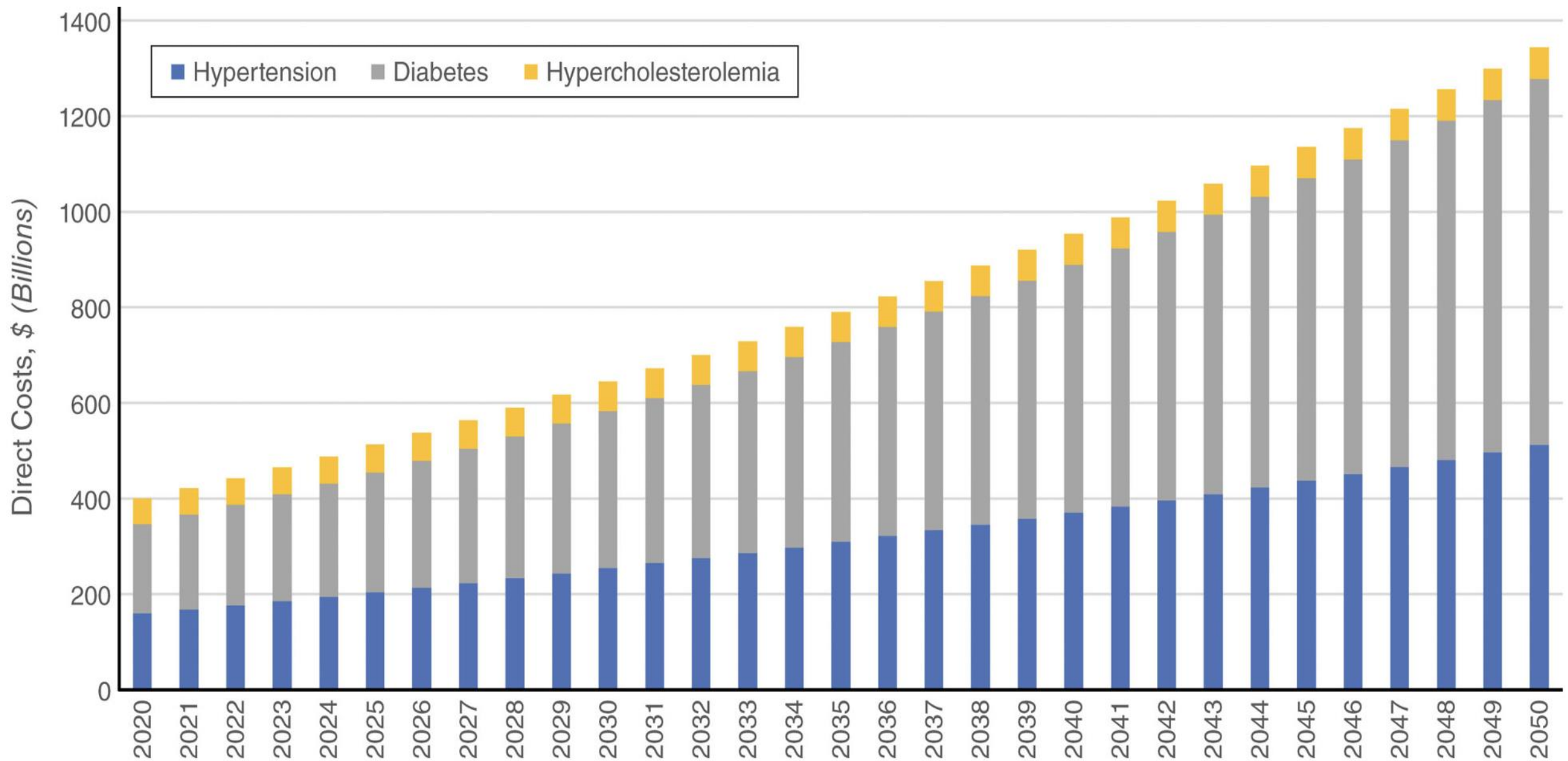
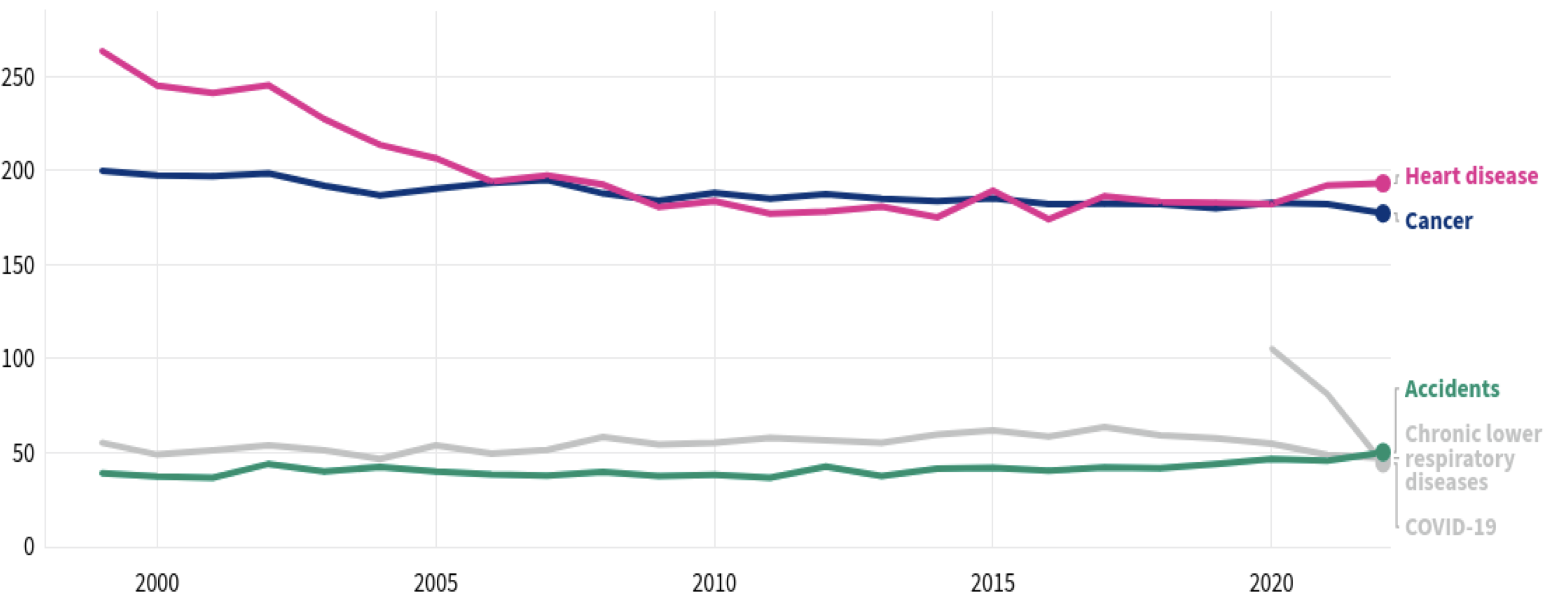


Figure 1. Population-level economic burden of key cardiovascular risk factors in US adults, 2020 to 2050. Our

The leading causes of death in Nebraska are consistently heart disease and cancer.

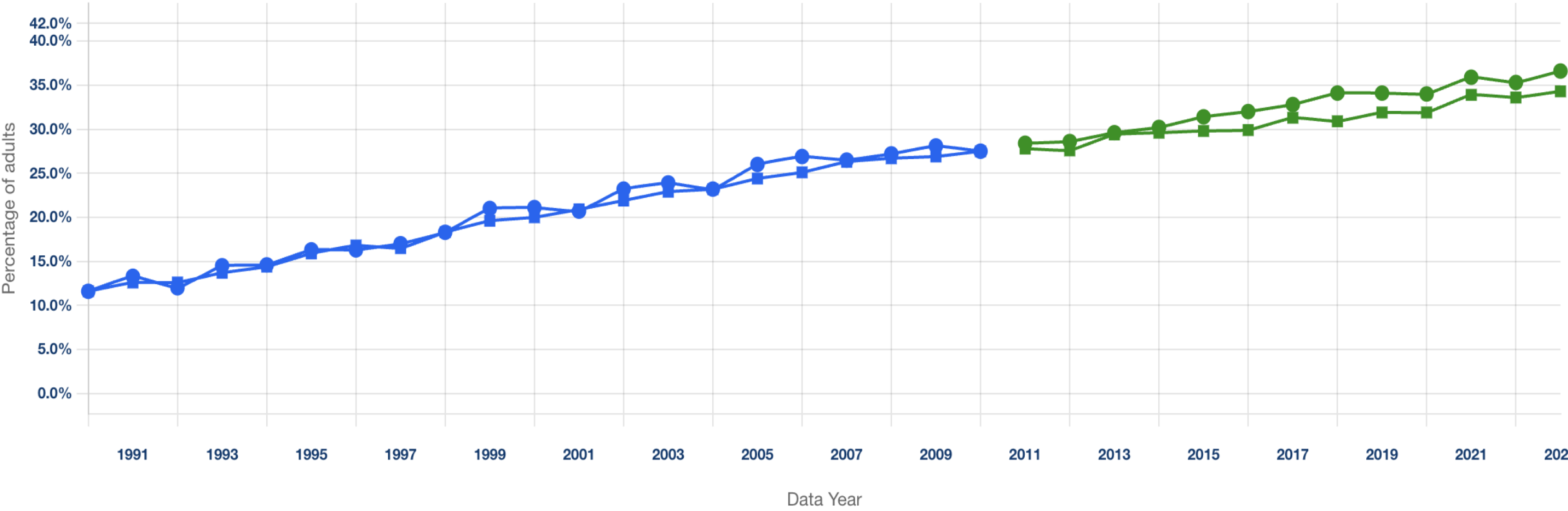
2022's top five causes of death per 100,000 people in Nebraska



Obesity Trends



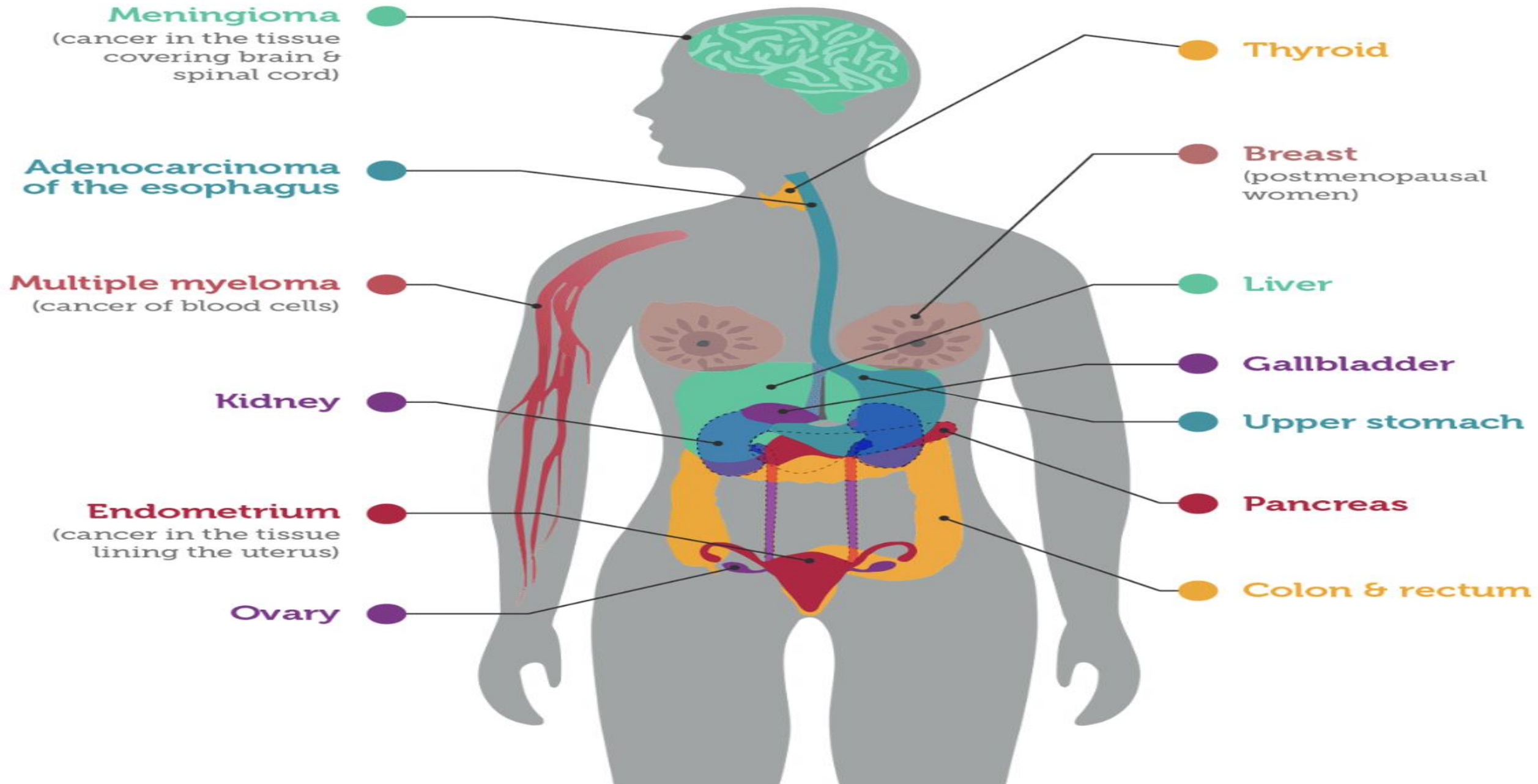
Percentage of adults who have a body mass index of 30.0 or higher based on reported height and weight



Nebraska

Line breaks indicate a change in methodology and may not be comparable

Cancers Associated with Overweight & Obesity





WE MUST ACT NOW

DESPITE THE US SPENDING MORE MONEY ON DIABETES AND CARDIOMETABOLIC DISORDERS THAN ANY OTHER PLACE IN THE WORLD, OUR RATES OF CARDIOMETABOLIC DISORDERS CONTINUE TO RISE.

REACTIVE



**Come with Me, And
You'll See, Why I'm On
So Many Medications.**

PROACTIVE



**WHAT SHOULD WE
SCREEN? WHEN
SHOULD WE
SCREEN?**

Resources

- 2026 AHA/ACC/ADA/ASN Guideline for the Prevention, Detection, Evaluation, and Management of Cardiovascular-Kidney-Metabolic Syndrome: Clinical Practice Guidelines
- Cardiometabolic Health in Pregnancy: Journal of the American College of Cardiology
- Endocrine Society: Obesity Guidelines – To be published soon
- ACOG Guidelines



Cardiometabolic Health in Pregnancy: Prevention, Management, and Long-Term Implications

Authors: Colleen M. Harrington , Amy Sarma, Amanda Jowell, Jessica Passarelli, Camille Powe, Natalie A. Bello, Jennifer Lewey, Melinda B. Davis, Lily Nedda Dastmalchi, Garima Sharma, Michael Honigberg, and Nandita Scott | [AUTHORS INFO & AFFILIATIONS](#)

Publication: JACC: Advances • Volume 5, Number 6_Part_1

Highlights

- Cardiometabolic risk spans the preconception-pregnancy-postpartum continuum.
- Hypertension and hyperglycemia are key drivers of maternal and intergenerational risk.
- The postpartum period is a high-risk, underutilized window for prevention.
- Multidisciplinary, longitudinal care is essential to reduce risk and disparities.

Identify Patients at Risk – Pre-conception

- Individuals with metabolic risk factors include:
 - Pre-pregnancy obesity
 - PCOS
 - Type 2 Diabetes
 - Metabolic Syndrome
 - History of gestational diabetes

Risk factors for fatty liver in

PCOS

@The.PCOS.Dietitian

Higher rates of fatty liver in PCOS are possibly due to:

- Insulin resistance
- High levels of androgens
- Increased abdominal visceral fat
- High blood pressure
- Metabolic syndrome
- Higher levels of triglycerides
- Obstructive sleep apnea
- Genetics
- High LDL chol
- Low HDL chol
- Type 2 diabetes



**Polyendocrine
Metabolic Ovarian
Syndrome:
Cardiometabolic Risk,
Gestational Diabetes
Risk**

**47% of women with PMOS
have MAFLD regardless of BMI**

Pre- conception Lab Studies and Score Calculators

CBC

CMP

HbA1c

Fasting Lipid Panel

C-peptide, fasting insulin level, or stimulated C-peptide 1-2 hours after a meal

What Do the Labs Tell Us?

- Elevated fasting glucose, elevated fasting or post-prandial C-peptide/insulin levels, and/or elevated Triglycerides/Cholesterol/Low HDL/elevated LDL is highly predictive of underlying insulin resistance, even if the HbA1c is normal.
- Calculate a Fibrosis-4 Index using platelets, AST/ALT, age (Use MD-Calc, include in EMR)

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

CAVEAT....

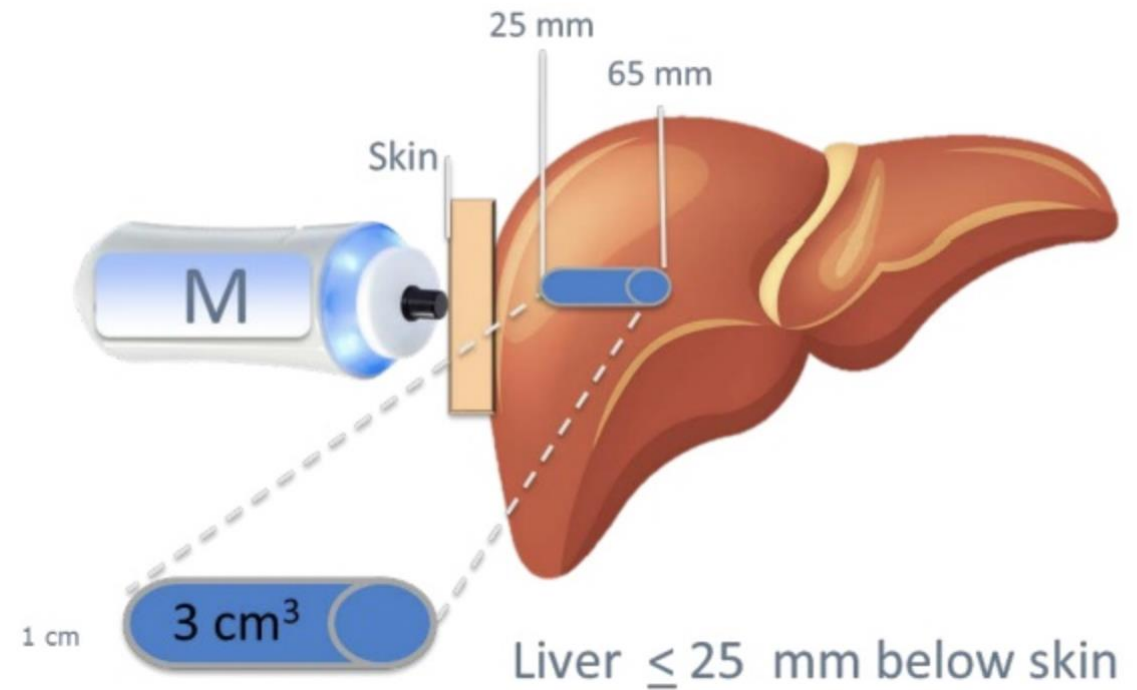
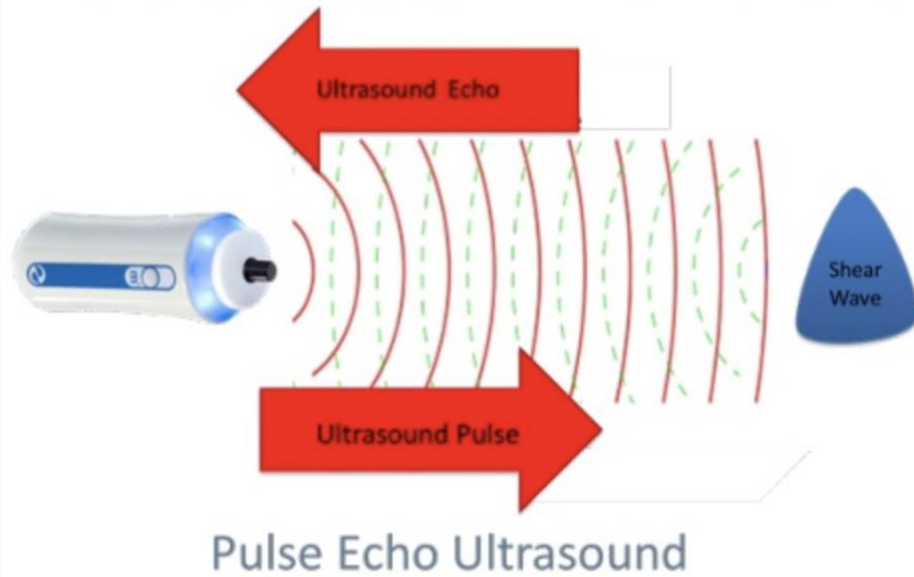
1. Not all patients with NASH/NAFLD have elevated liver enzymes.
2. In those with elevated liver enzymes, it is important to assess for secondary causes of liver disease. The conditions include, but not limited to;
 1. Hemochromatosis
 2. Hepatitis
 3. Lipodystrophy
 4. HELLP Syndrome
 5. Alcohol related liver damage
 6. Drug use
 7. Glycogen storage diseases

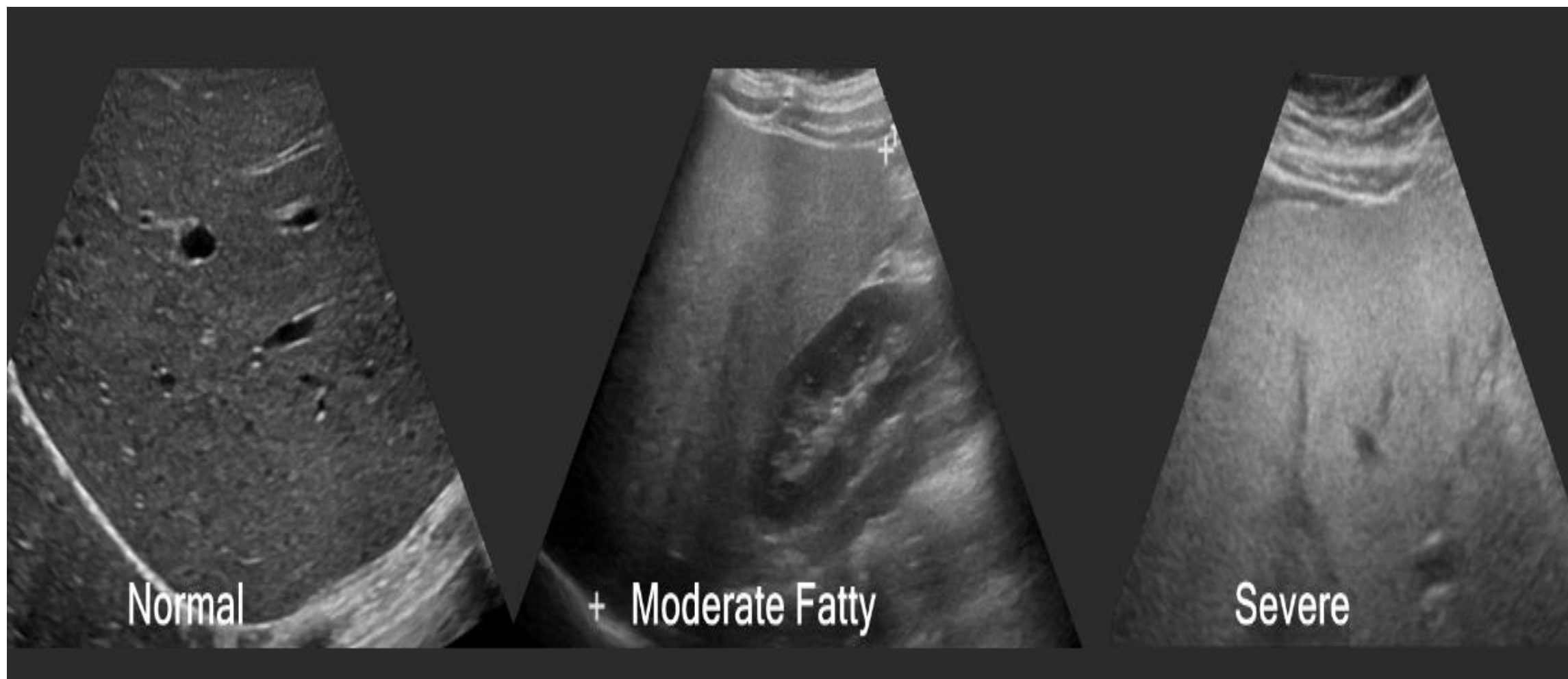
Interpretation of Fib-4 and Next Steps

- Low Risk (<1.30 to 1.45): Low chance of advanced liver fibrosis
- Intermediate Risk (1.46 to 2.67) : Additional testing warranted (Imaging)
- High Risk (>2.67 to >3.25) : Higher chance of advanced fibrosis or cirrhosis, warranting hepatology evaluation
- Intermediate Risk Patients:
 - Vibration Controlled Transient Elastography
 - MR Elastography

VCTE

Shear Wave Speed Measurement





MRE - Magnetic Resonance Elastography

- 92% to 100% sensitivity and 92% to 95% specificity for evaluation of hepatic steatosis compared to ultrasonography
- MRI with elastography is a better method for the identification of the degrees of fibrosis in patients with increased waist circumference/central abdominal obesity



Preconception Treatment of MAFLD

- Stage 1 – Lifestyle/dietary changes, weight loss, exercise programs, SMART goals
- Stage 2 – above + Rezdiffra (Resmetirom), Actos if diabetic, GLP-1 agonists associated with weight loss
- Stage 3 – Same as Stage 2
- Stage 4 – Hepatology referral

Lifestyle and Dietary Recommendations

- A heart healthy diet before pregnancy associated with lower risk of :
 - MAFLD
 - Gestational Diabetes
 - Pre-term birth
 - Hypertensive Disorders of Pregnancy
- Dietary patterns recommended – rich in vegetables, fruit, whole grains, nuts, legumes, and fish (careful of mercury content)
 - DASH diet
 - Mediterranean Diet
- At least 150-300 minutes of moderate exercise weekly pre-conception
- ACOG – at least 150 minutes of moderate intensity aerobic and/or strength training exercise during pregnancy recommended

Preconception, Postpartum Treatments: American Heart Association Guidelines for Cardiometabolic Disorders



Lifestyle + Dietary changes



GLP-1 agonists are gold standard in treatment for obesity, diabetes.



Treatment of MAFLD – Rezdiffra, Actos, ongoing studies on Mounjaro



Hypertension management

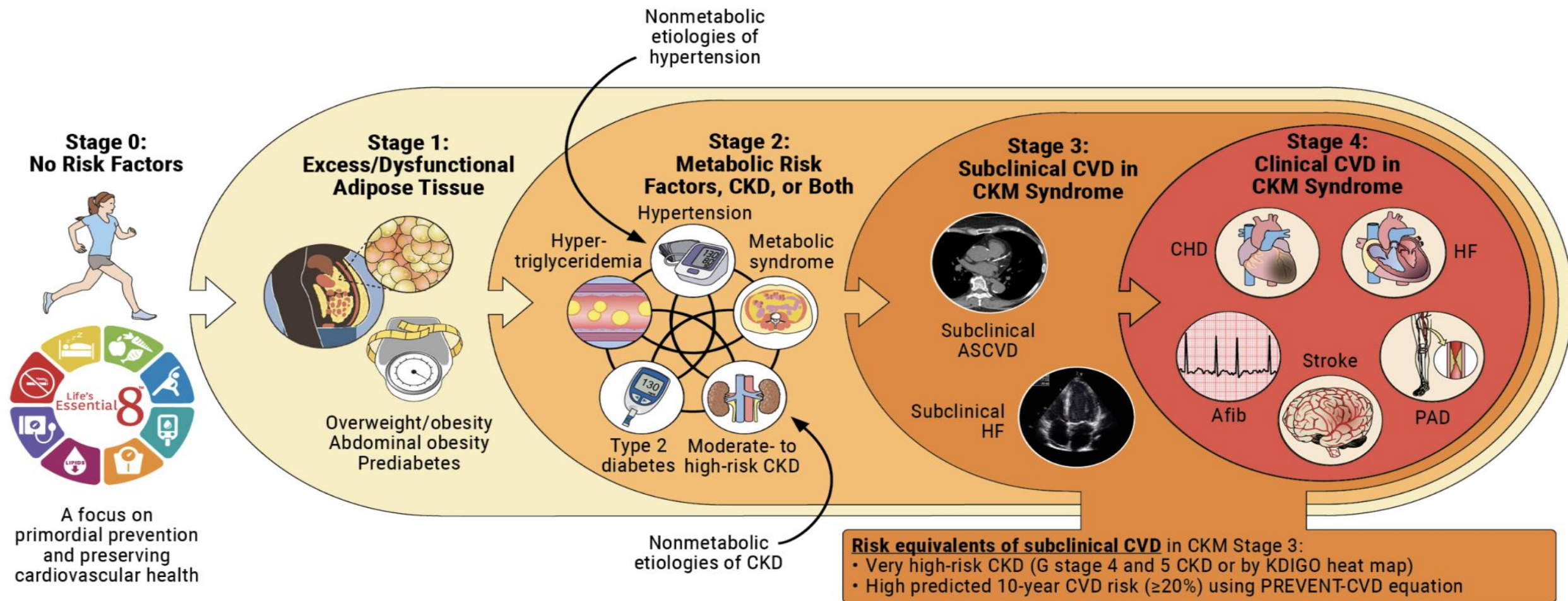


Hyperlipidemia management

MOST IMPORTANT

- Identify patients at highest risk early on
- Multidisciplinary, longitudinal care is the most essential to reduce risk and disparities (AHA CKM guidelines)

Stages of CKM Syndrome



MULTIDISCIPLINARY APPROACH



WE INVITE YOU....

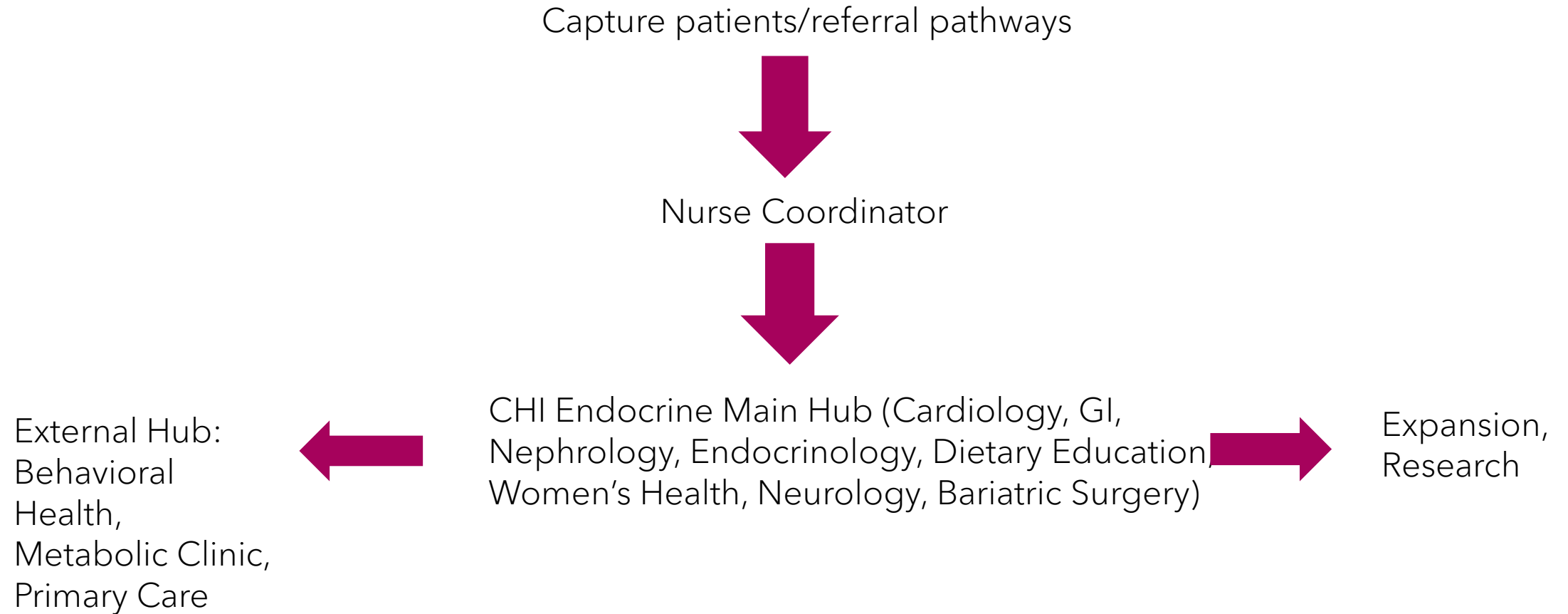
1. Improve regional population health statistics
2. Collaborate in a multidisciplinary approach rather than siloed patient care
3. Improve quality care in PREVENTION
4. Decrease cost of healthcare for our patients and healthcare system



CHI Multidisciplinary Cardiometabolic Center of Excellence

BETTER OUTCOMES. LOWER COSTS. HEALTH EQUITY REALIZED

Cardiometabolic Center - Framework



Conclusions

- I hope this presentation allows you to view Gestational Diabetes in a different lens, as a continuum of Cardiometabolic Disorders
- Emphasize importance of screening for Metabolic Associated Fatty Liver Disease and how it contributes to development of gestational diabetes/type 2 diabetes, hyperlipidemia, and increased cardiovascular mortality
- Introduce new Guidelines for Cardiometabolic Disorders
- Introduce the CHI Multidisciplinary Cardiometabolic Center as a Resource for your patients, for education, and for research

THANK YOU

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UNIVERSITY
MEDICAL CENTER

