



Maternal Diabetes and Cardiovascular Malformations

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Outline

- Pregnancy outcomes associated with
 - ◆ Pre-existing diabetes (PDM)
 - ◆ Gestational diabetes (GDM)
- Possible implications for follow-up of GDM and research

Pre-existing Diabetes and Pregnancy: Maternal Complications

- Spontaneous abortion
- Hypoglycemia, ketoacidosis
- Pregnancy-induced hypertension
- Pyelonephritis, other infections
- Polyhydramnios
- Preterm labor
- Cesarean delivery

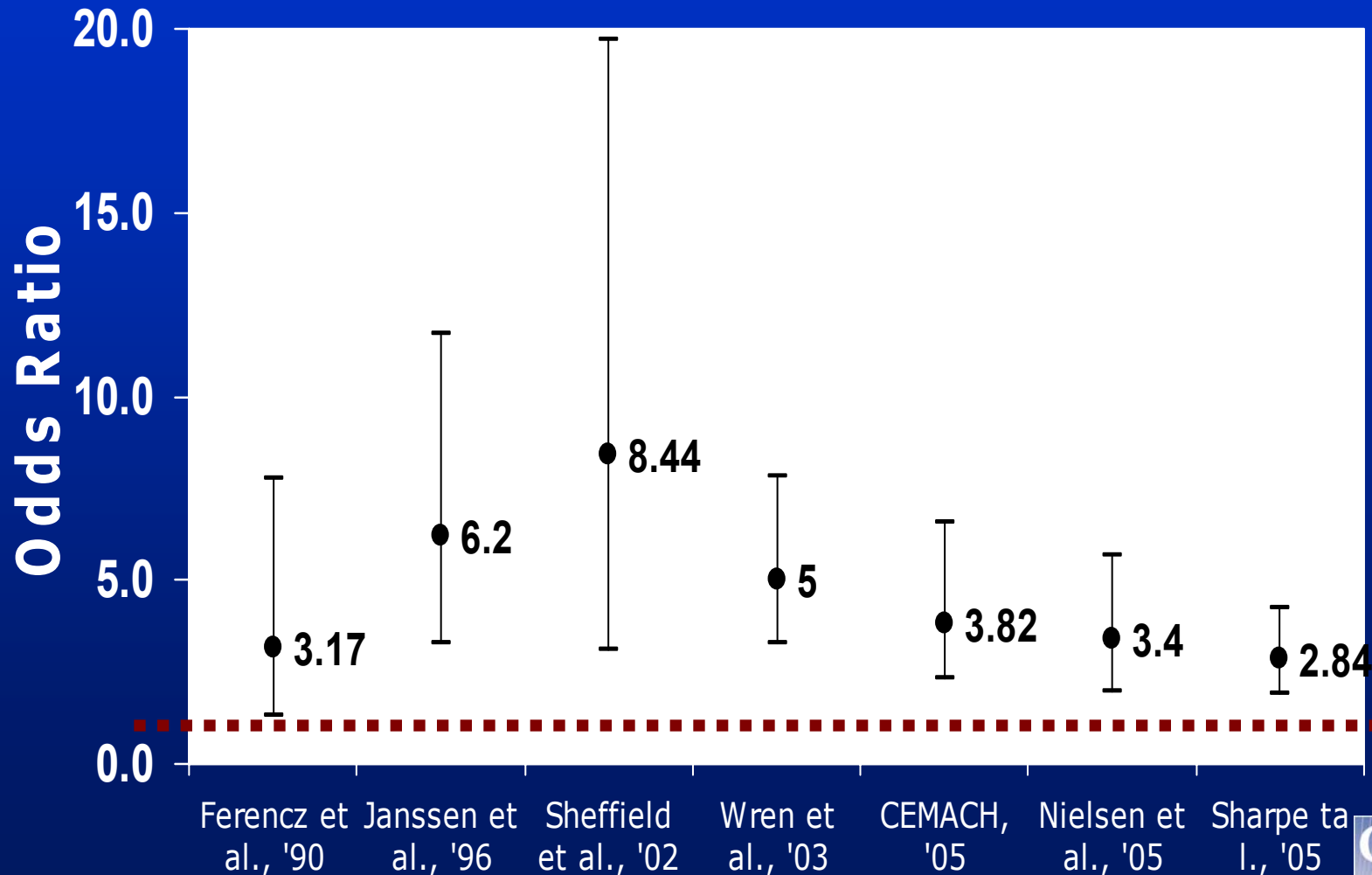
Pre-existing Diabetes and Pregnancy: Fetal and Perinatal Complications

- **Birth defects**
- Birth injury
- Birth asphyxia
- Cardiac hypertrophy
- Heart failure
- Hypocalcemia
- Hypoglycemia
- Hypomagnesemia
- Increased red blood cells
- Jaundice
- Macrosomia
- Neurological instability
- Organomegaly
- Respiratory distress
- Small left colon syndrome
- Stillbirth

Public Health Significance of Congenital Heart Defects (CHD)

- 1 in 110 births (8-9 per 1000 births)
 - ◆ ~ 8000-9000 affected infants each year
- 1 in 4 major defects
- 35-50% infant deaths due to birth defects
- Increased risk of poor developmental outcomes

Studies of Maternal Pregestational Diabetes and Risk of CHD



Strategies and Challenges for the Prevention of CHD Associated with PDM

- Strategies
 - ◆ Pregnancy planning
 - ◆ Glycemic control, particularly during the periconceptional period
- Challenges
 - ◆ Diagnosed before pregnancy
 - ★ Unplanned pregnancies
 - ★ Effective glycemic control is a complex task
 - ◆ Undiagnosed before pregnancy

Gestational Diabetes Mellitus (GDM)

- Glucose intolerance beginning or first recognized during pregnancy
 - ◆ May include some women with unrecognized type 2 diabetes
- Complicates 4-8% of pregnancies / year

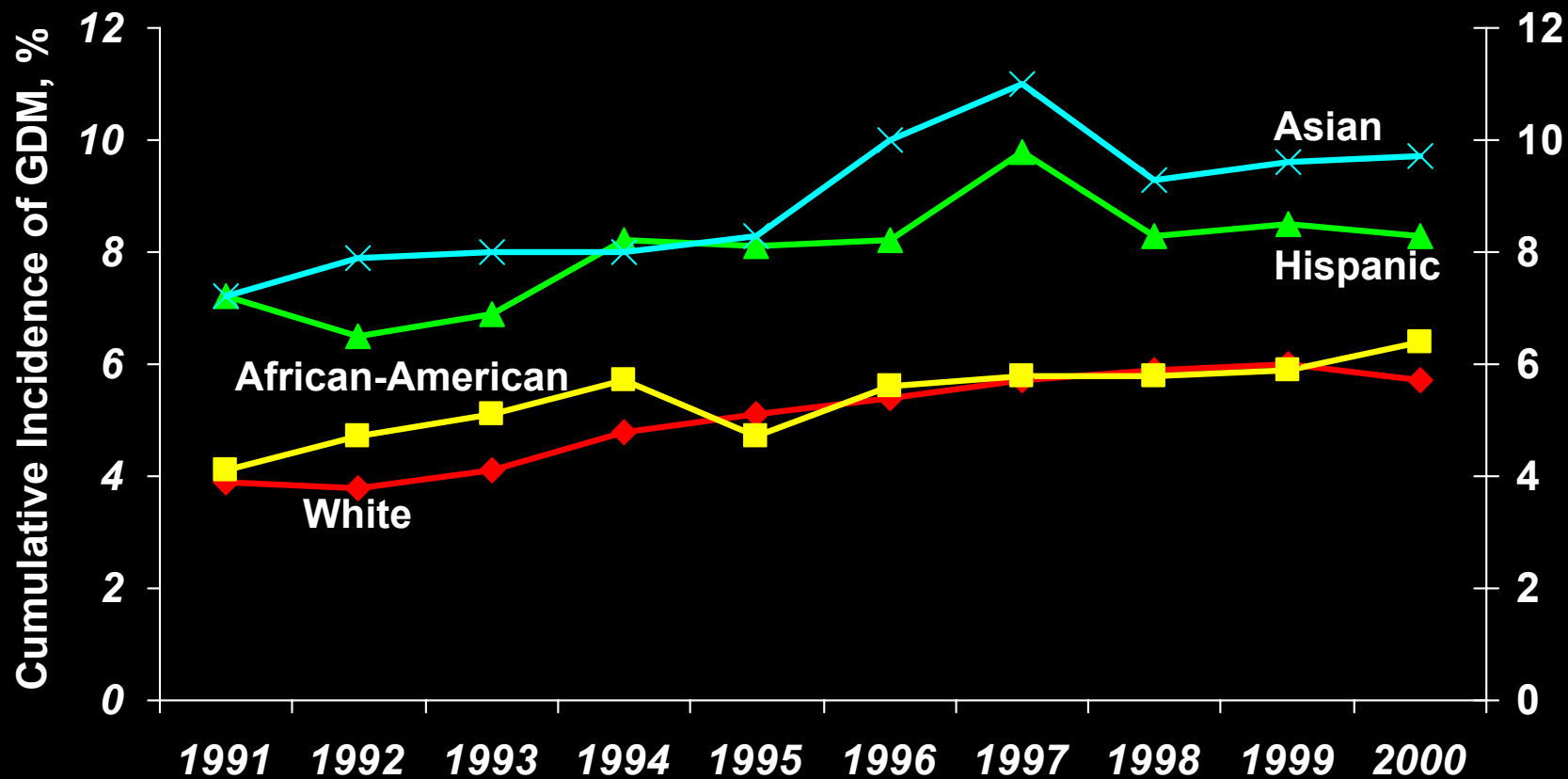
Concerns about GDM: Index Pregnancy

- Hypertensive disorders
- Intrauterine fetal death
- Fetal macrosomia
- Fetal dystocia (fractures, nerve palsies)
- Cesarean delivery
- Neonatal hypoglycemia
- Jaundice
- Polycythemia
- Hypocalcemia
- Hypoglycemia

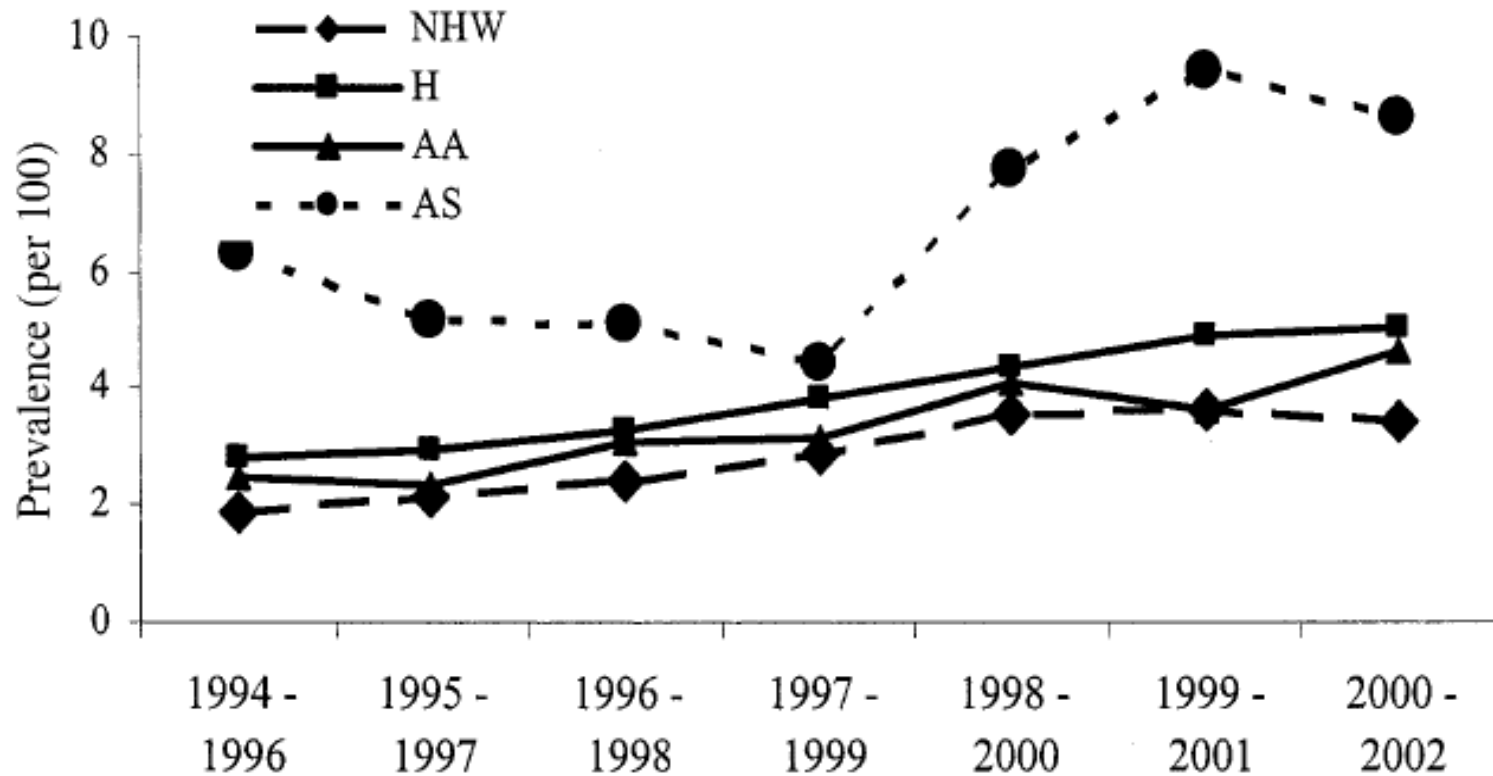
Concerns about GDM: Long Term

- Subsequent pregnancies at increased risk of recurrence (recurrence rate of 35%–50%)
- Development of type 2 diabetes
 - ★ As many as 70% of affected women will progress to type 2 diabetes in their lifetime
- Increasing prevalence

Age-adjusted cumulative incidence of gestational diabetes mellitus, Kaiser Permanente, Northern California GDR



Age-adjusted Prevalence of GDM, Kaiser Permanent, Colorado



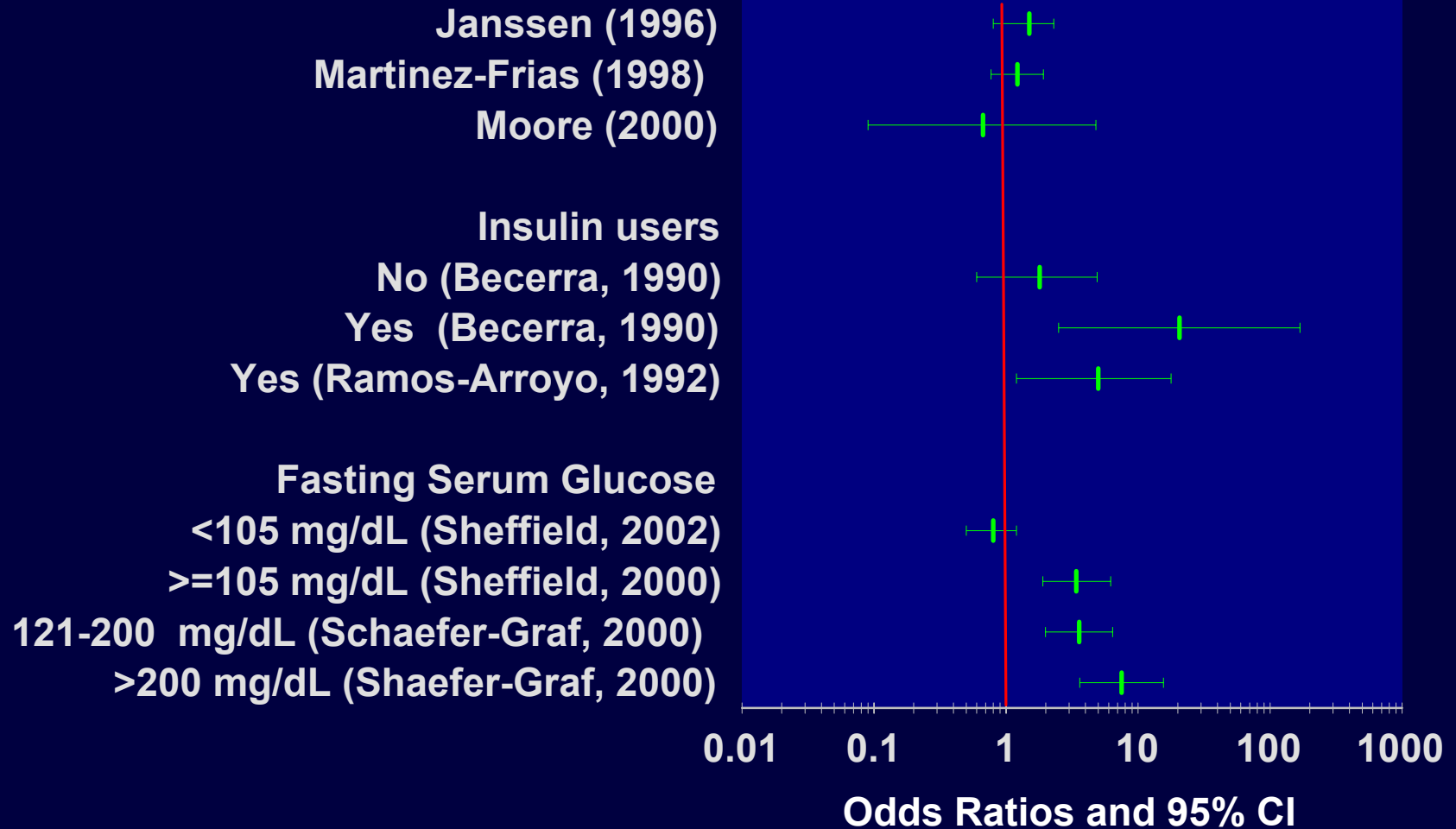
Dabelea et al (2005)

DIABETES CARE, VOLUME 28, NUMBER 3, MARCH 2005

Is GDM Associated with Heart Defects?

- Most published studies have reported no associations of GDM with risk for heart defects
- However, stratification of GDM by level of hyperglycemia suggests an association of GDM with increased FBS and heart defects

Association of Heart Defects and GDM by Insulin Use or FBS Levels



Question

- Is GDM associated with an increased risk for heart defects in a population-based setting in more recent years?

Data Source: The Baltimore-Washington Infant Study (BWIS)

- Case-control study of heart defects in Maryland, District of Columbia, and Northern Virginia (1981-1989)
- Cases
 - ◆ Ascertained from hospital and community searches
 - ◆ Confirmed by echocardiogram, cardiac catheterization, surgery, or autopsy before 1 year of age
 - ◆ Participation: >90%
- Controls
 - ◆ Random sample of all live-born infants without CVM
 - ◆ Stratified by month and year of birth and hospital of birth
 - ◆ Participation: 78% were 1st choices and 17% were 2nd choices
- Home interviews

Inclusions and Exclusions

■ Cases

- ◆ Singleton infants with CHD (n=2,551)
- ◆ Exclusions
 - ★ Chromosomal disorders, syndromes, rare subtypes

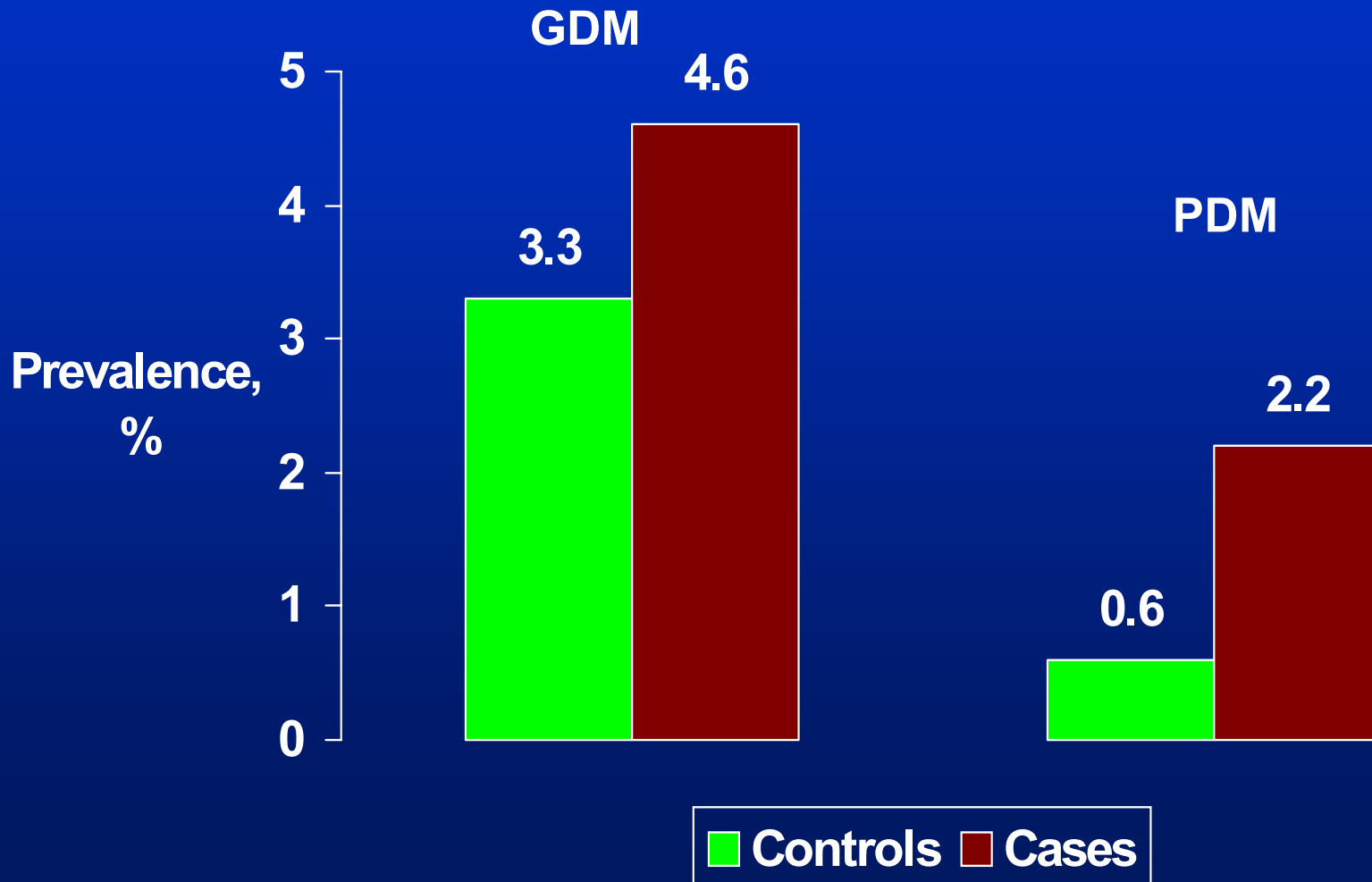
■ Controls

- ◆ Singleton infants w/o defects (n=3,494)

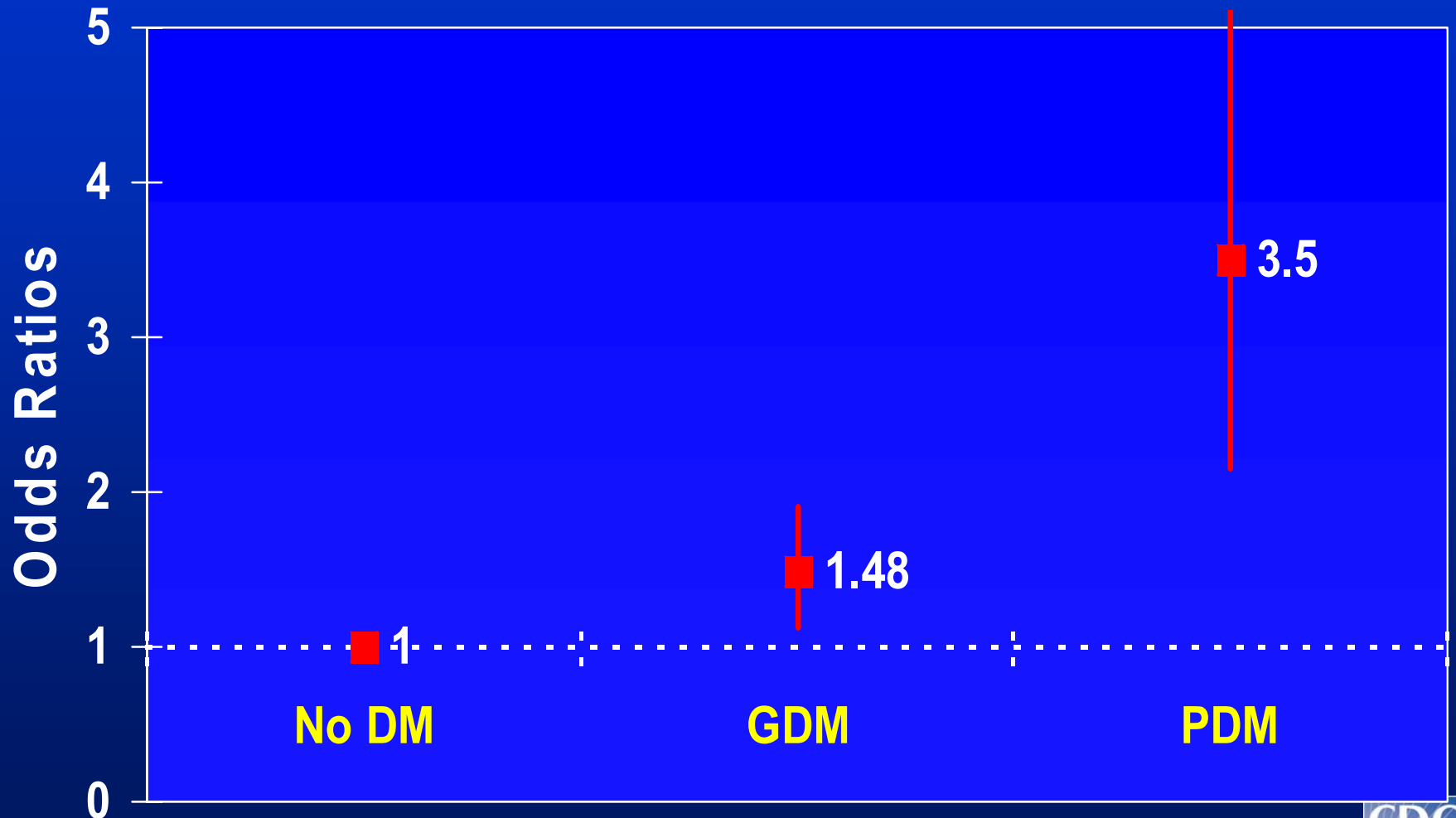
Classification of Maternal Diabetes based on Self-reports

- Ever had diabetes?
 - ◆ No = non diabetic
- If yes, Did you have diabetes only during this pregnancy?
 - ◆ Yes = gestational (GDM)
 - ◆ No = pre-gestational (PDM)

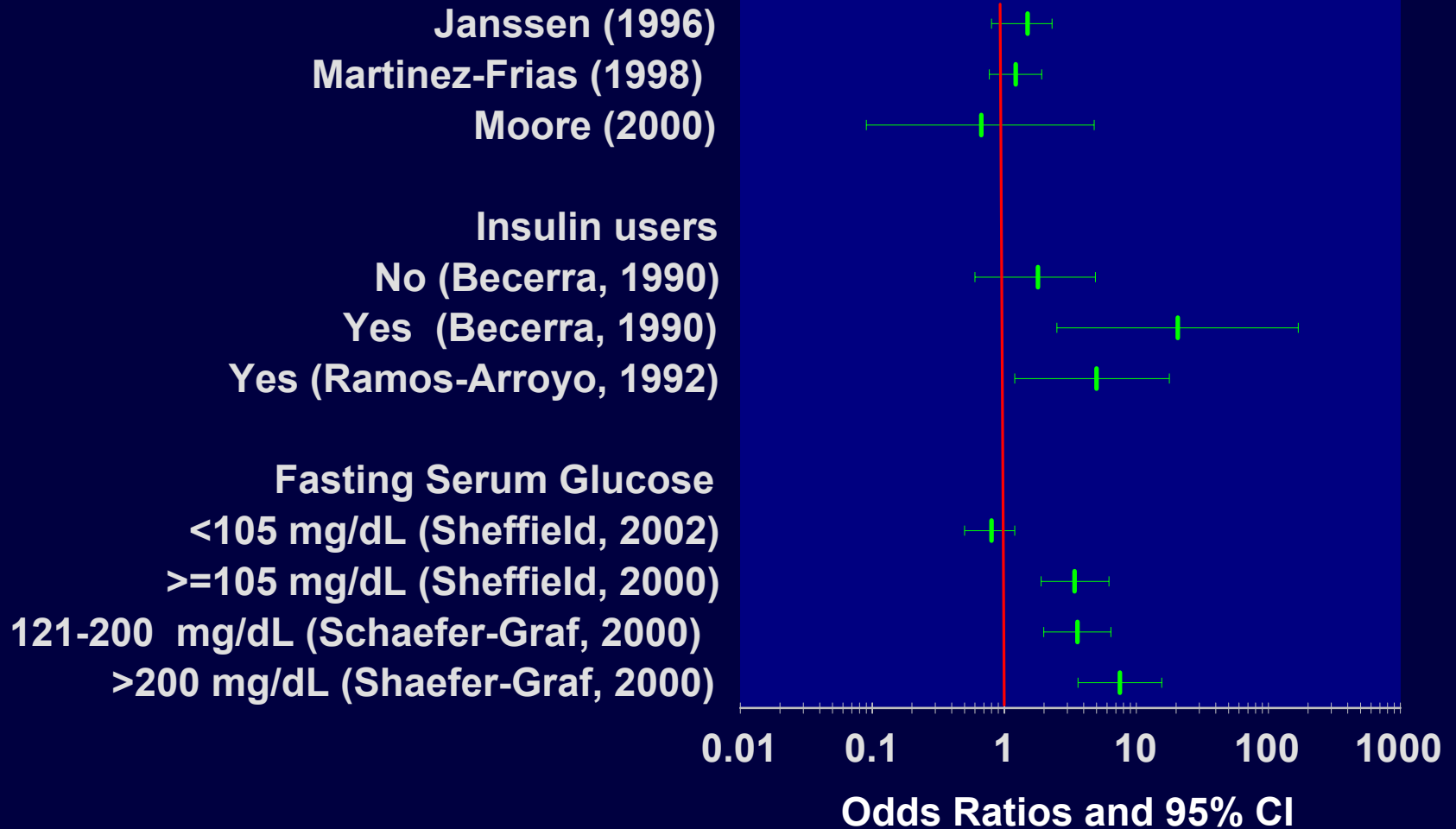
Prevalence of GDM and PDM, by Case-control Status



Odds Ratios for Heart Defects, GDM and PDM



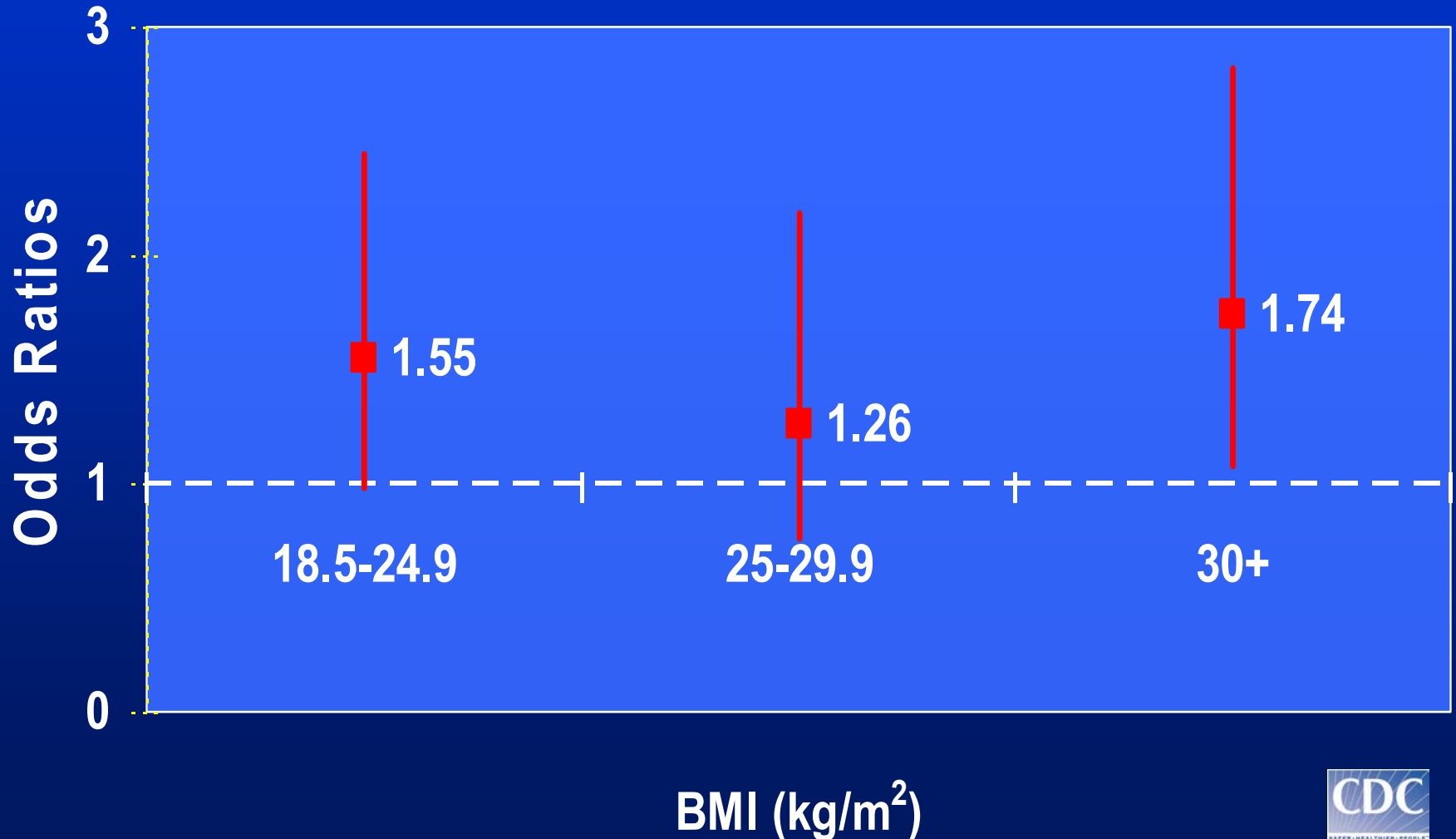
Association of GDM with Heart Defects varies by Insulin Use or FBS Level



If obesity is associated with \uparrow insulin resistance and \uparrow risk for GDM,

Is the association of heart defects with GDM due to an association with pre-pregnancy obesity / \uparrow insulin resistance?

Odds Ratios for Heart Defects and GDM, by Pre-pregnancy Weight Status (BMI)



Conclusion

- GDM appears to be associated with heart defects
 - ◆ However, the excess risk is limited to offspring of women with GDM and pre-pregnancy obesity
 - ★ => association might be with undiagnosed T2DM

Possible Implications for Follow-up

- Women diagnosed with GDM should have postpartum follow-up evaluations to determine baseline glycemic status
 - ◆ If T2DM or pre-diabetes, counseled re
 - ★ Management of diabetes
 - ★ Family planning
 - ◆ If normal,
 - ★ Counseled about recurrence risk of GDM
 - ★ Weight loss/control
 - ★ Screened for GDM in subsequent pregnancies

Possible Implications for Research

- Need to identify practical and effective strategies for screening and treating GDM
- Need to identify modifiable factors that might enable adequate periconceptional glycemic control in women at risk of GDM
- Identify practical recommendations for the prevention of birth defects associated with periconceptional hyperglycemia