Obesity and Adult Heart Disease Begin in the Womb

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Objectives

- Recognize the world wide epidemiology of obesity
- Describe the effects of in utero exposure to under and overnutrition on
  - Fetal obesity
  - Childhood obesity
  - Adult obesity and the Metabolic Syndrome
- Discuss possible effective interventions

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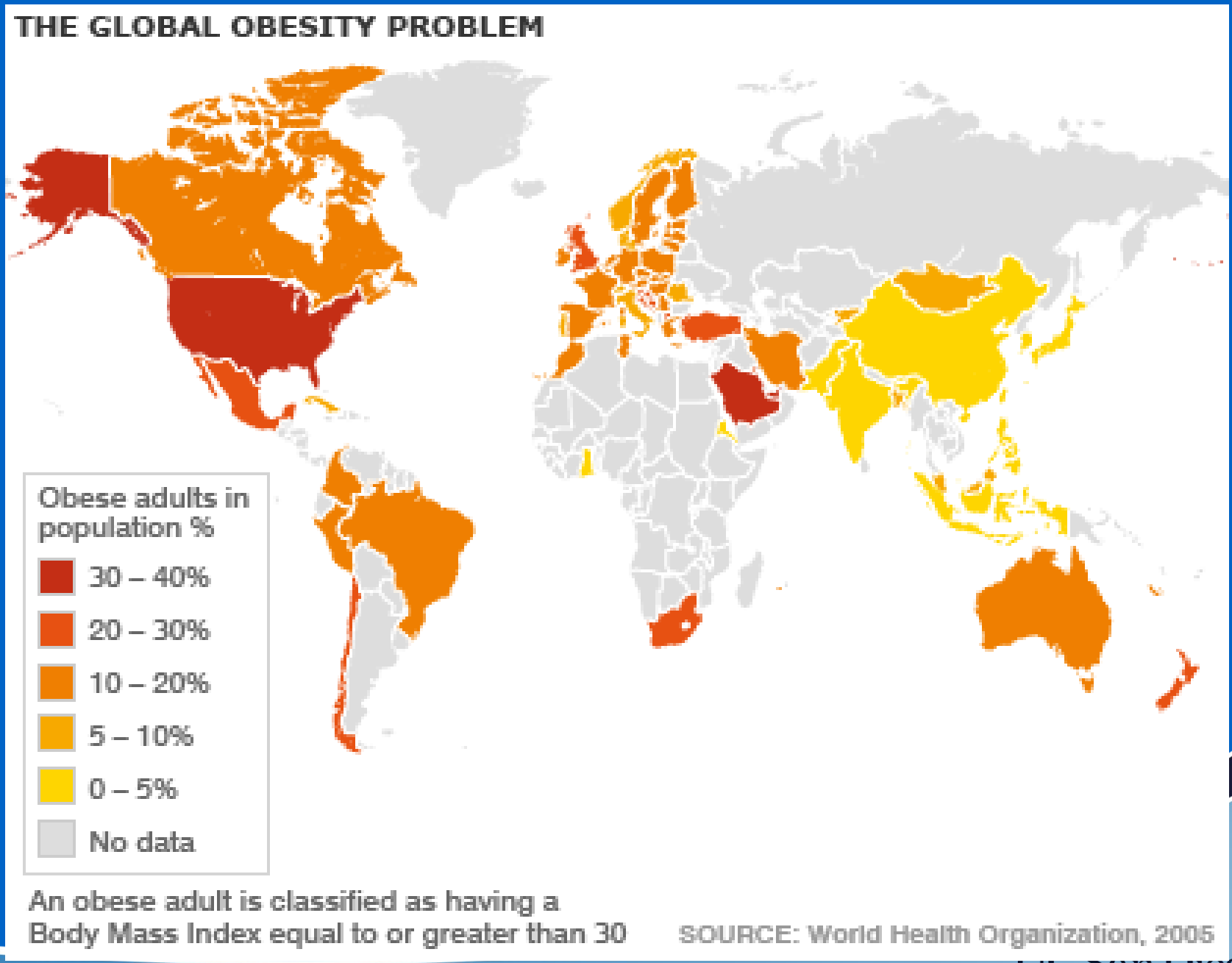
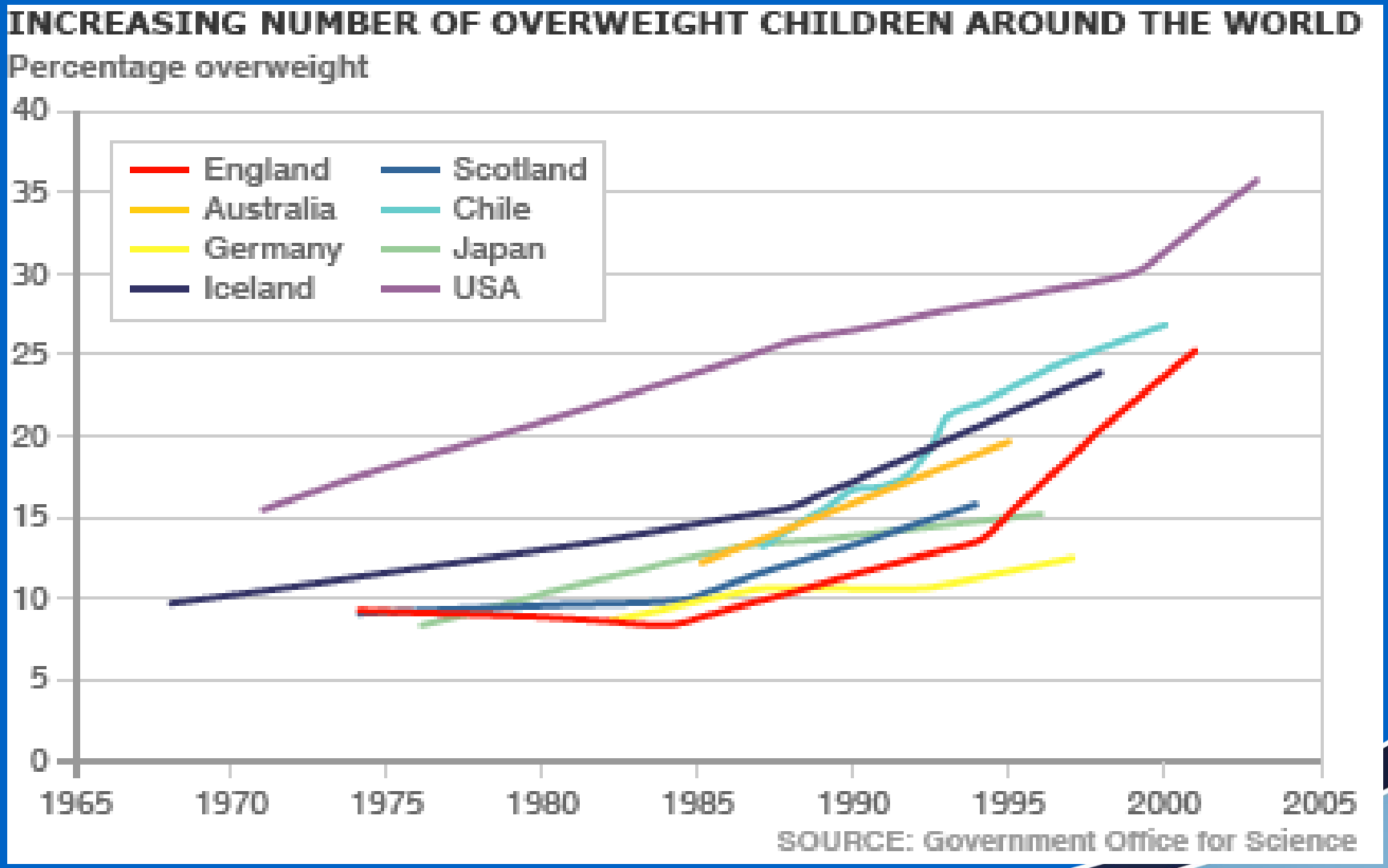


BBC 2 January 2008



BBC 2 January 2008

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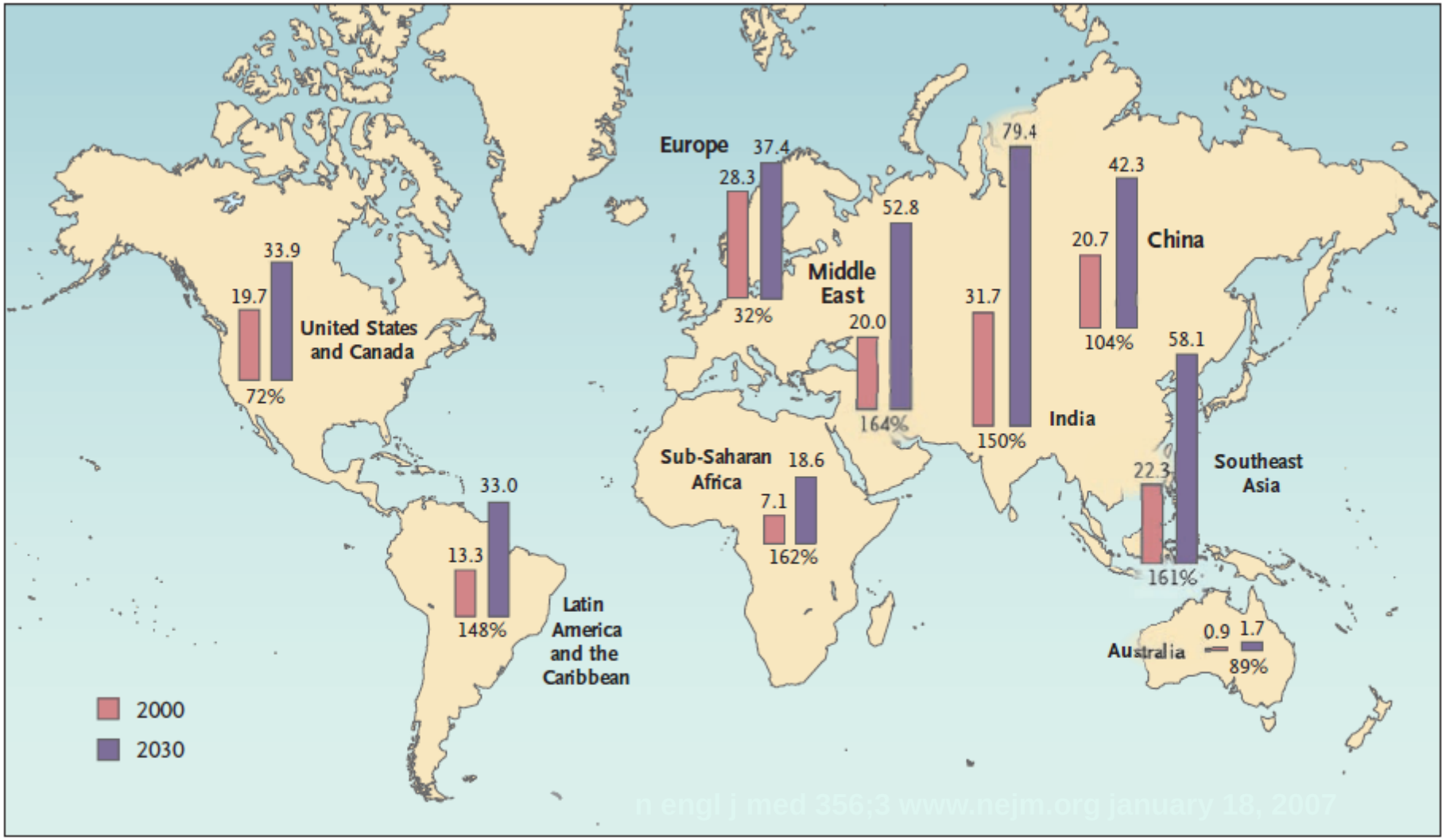
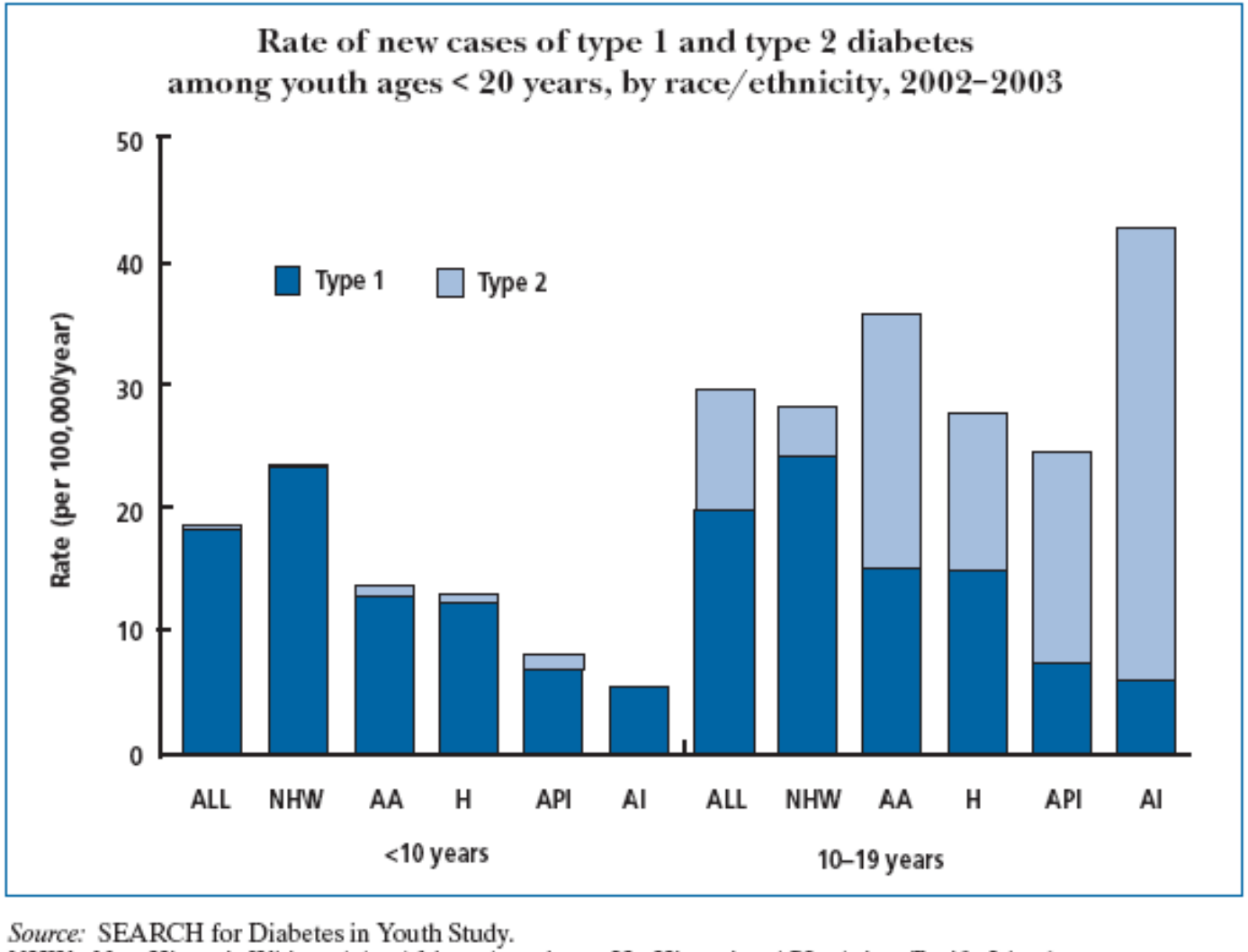
Millions of Cases of Diabetes in 2000 and Projections for 2030



Millions of Cases of Diabetes in 2000 and Projections for 2030, with Projected Percent Changes.

Data are from Wild et al.[3]



Source: SEARCH for Diabetes in Youth Study.
NHW=Non-Hispanic Whites; AA=African Americans; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

NIDDK. National Diabetes Statistics, 2007 fact sheet. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, 2008.

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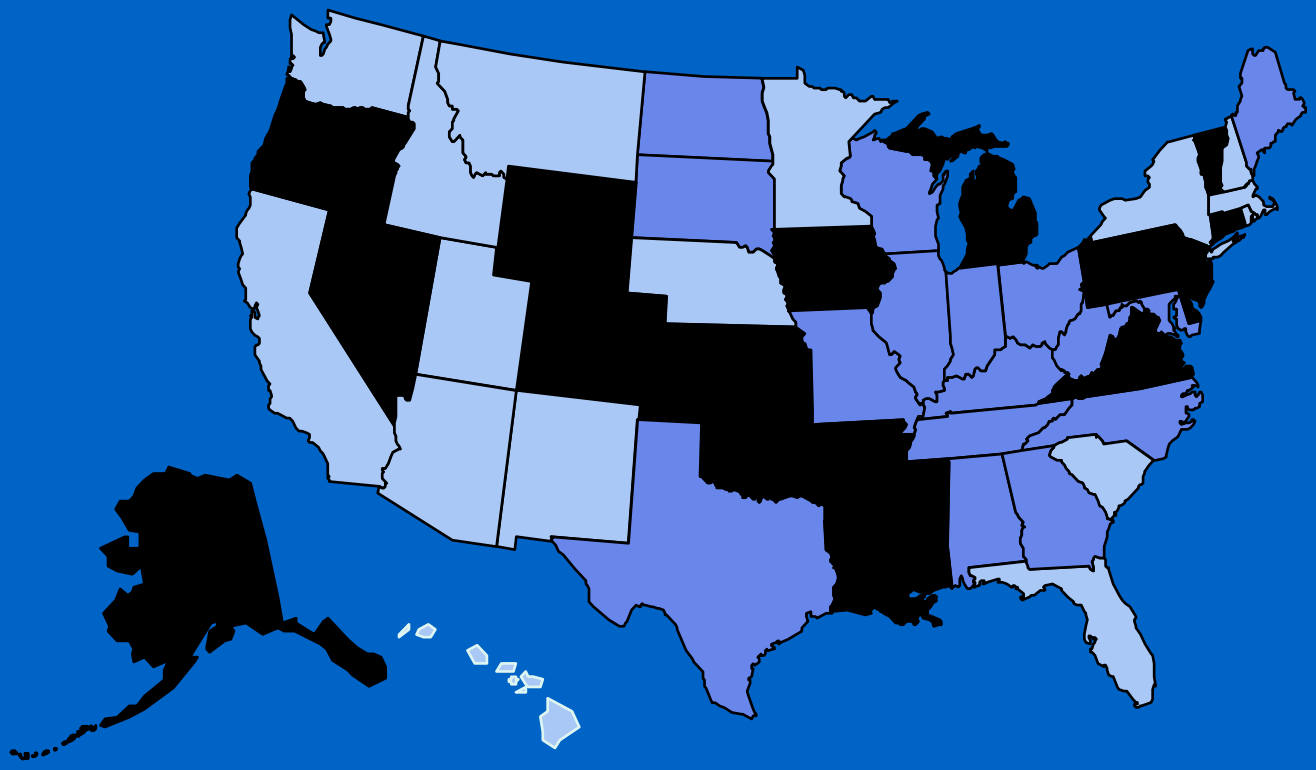
Obesity Trends* Among U.S. Adults

BRFSS, 1987

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



No Data | <10% | 10%–14%

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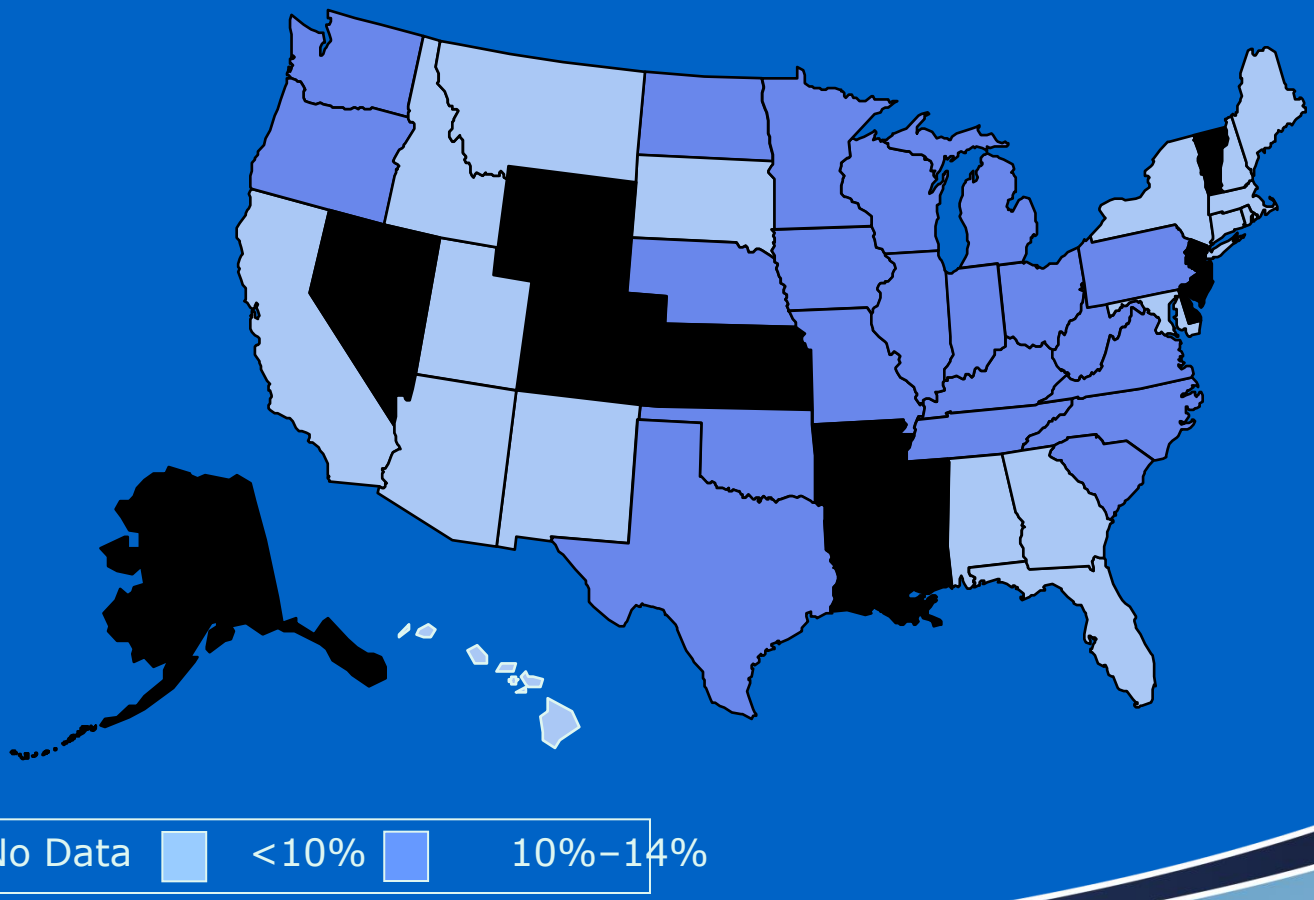
Obesity Trends* Among U.S. Adults

BRFSS, 1989

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



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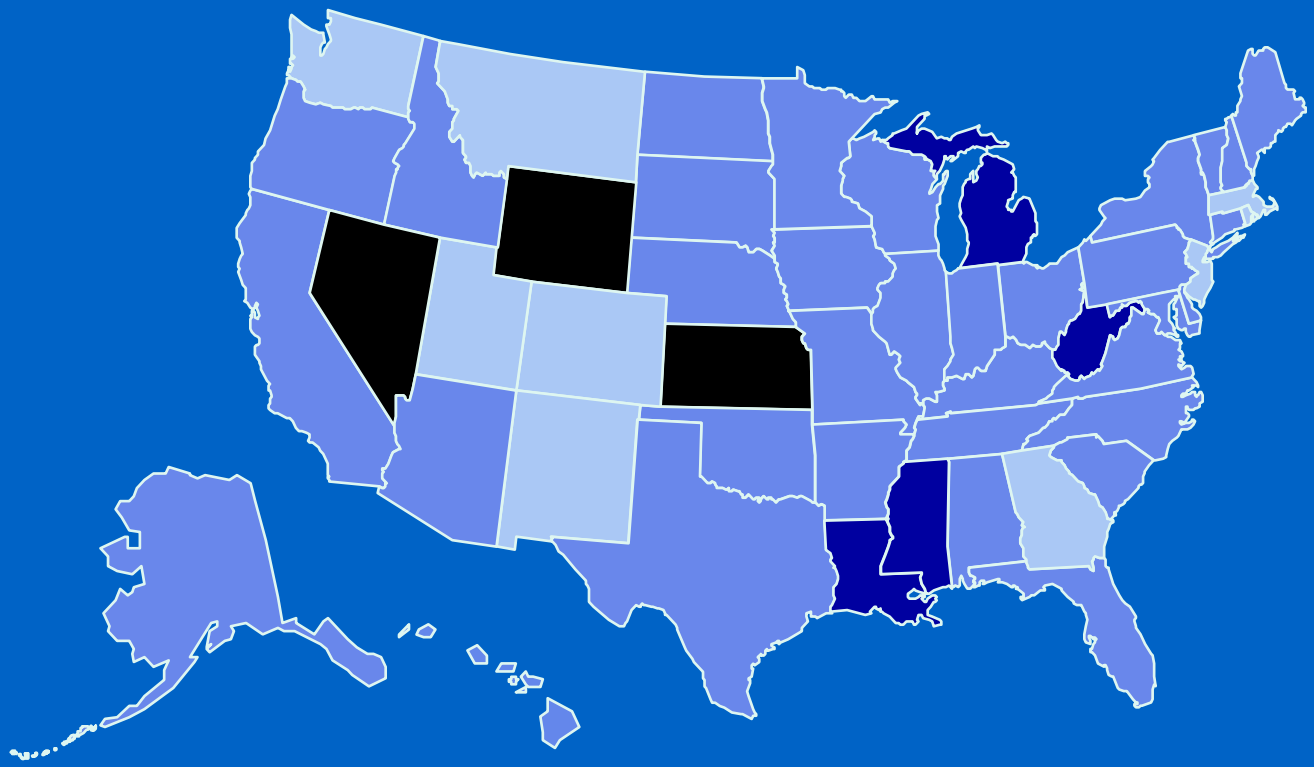
Obesity Trends* Among U.S. Adults

BRFSS, 1991

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



No Data | <10% | 10%–14% | 15%–19%

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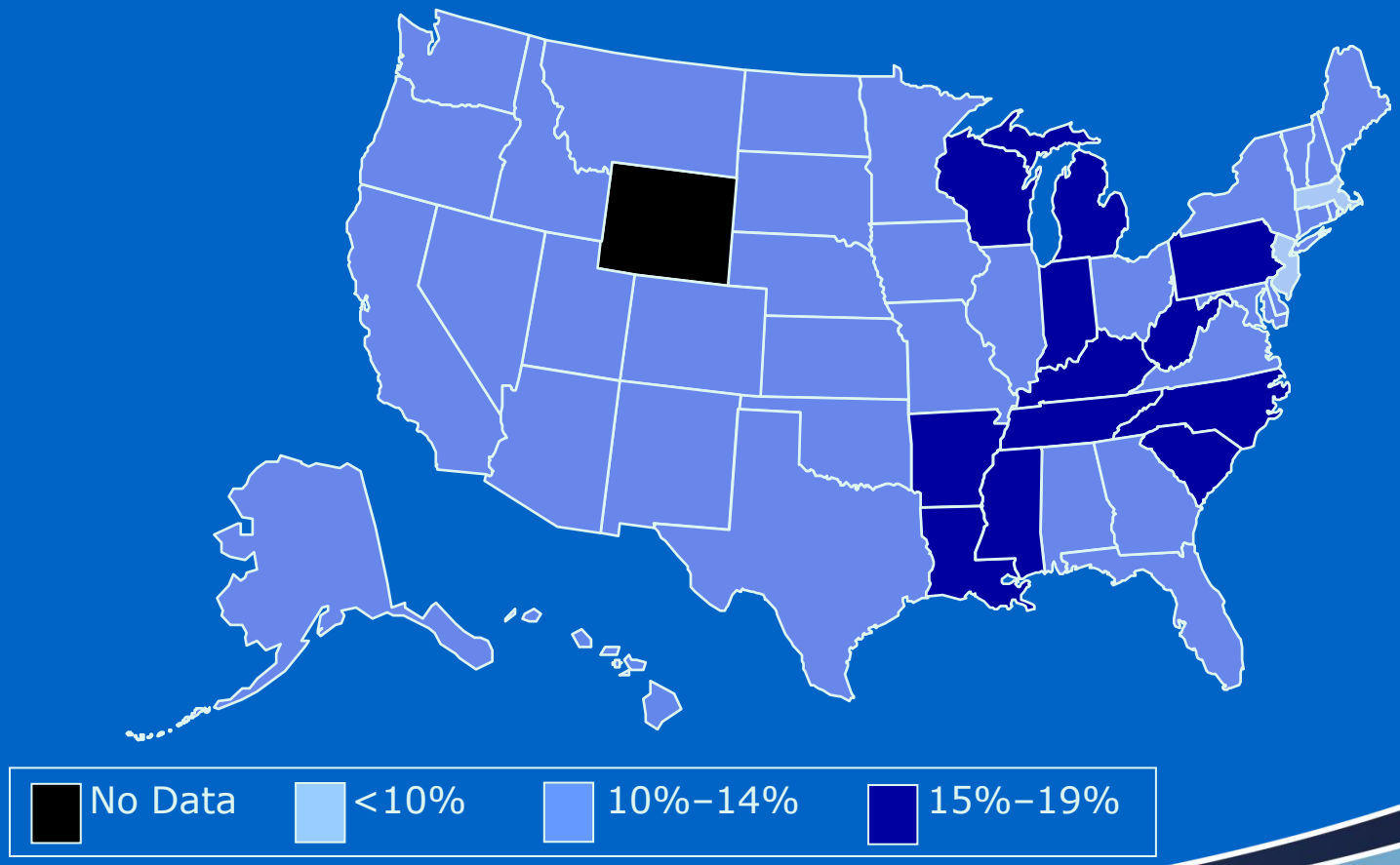
Obesity Trends* Among U.S. Adults

BRFSS, 1993

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



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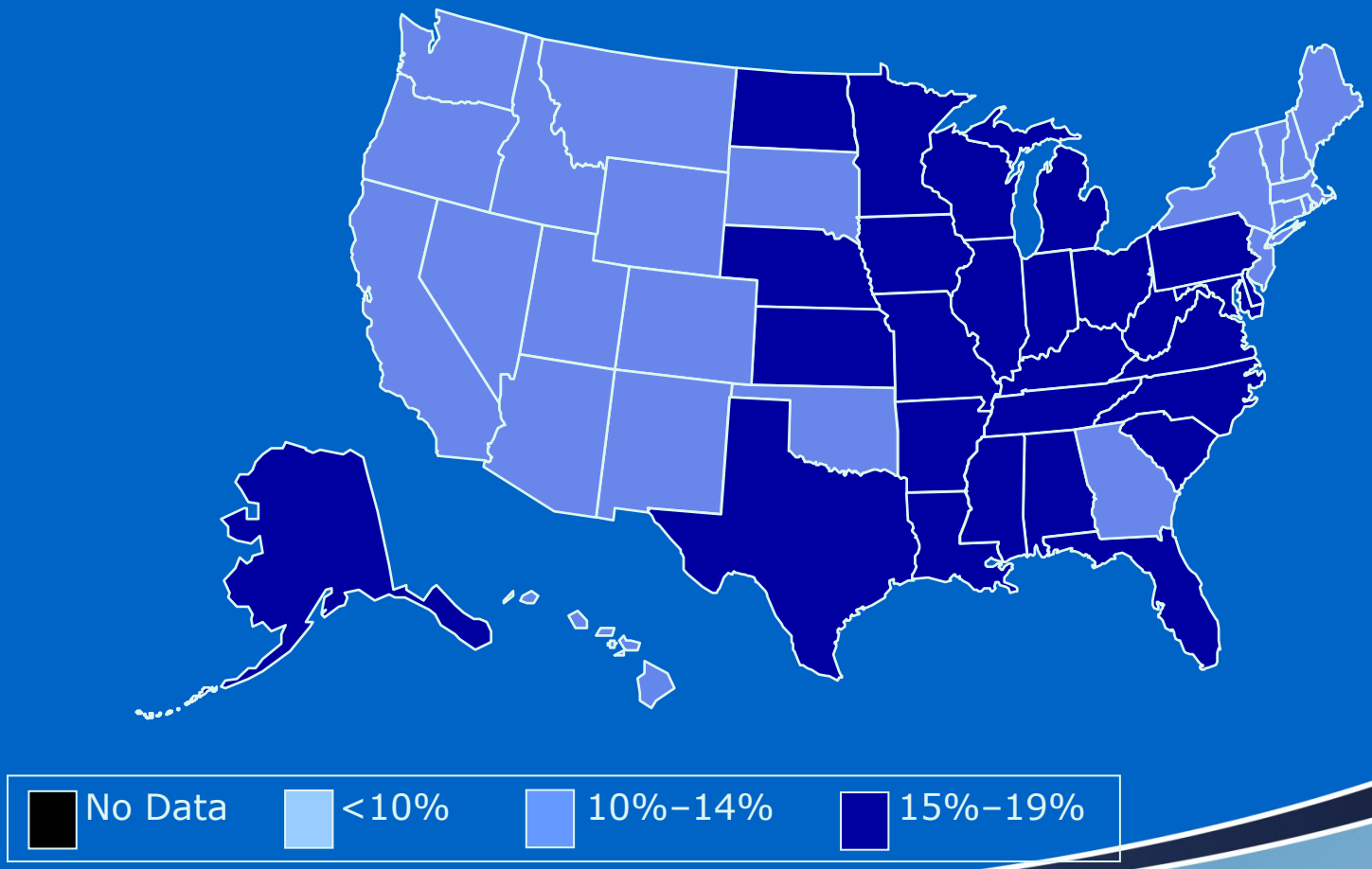
Obesity Trends* Among U.S. Adults

BRFSS, 1995

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



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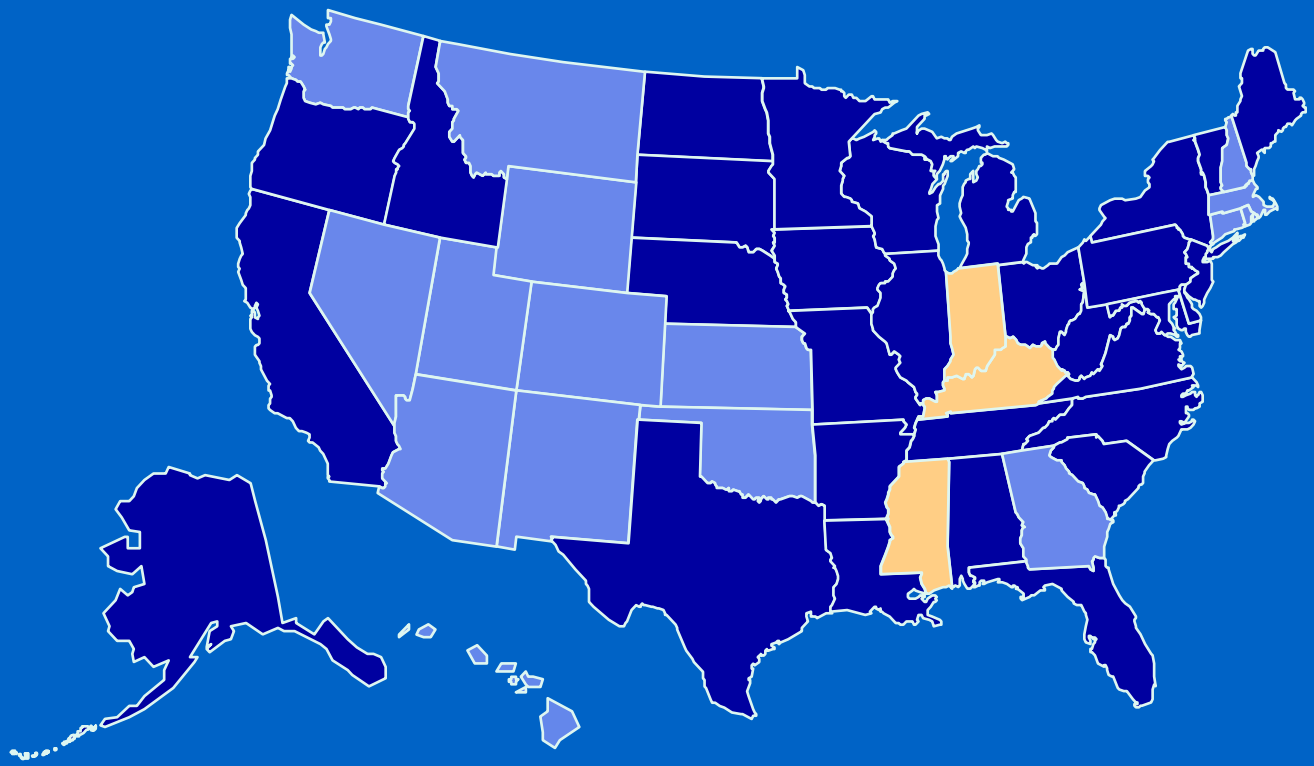
Obesity Trends* Among U.S. Adults

BRFSS, 1997

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



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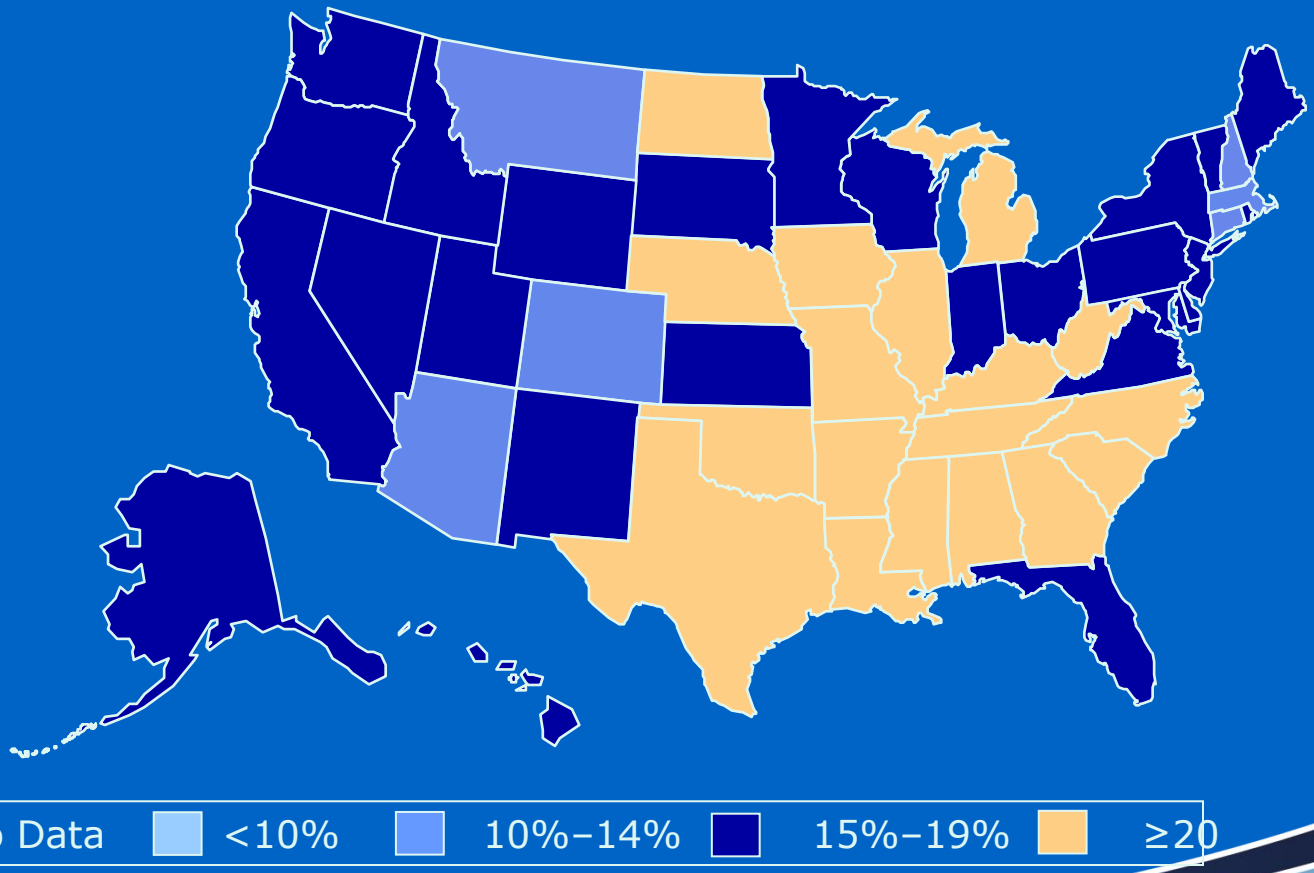
Obesity Trends* Among U.S. Adults

BRFSS, 1999

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



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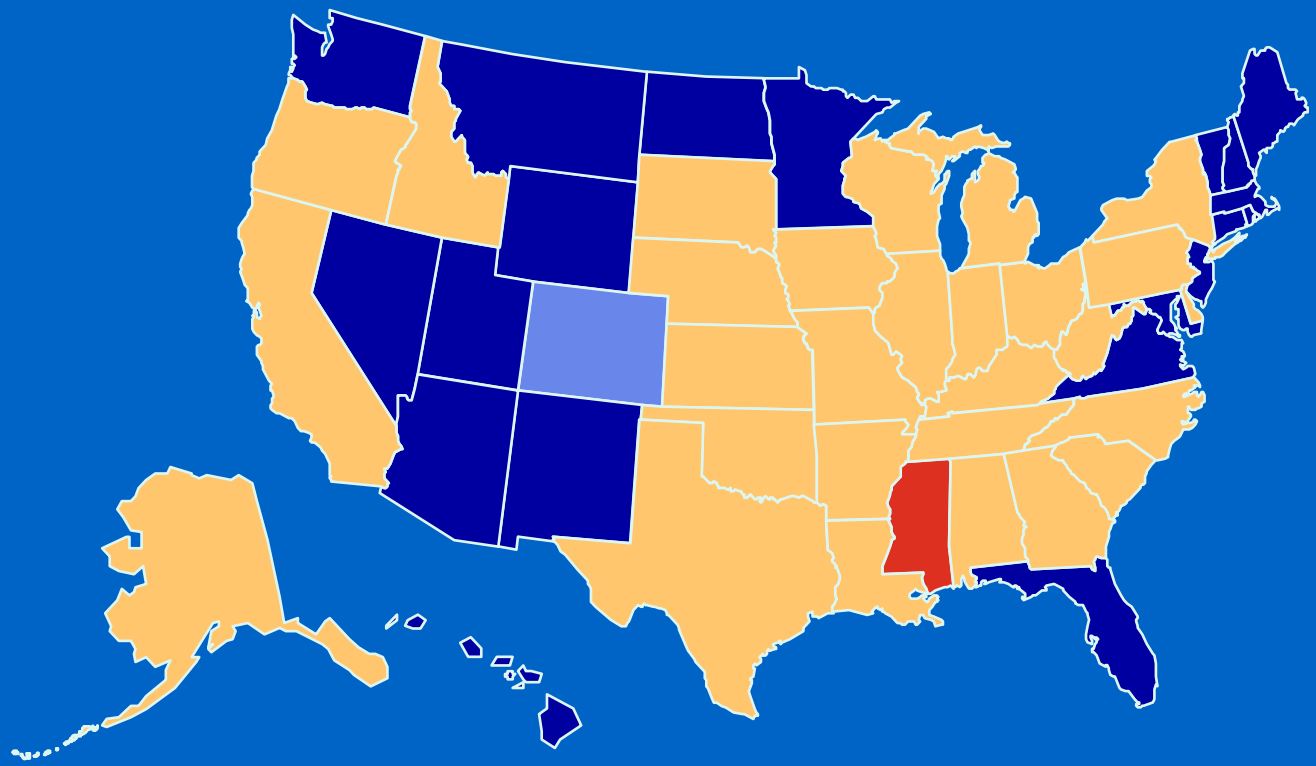
Obesity Trends* Among U.S. Adults

BRFSS, 2001

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” woman)



No Data | <10% | 10% - 14% | 15% - 19% | 20% - 24% | 25% - 29% | ≥30%

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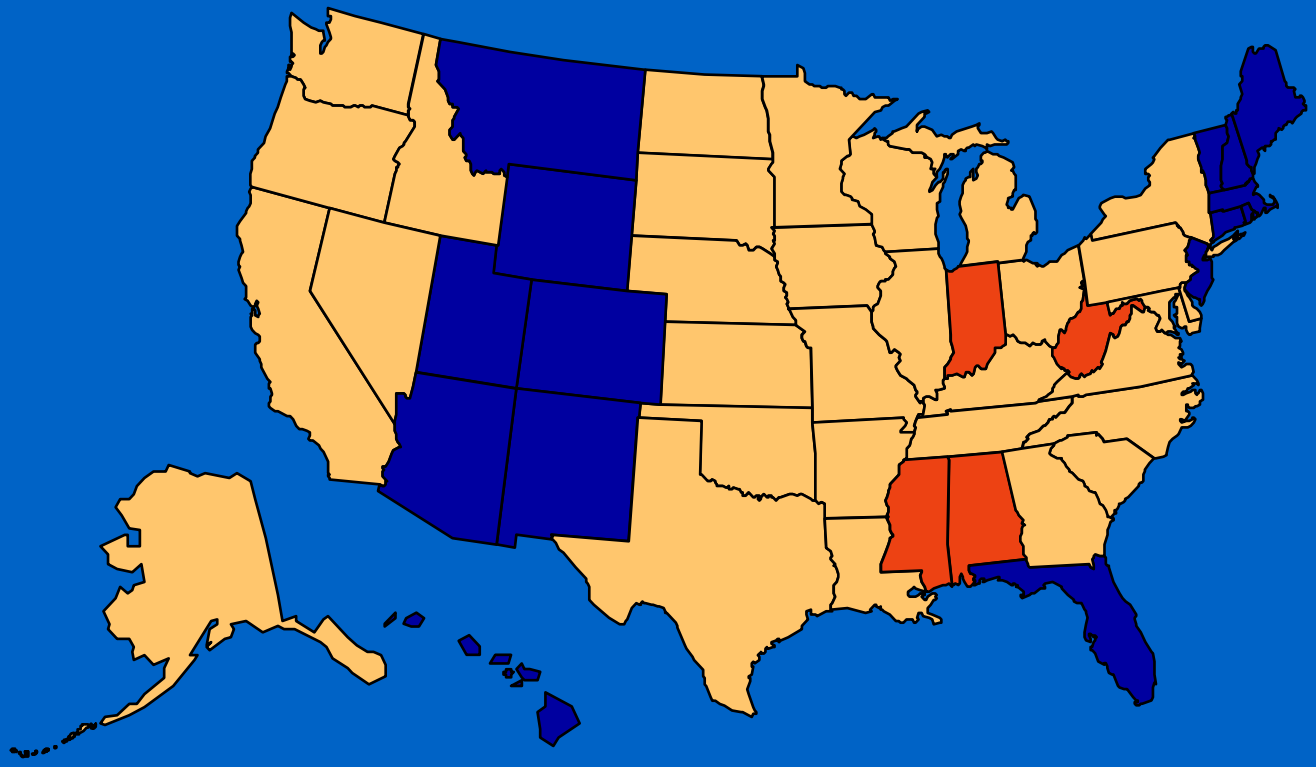
Obesity Trends* Among U.S. Adults

BRFSS, 2003

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



No Data | <10% | 10%–14% | 15%–19% | 20%–24% | 25%–29% | ≥30%

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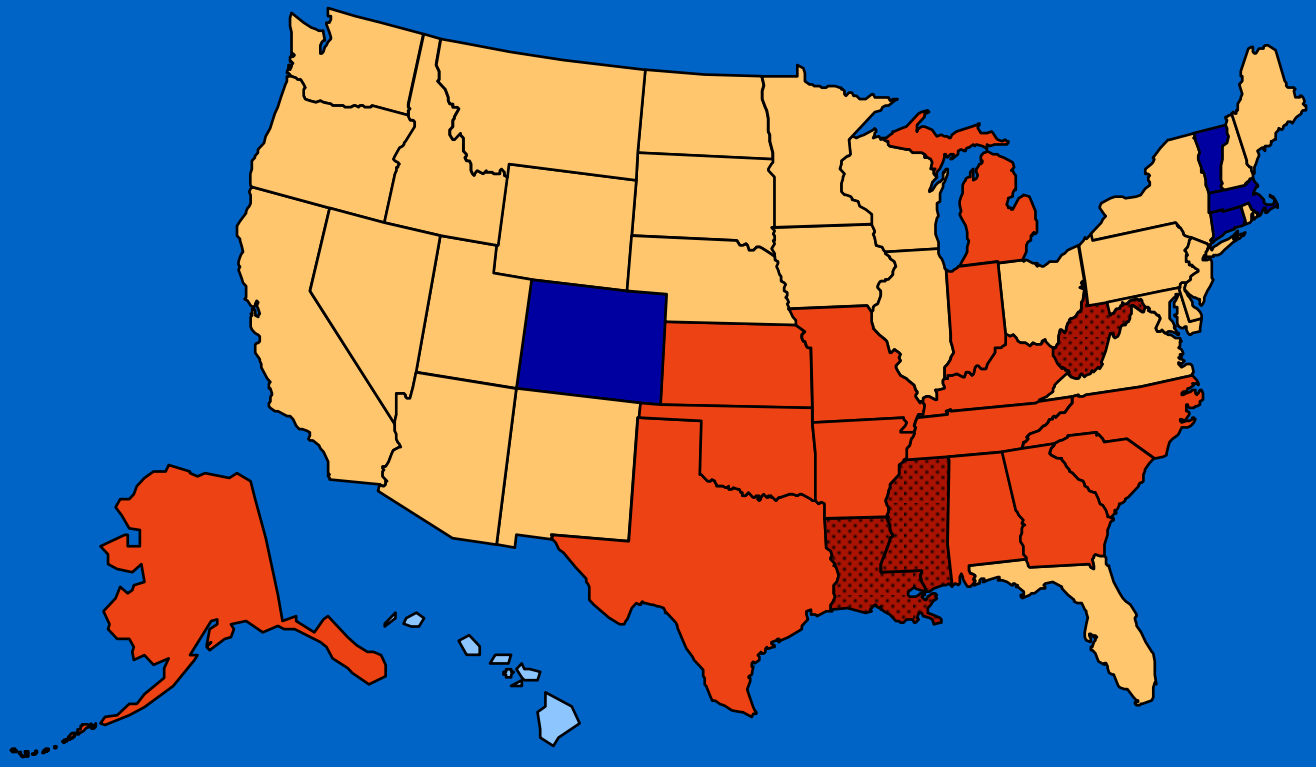
Obesity Trends* Among U.S. Adults

BRFSS, 2005

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



No Data | <10% | 10%–14% | 15%–19% | 20%–24% | 25%–29% | ≥30%

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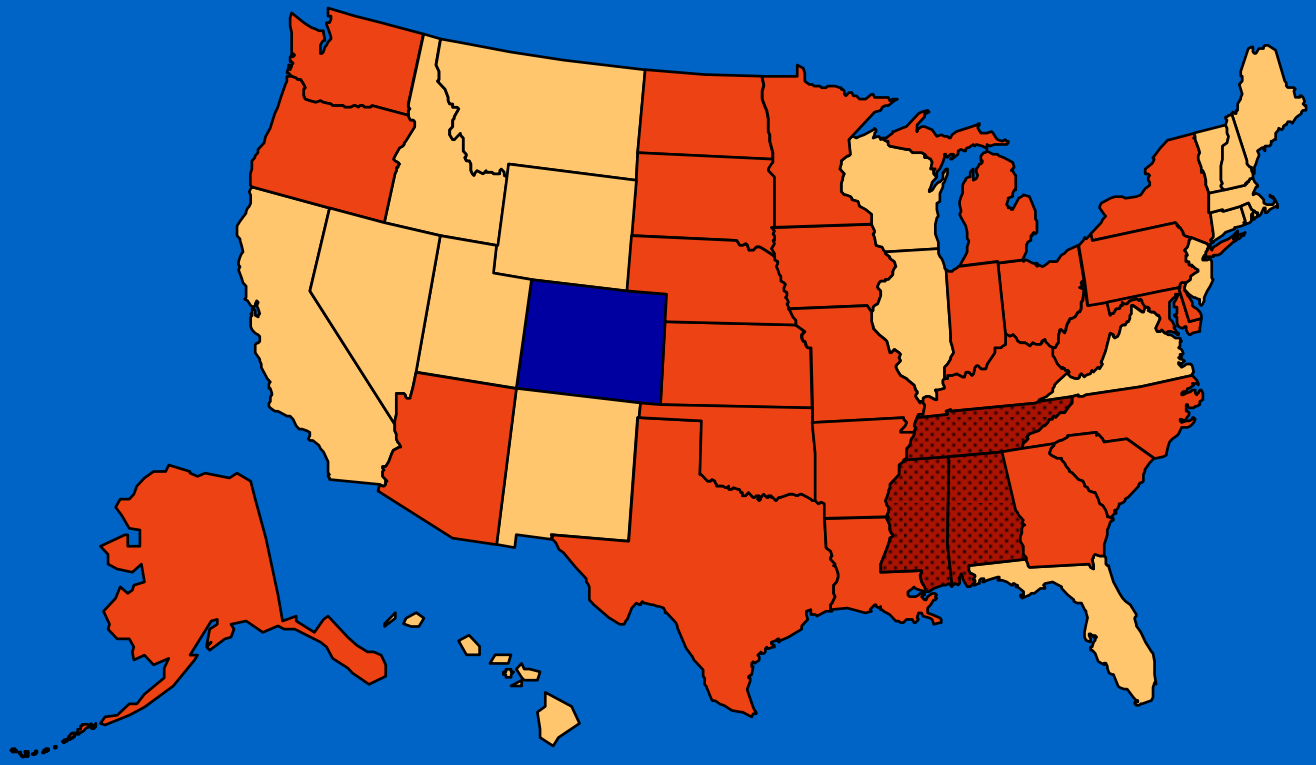
Obesity Trends* Among U.S. Adults

BRFSS, 2007

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)



No Data | <10% | 10%–14% | 15%–19% | 20%–24% | 25%–29% | ≥30%

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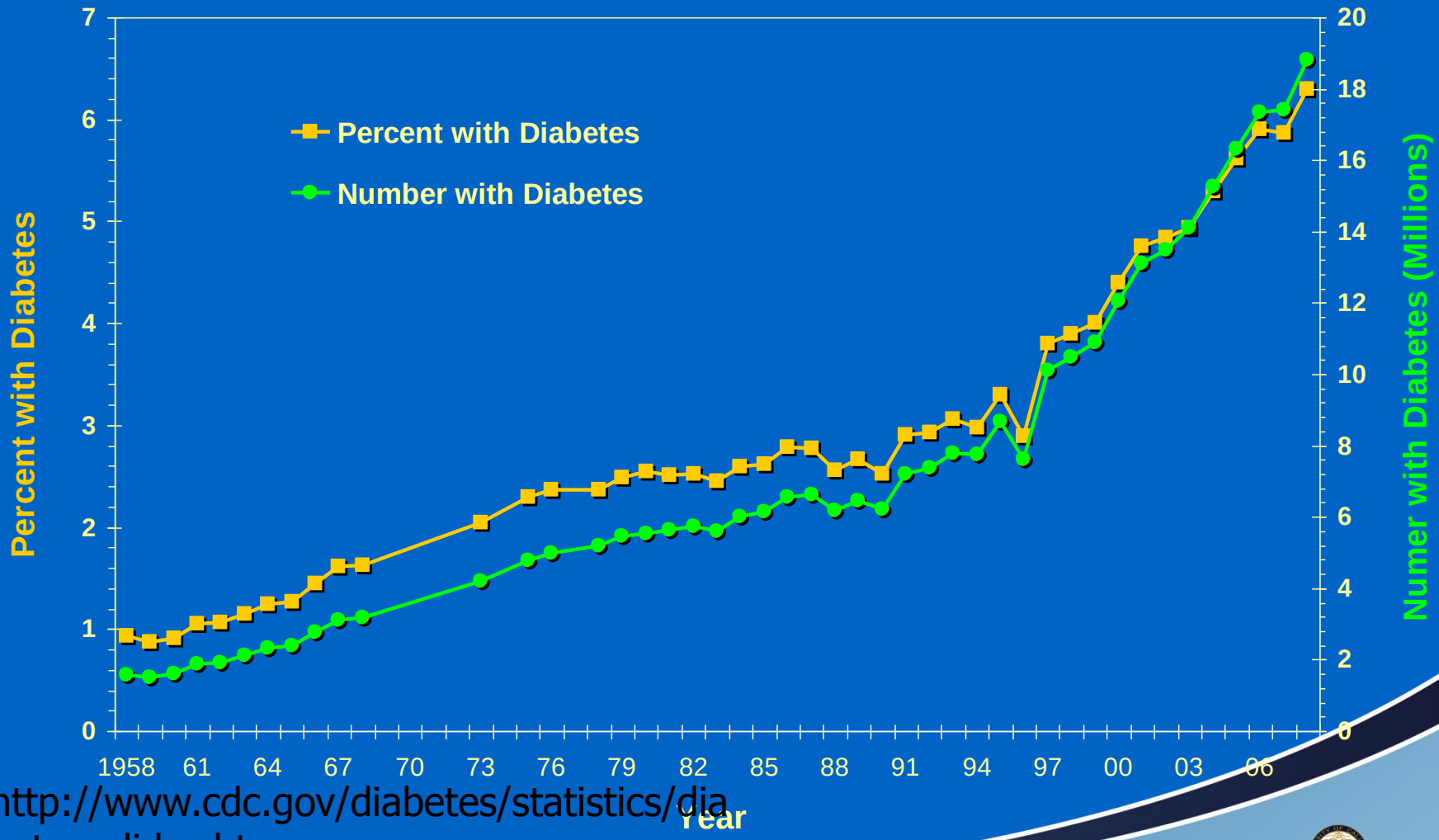
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008



http://www.cdc.gov/diabetes/statistics/diabetes_slides.htm

CDC's Division of Diabetes Translation. National Diabetes Surveillance System, available at http://www.cdc.gov/diabetes/statistics

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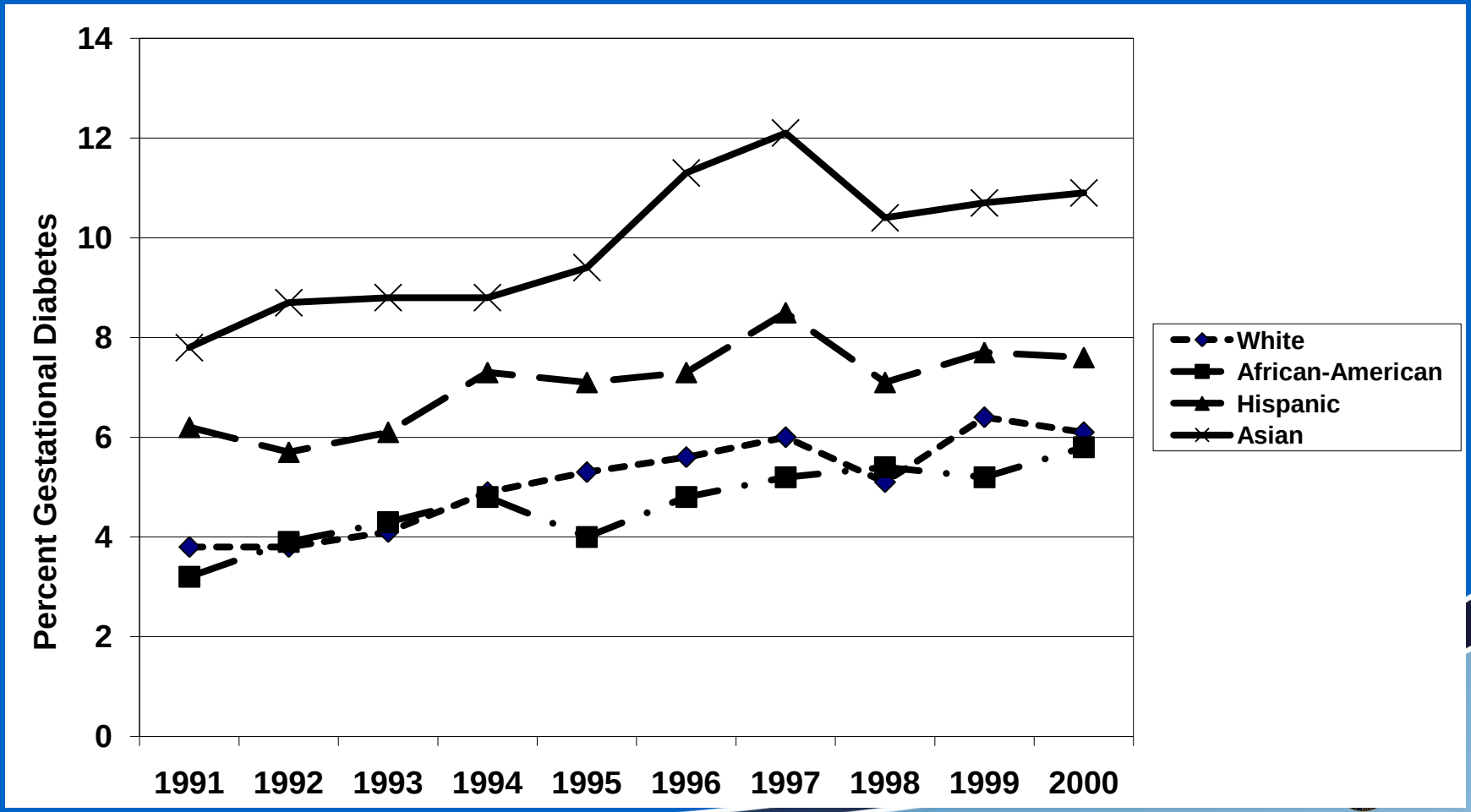
Prevalence of GDM in Colorado 1991-2000 (Kaiser)



Dabalea et al, Diabetes Care 28:579–584, 2005

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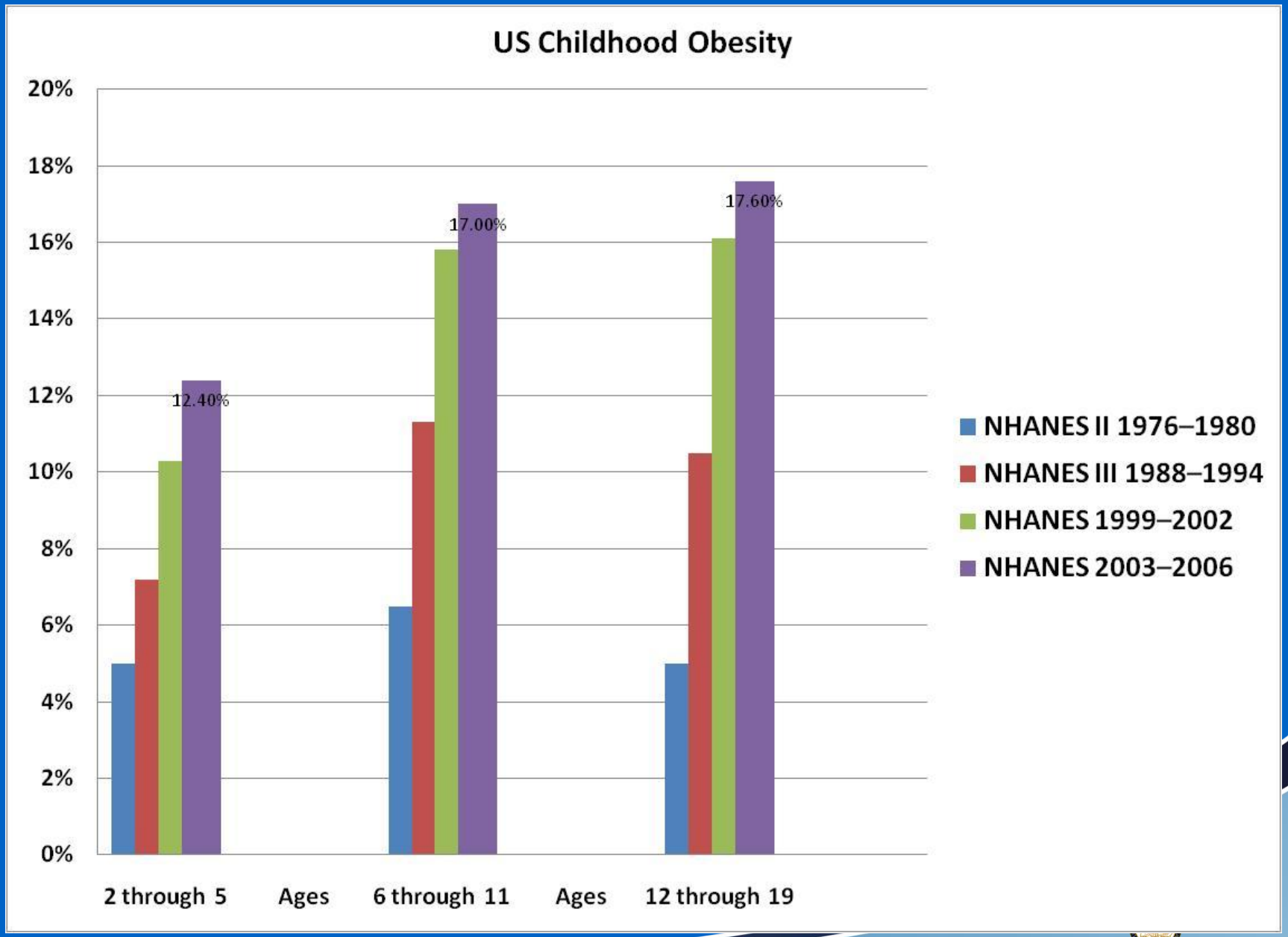

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The Worldwide Avalanche of Type 2 Diabetes is…

a potential avalanche of anomalous and obese newborns

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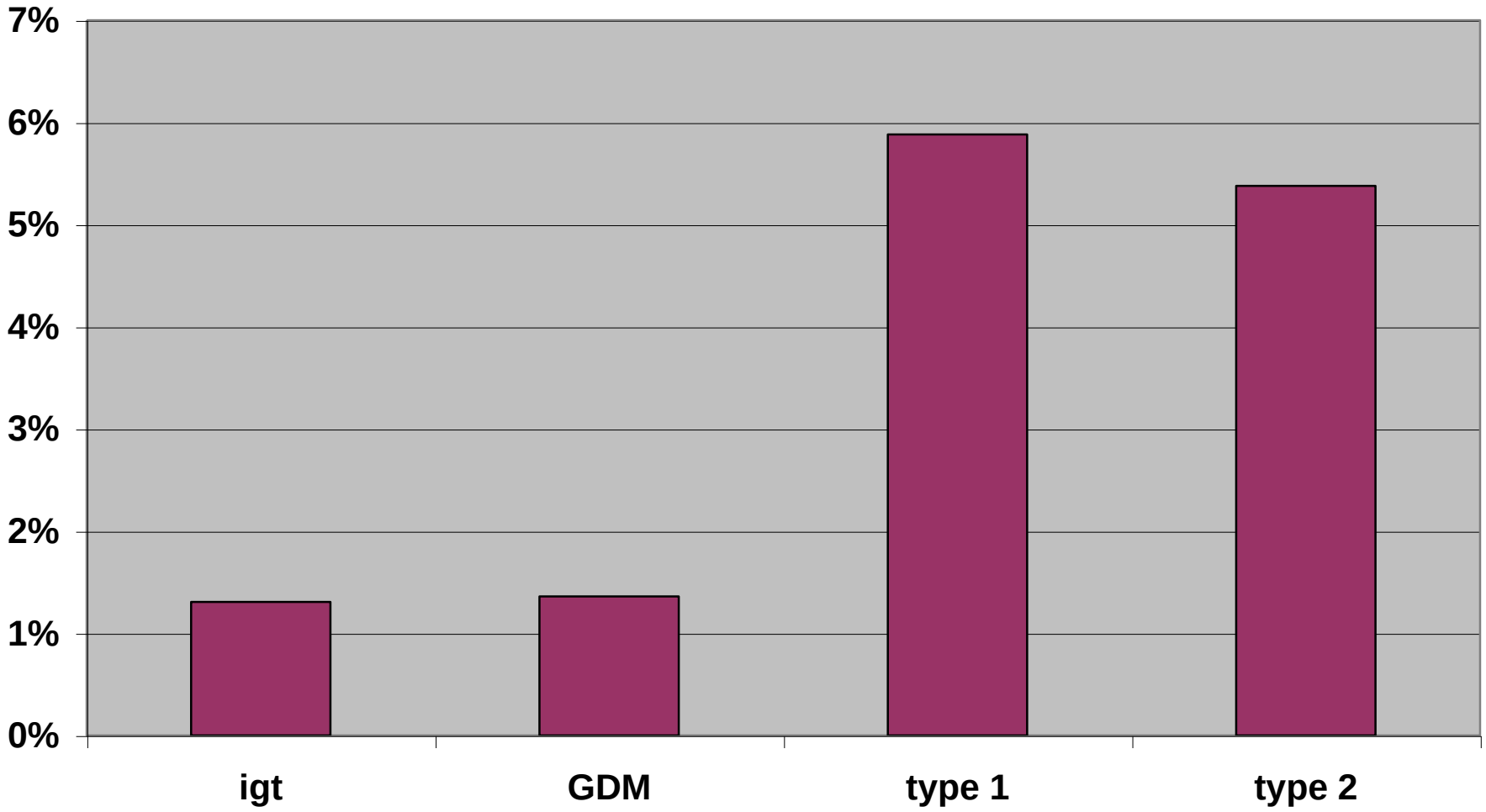
Fetal Anomalies

California Sweet Success Data 2004



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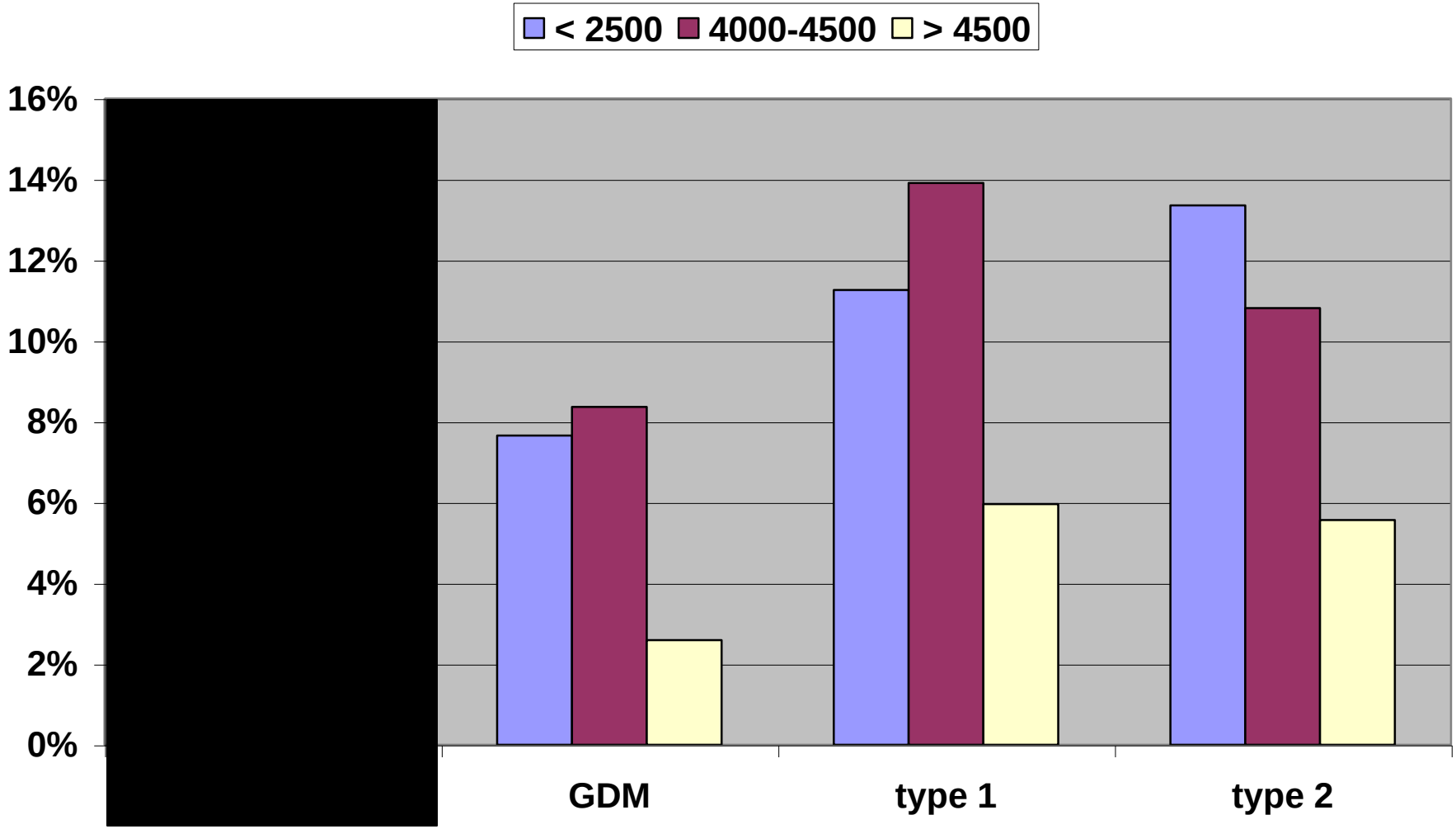
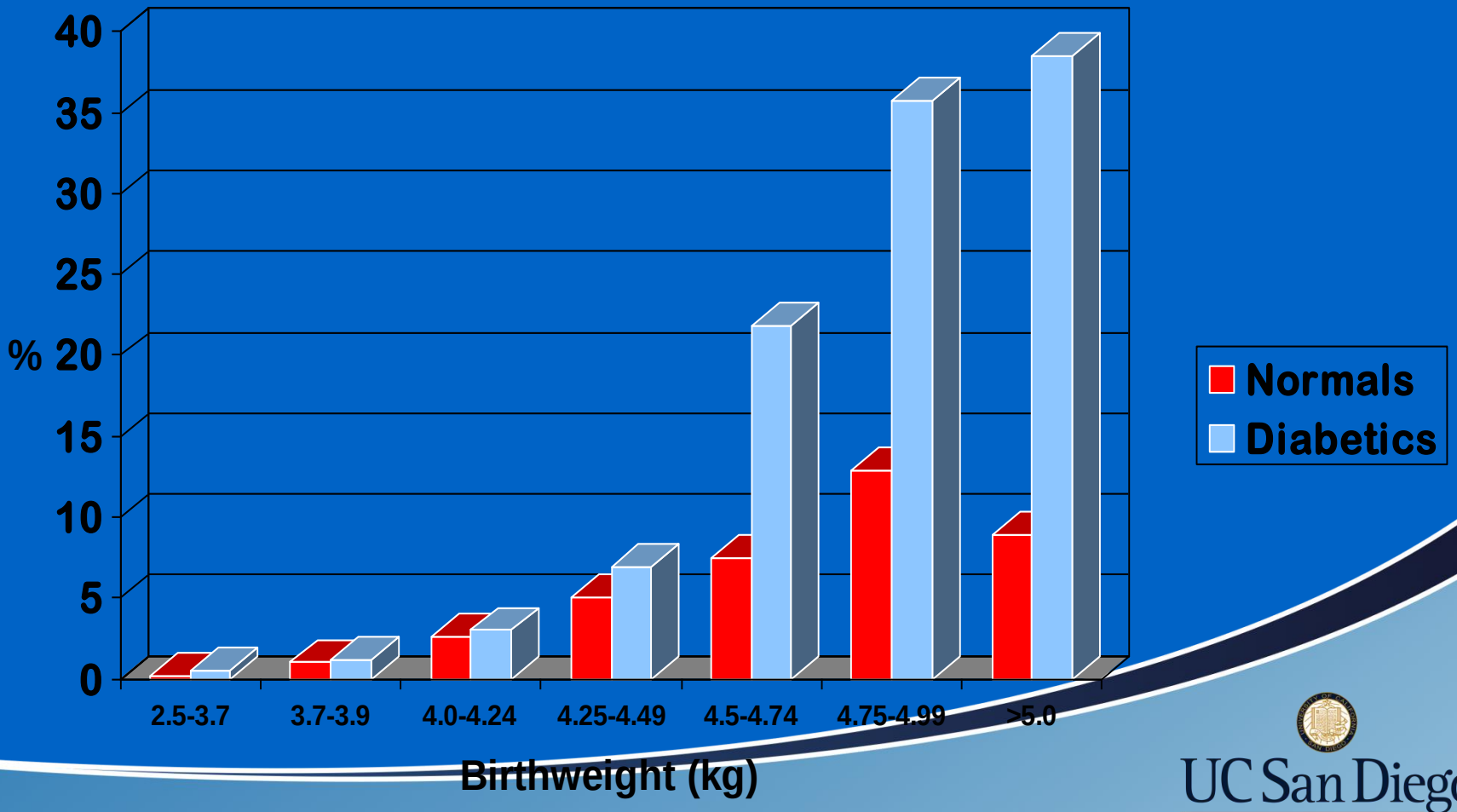
Birthweight

California Sweet Success Data 2004



Shoulder Dystocia Risk



Langer et al, Am J Obstet Gynecol 1991;165:831

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Do the fetal morbidities of obesity and diabetes in pregnancy stop with delivery?

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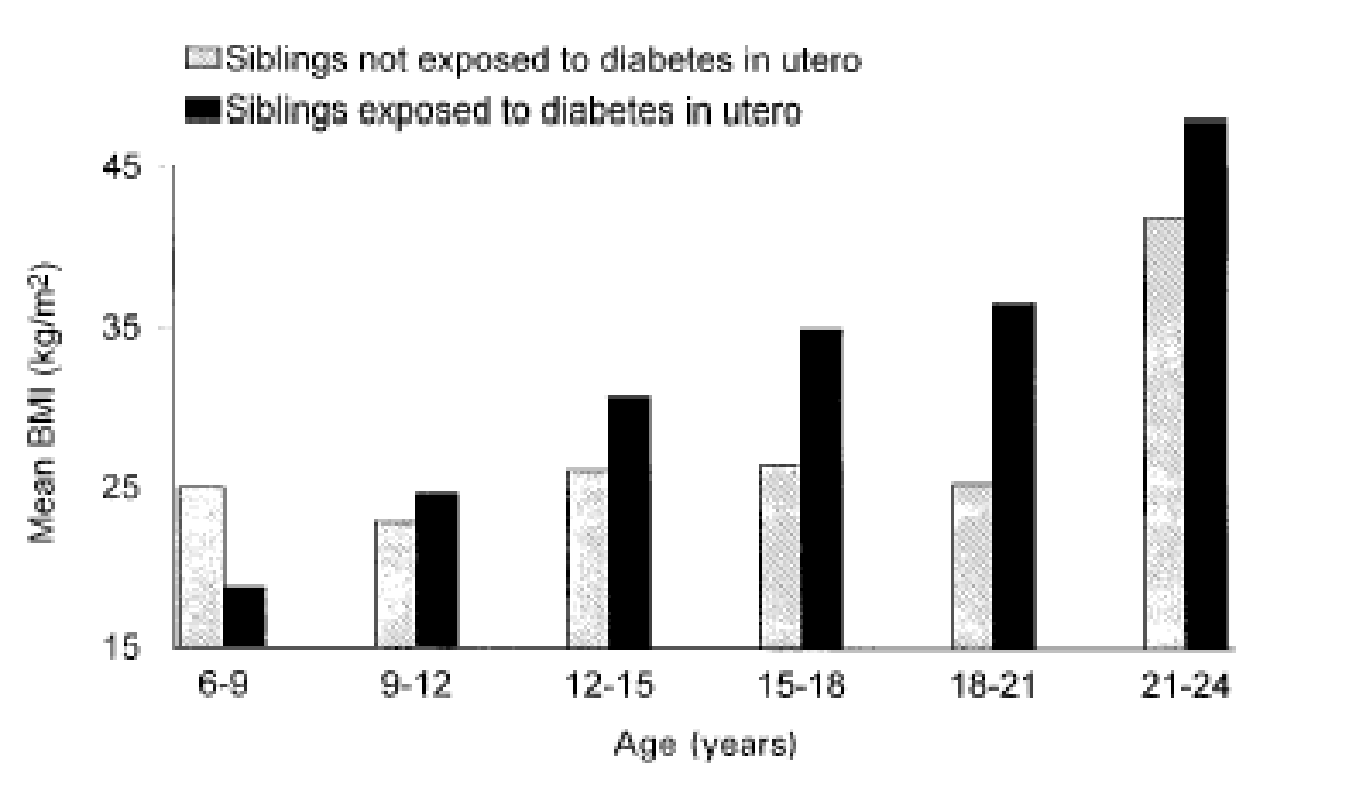
Adult Obesity After Prenatal Diabetes Exposure



Dabelea et al, *Diabetes* 49:2208–2211, 2000

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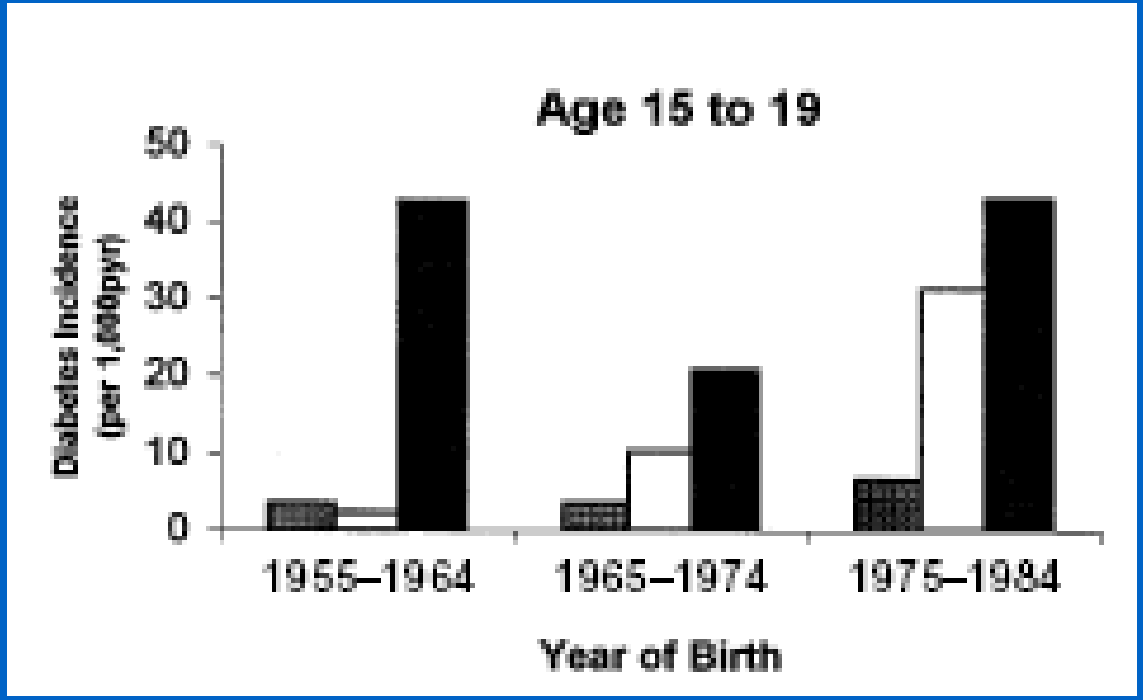
Incidence of Childhood Diabetes by In Utero Exposure



Pima Indian Longitudinal Study

Hatched bars: **non diabetic mother (x 10 years PP)**
White bars: **pre-diabetic (IGT)**
Black bars: **Type 2 mother**

Lindsay et al, ***Diabetes Care*** **23:1249–1254, 2000**

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The Legacy of Fetal Obesity is More than Adult Obesity and Diabetes

Metabolic Syndrome

- Obesity
- Diabetes
- Dyslipidemia/Heart Disease
- Hypertension

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Metabolic Syndrome Definitions

- Abdominal obesity = Waist circumference
  - Male >40”; **Female >35”**
- Atherogenic dyslipidemia
  - TG ≥ 150 mg/dl
  - HDL: Male <40 mg/dl; **Female <50 mg/dl**
- Blood pressure ≥130/≥85 mm Hg
- Insulin resistance ± glucose intolerance
  - FBG ≥110 mg/dl

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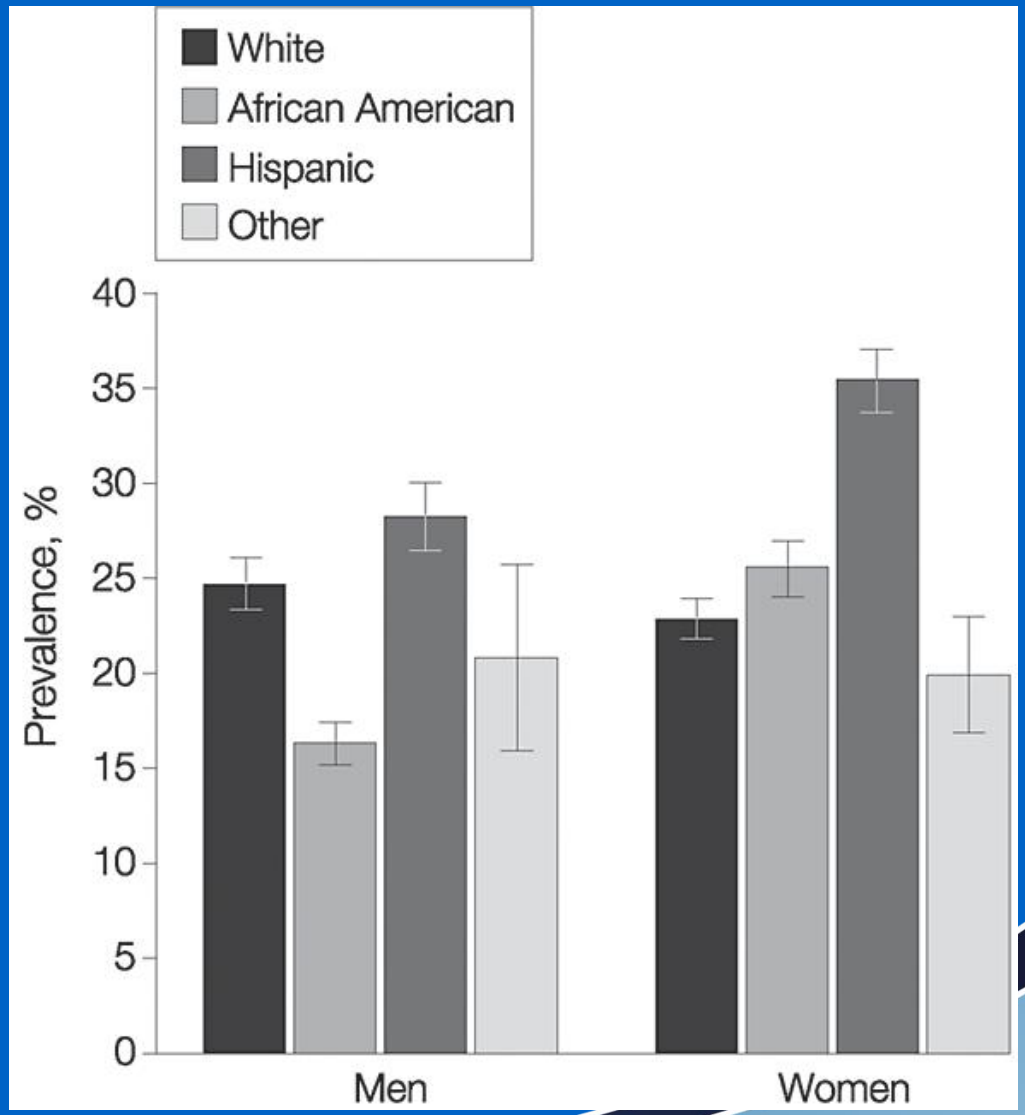
Prevalence of Metabolic Syndrome in U.S. Adults



Ford et al. *JAMA.* 2002;287:356-359.

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Excess adipose liberates excess inflammatory factors

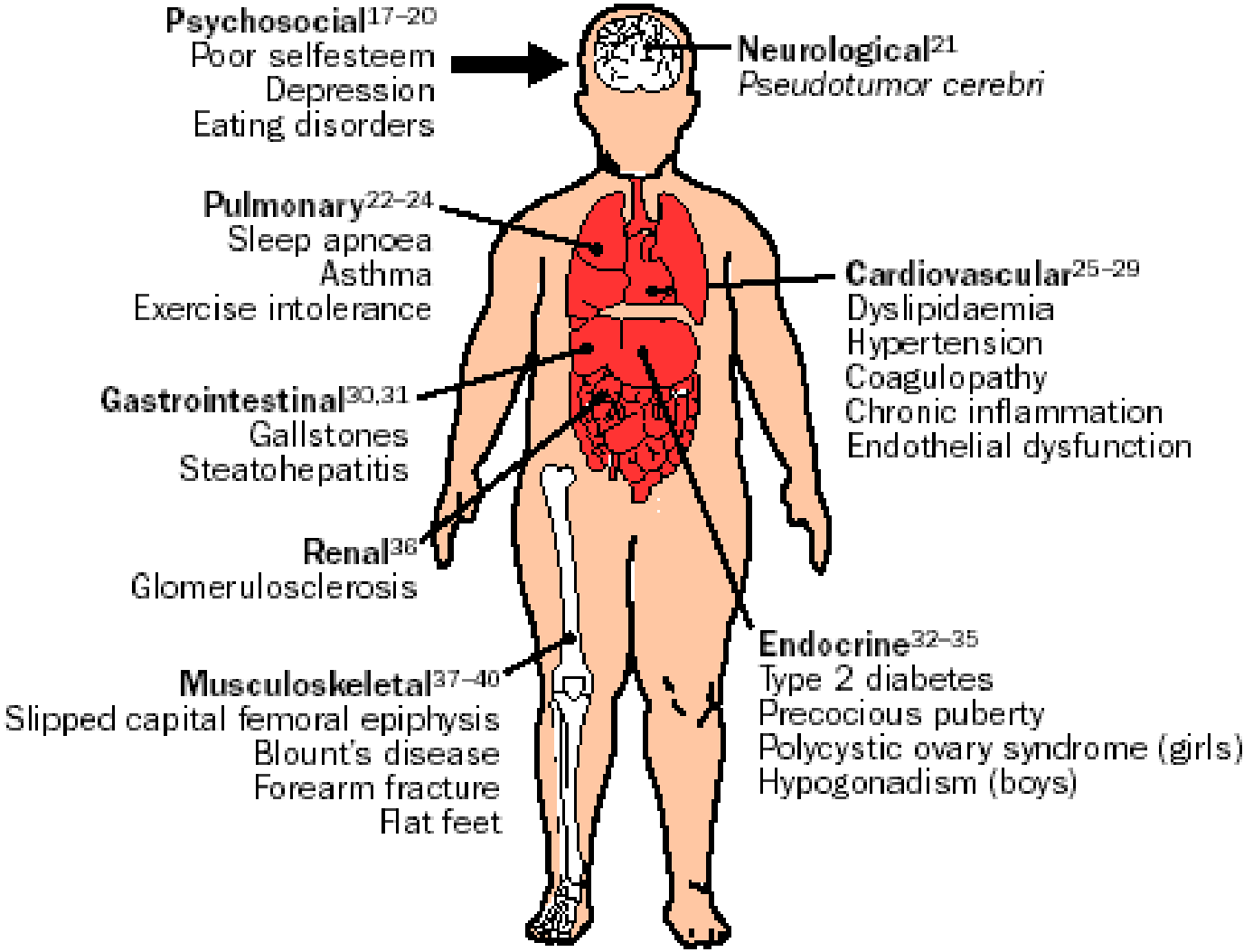

Figure 2: **Complications of childhood obesity**

How does altered fetal nutrition permanently program tissues and regulatory systems?

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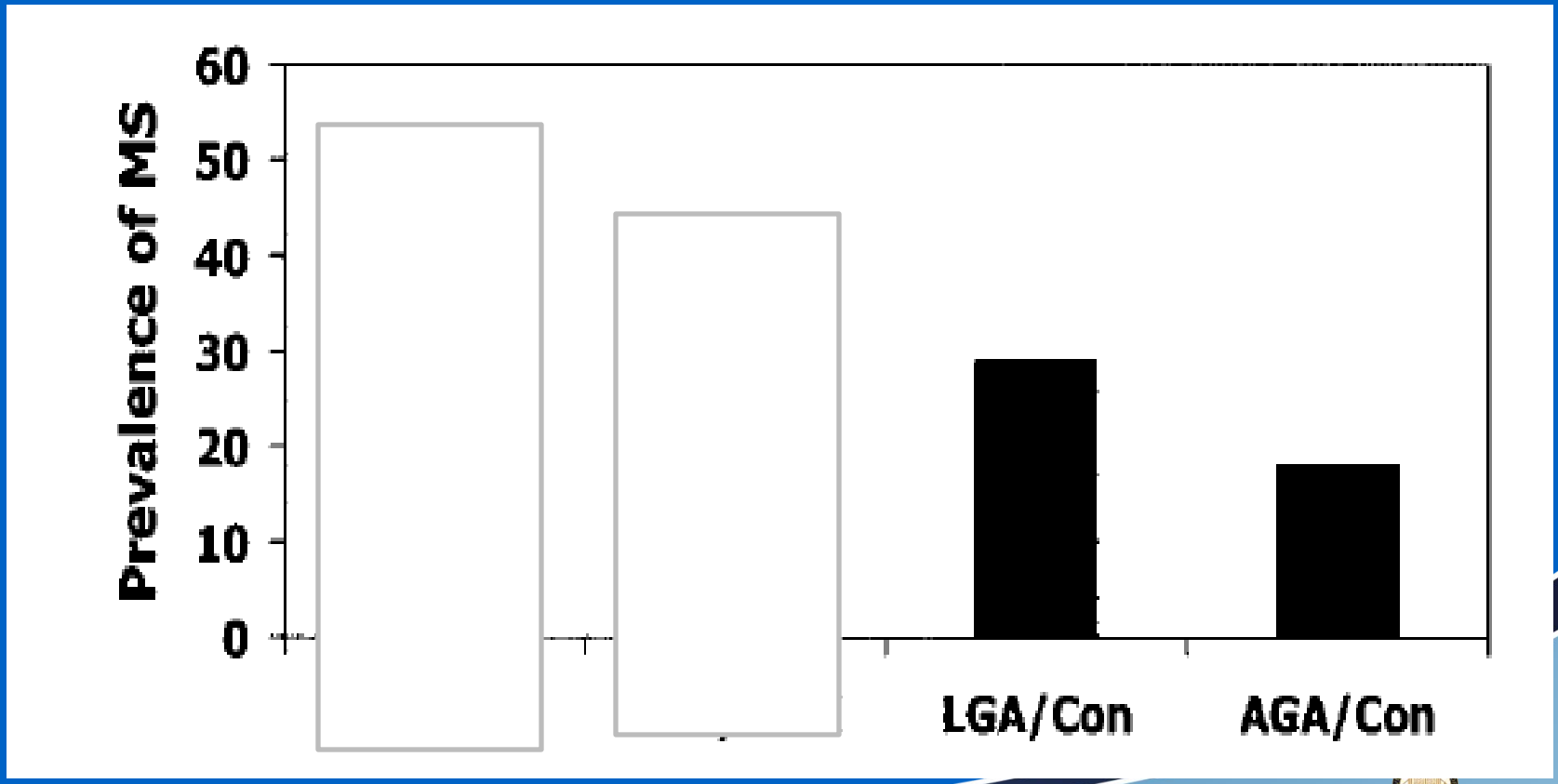
Childhood Metabolic Syndrome: Effect of Maternal GDM



Charlotte M. Boney, Anila Verma, Richard Tucker and Betty R. Vohr
Pediatrics 2005;115;290-296

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Childhood Metabolic Syndrome and Maternal GDM

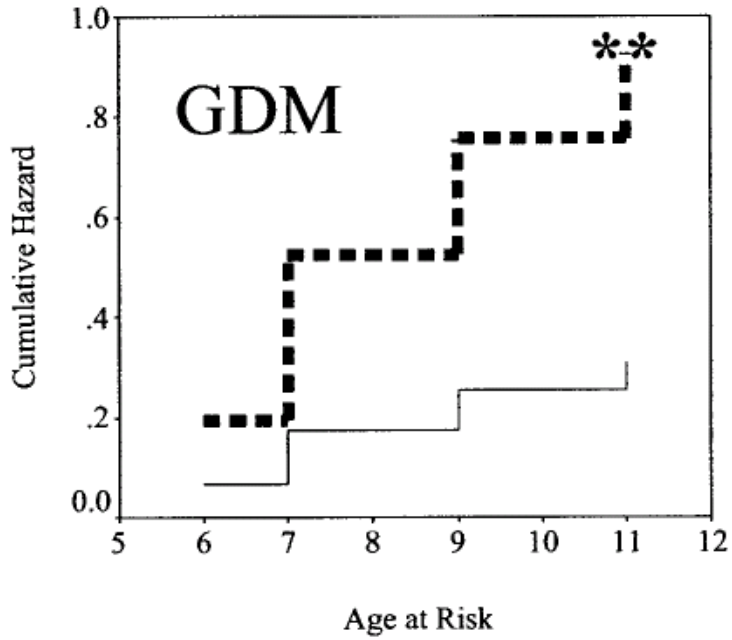
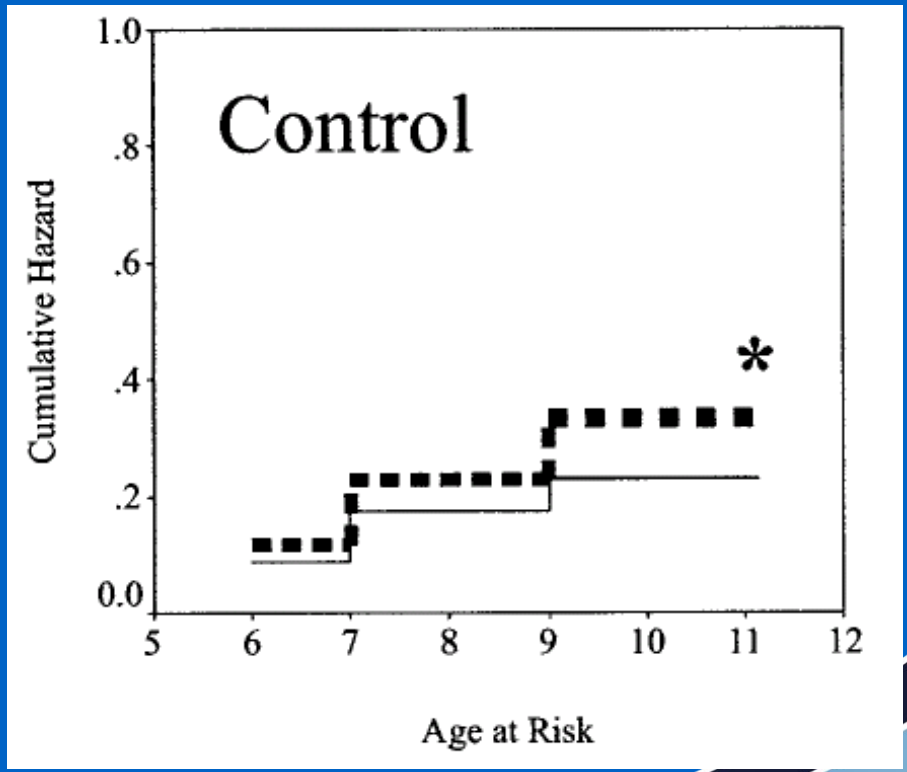


Fig 2. Cumulative hazard (risk) function for development of MS according to birth weight. Children were divided into control (n = 83) (*P = .56) and GDM (n = 92) (**P = .004) groups. The



Charlotte M. Boney, Anila Verma, Richard Tucker and Betty R. Vohr
Pediatrics 2005;115;290-296

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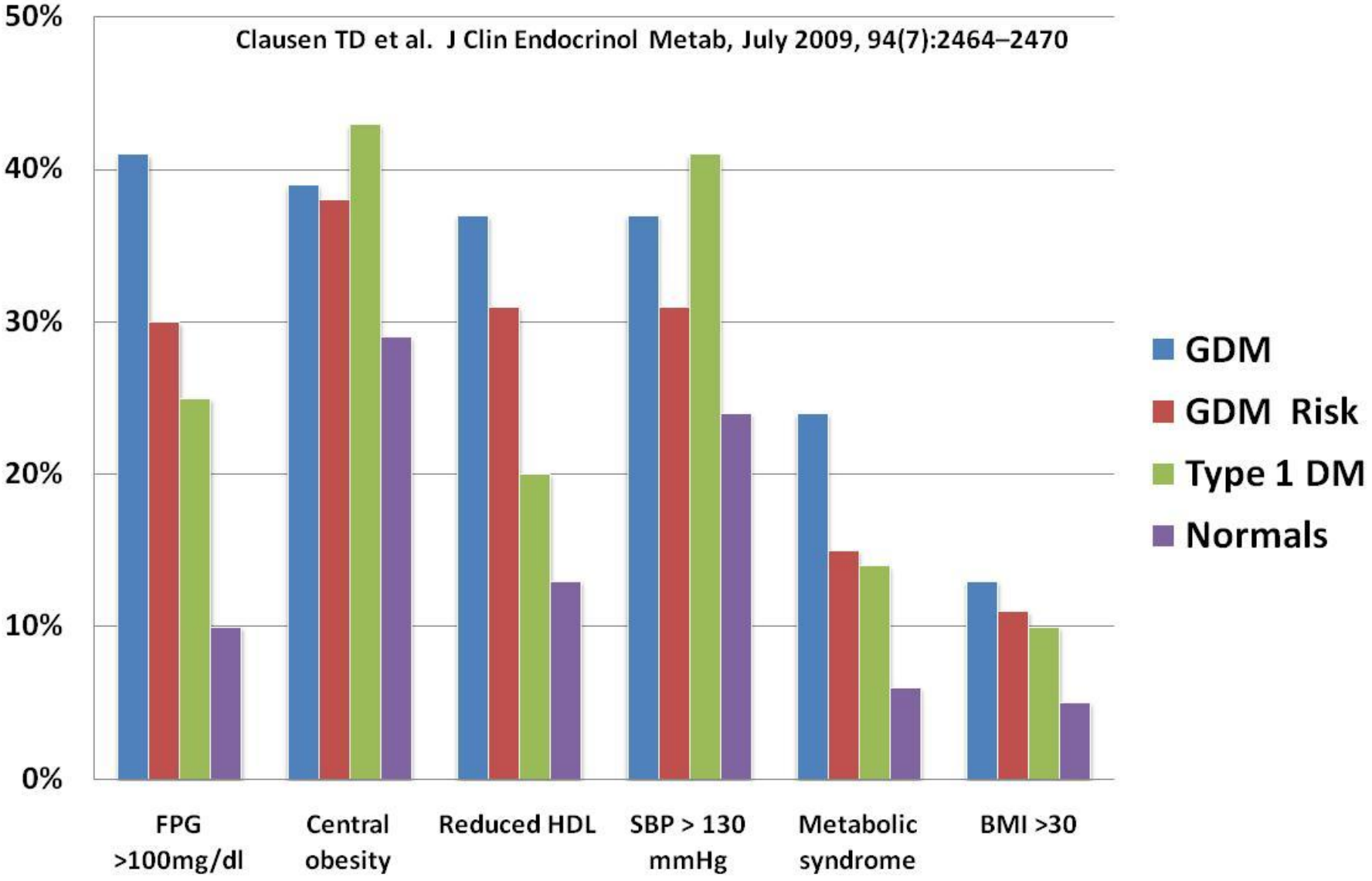
Offspring at 27 (4.5 SD) Years of Age by Maternal Metabolic Status
N=597



Can Treatment of GDM Prevent Adult Diabetes, Metabolic Syndrome and Excess Cardiovascular Morbidity and Mortality?

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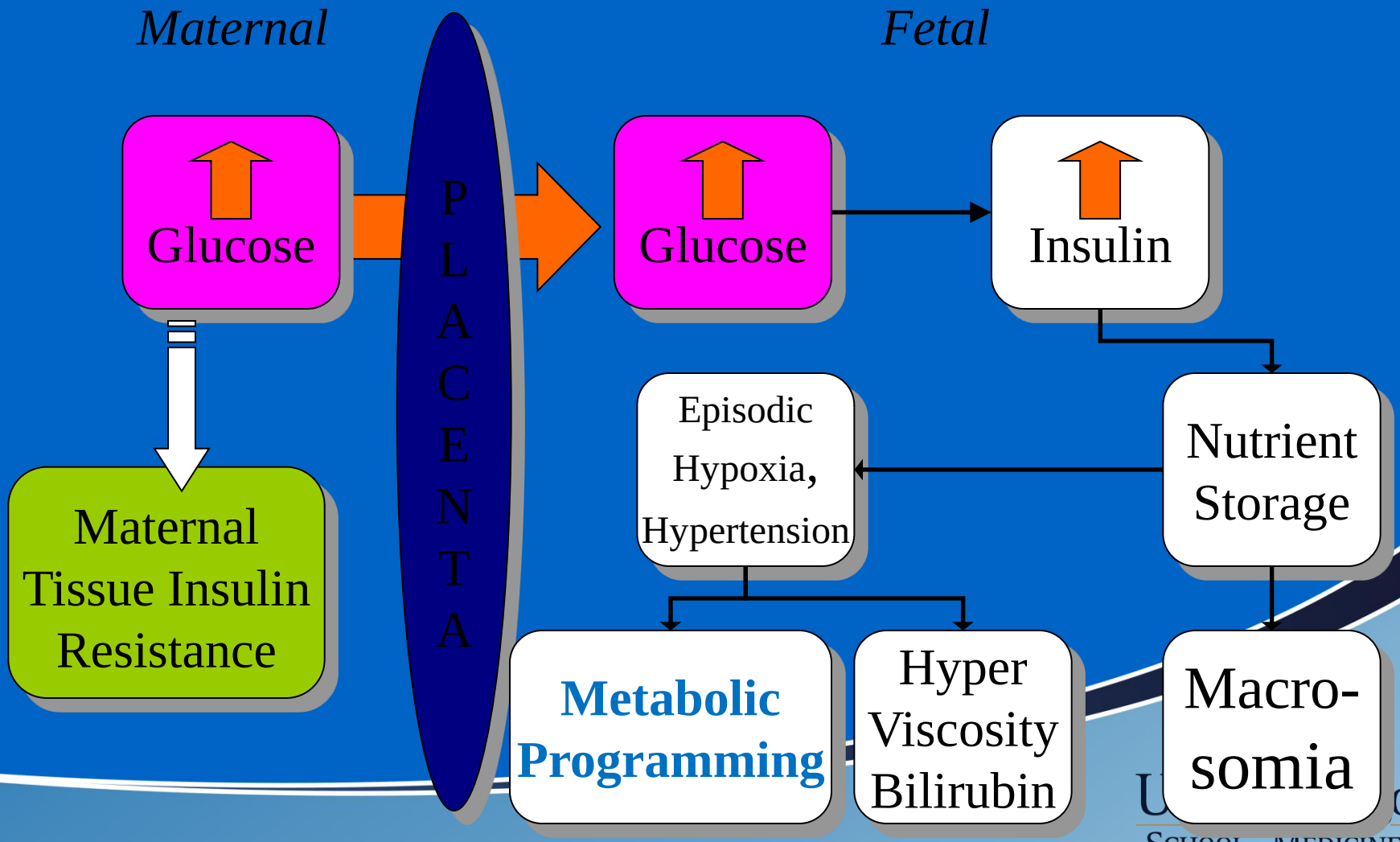
Pathophysiology of Fetal Morbidity in Diabetes



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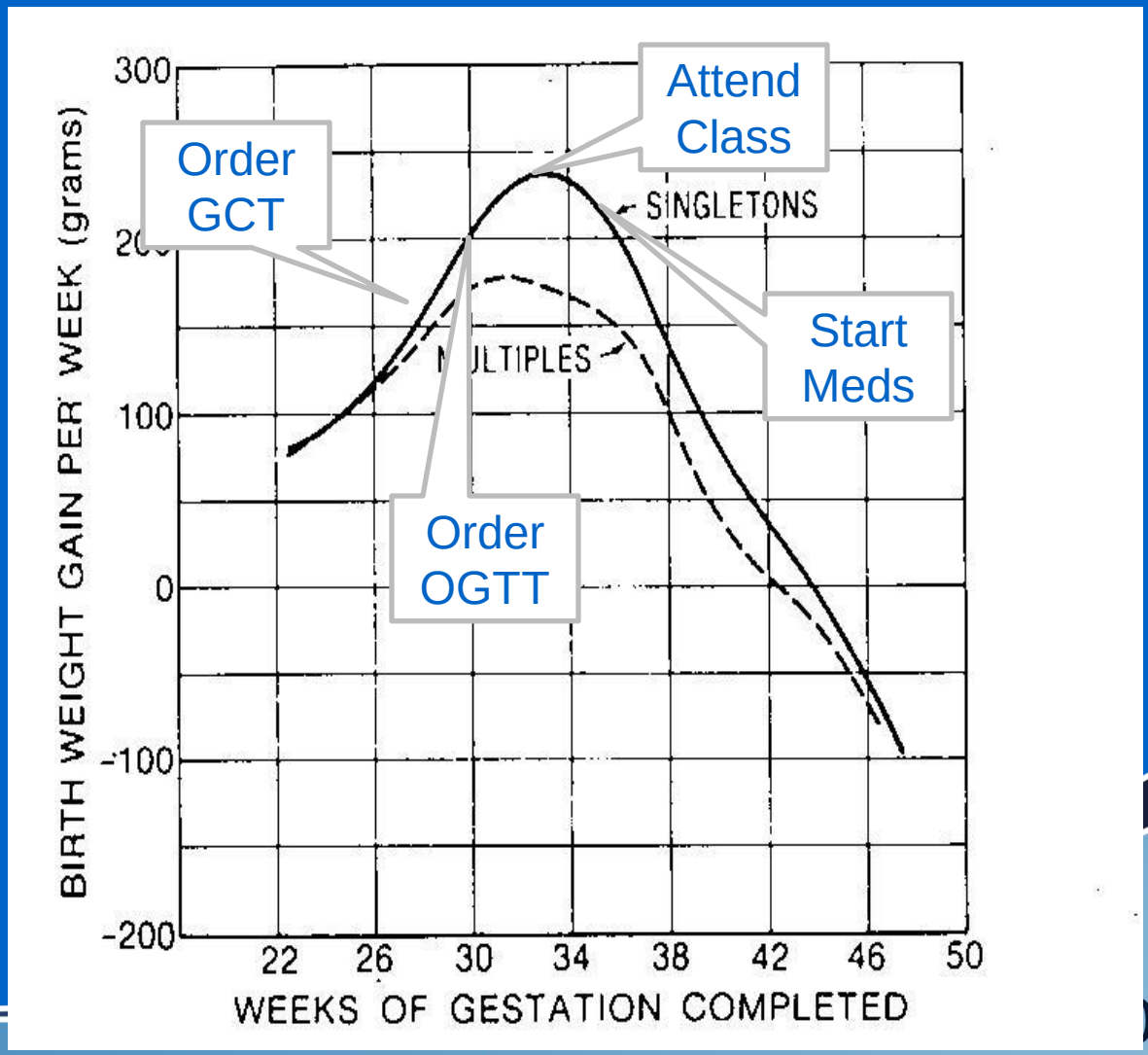
Fetal Growth Dynamics

The metaboli cclock Is ticking!




9#14oz,
cesarean

GDM Treatment RCT: "ACHOIS"

- 24 – 34 weeks
- 50-g oral GCT >140 mg/dl AND
- 75-g OGTT FBS < 140 AND
  2 hr 140 -198 mg/dl
- Intervention Group: 4x/d glucose, diet counseling, high-risk management
- Control Group: standard management

Crowther, C. et al. N Engl J Med 2005;352:2477-2486

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Infant Outcomes

Outcome	Rx Group	Control	AOR	P value
Birthweight	3335±551	3482±660	-145	<0.001
LGA	13%	21%	0.62	<0.001
Macrosomia	10%	21%	0.47	<0.001
SGA	7%	7%	0.88	0.59
NN hypoglycemia	7%	5%	1.42	0.16

Crowther, C. et al. N Engl J Med 2005;352:2477-2486

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NICHD Mild GDM RCT

- Determine if GDM treatment reduces perinatal morbidity and obstetric complications
- 'Mild GDM' = Normal FPG (< 95) but 2 other abnormal OGTT values
- Glucose treatment targets: FBG < 95, 2 h PP < 120 mg/dl

Landon MB, Spong CY, Thom E et al.
N Engl J Med. 2009 Oct 1;361(14):1339-48

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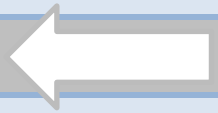
Mild GDM RCT: Outcomes

Outcome	Treated	Untreated	RR	Value
Birthweight g	3302 +/- 502	3408+/-589		0.0005
Birthweight > 4000g	5.9	14.3	0.41	0.0001
LGA %	7.1	14.5	0.49	0.0003
Fat mass g	427+/-198	464+/-222		0.003
Preterm %	9.5	11.6	0.81	0.28
SGA %	7.5	6.4	1.18	0.49
NICU Admit %	9	11.6	0.77	0.19
IV Glucose	5.3	6.8	0.77	0.32
RDS	1.9	2.9	0.66	0.33



Landon MB, Spong CY, Thom E et al.
N Engl J Med. 2009 Oct 1;361(14):1339-48

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IF GDM TREATMENT REDUCES FETAL AND NEWBORN OBESITY, WHO SHOULD BE TREATED?

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Hyperglycemia and Adverse Pregnancy Outcomes (HAPO)

- 25,505 pregnant women at 15 centers in 9 countries
- 75-g OGTT testing at 24 to 32 weeks of gestation.
- Exclusions: FPG > 105 mg/dl) and 2-hour PG >200 mg/dl.
- Primary outcomes were
  - birth weight above the 90th percentile
  - primary CS
  - neonatal hypoglycemia
  - cord-blood serum C-peptide level above the 90th percentile.

The HAPO Study Cooperative Research Group. N Engl J Med 2008;358:1991-2002

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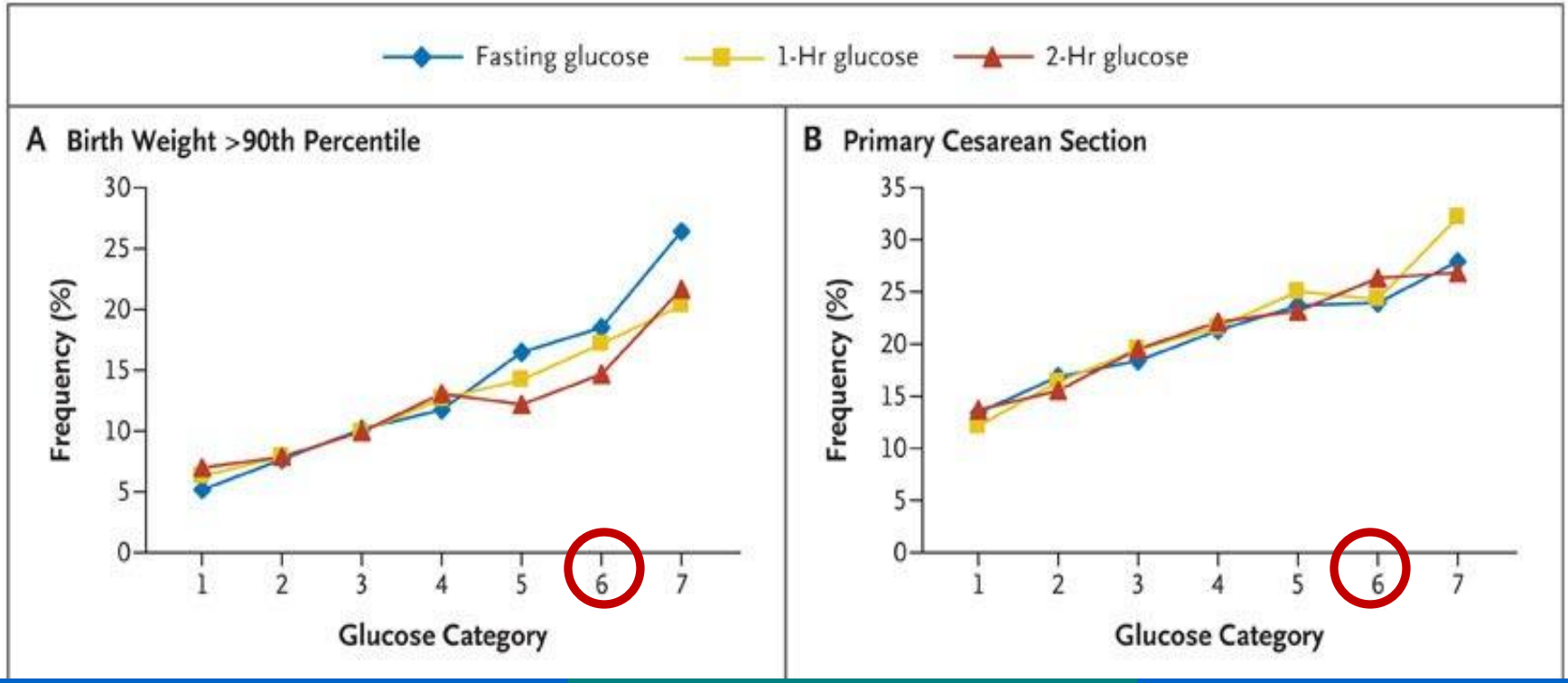

	fpg	*1 hr PP*
1	< 75	< 106
2	75-79	106-132
3	80-84	133-155
4	85-89	156-171
5	90-94	172-193
6	95-99	194-211
7	≥100	≥212

The HAPO Study Cooperative Research Group. I
Engl J Med 2008;358:1991-2002

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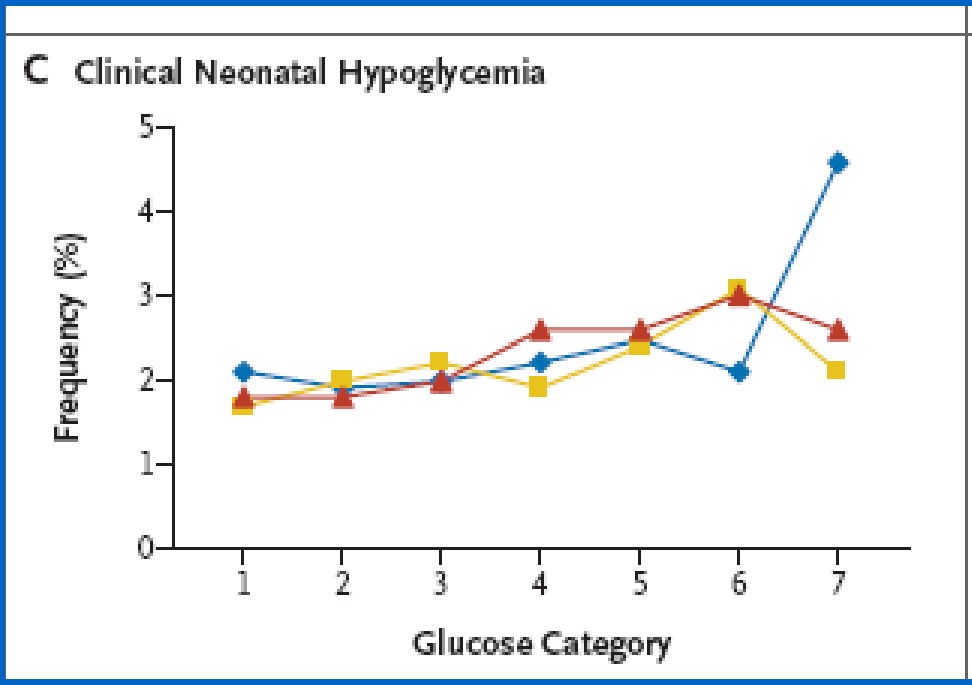

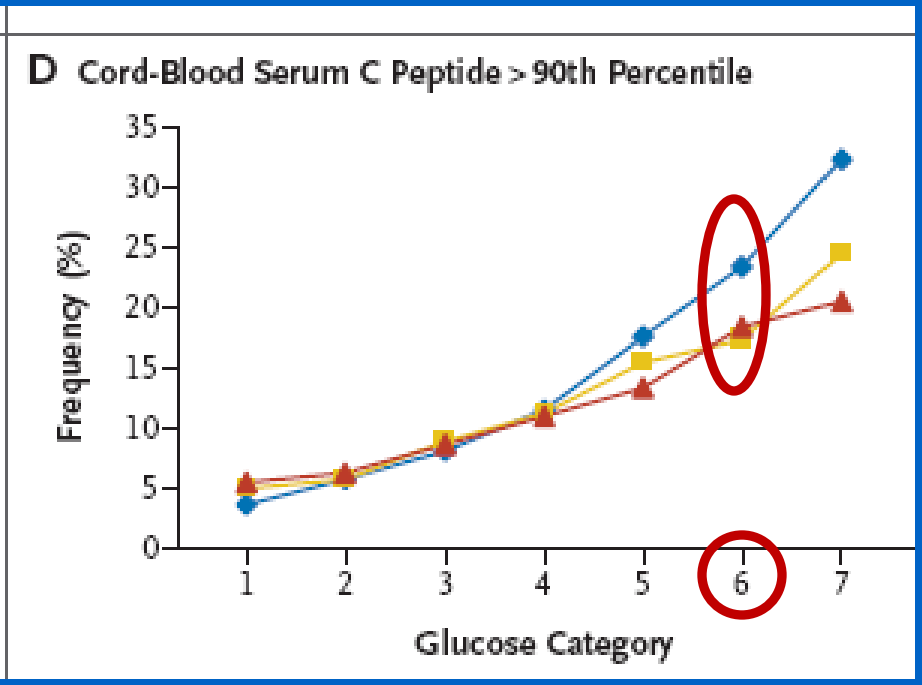

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The HAPO Study Cooperative Research Group. N Engl J Med 2008;358:1991-2002

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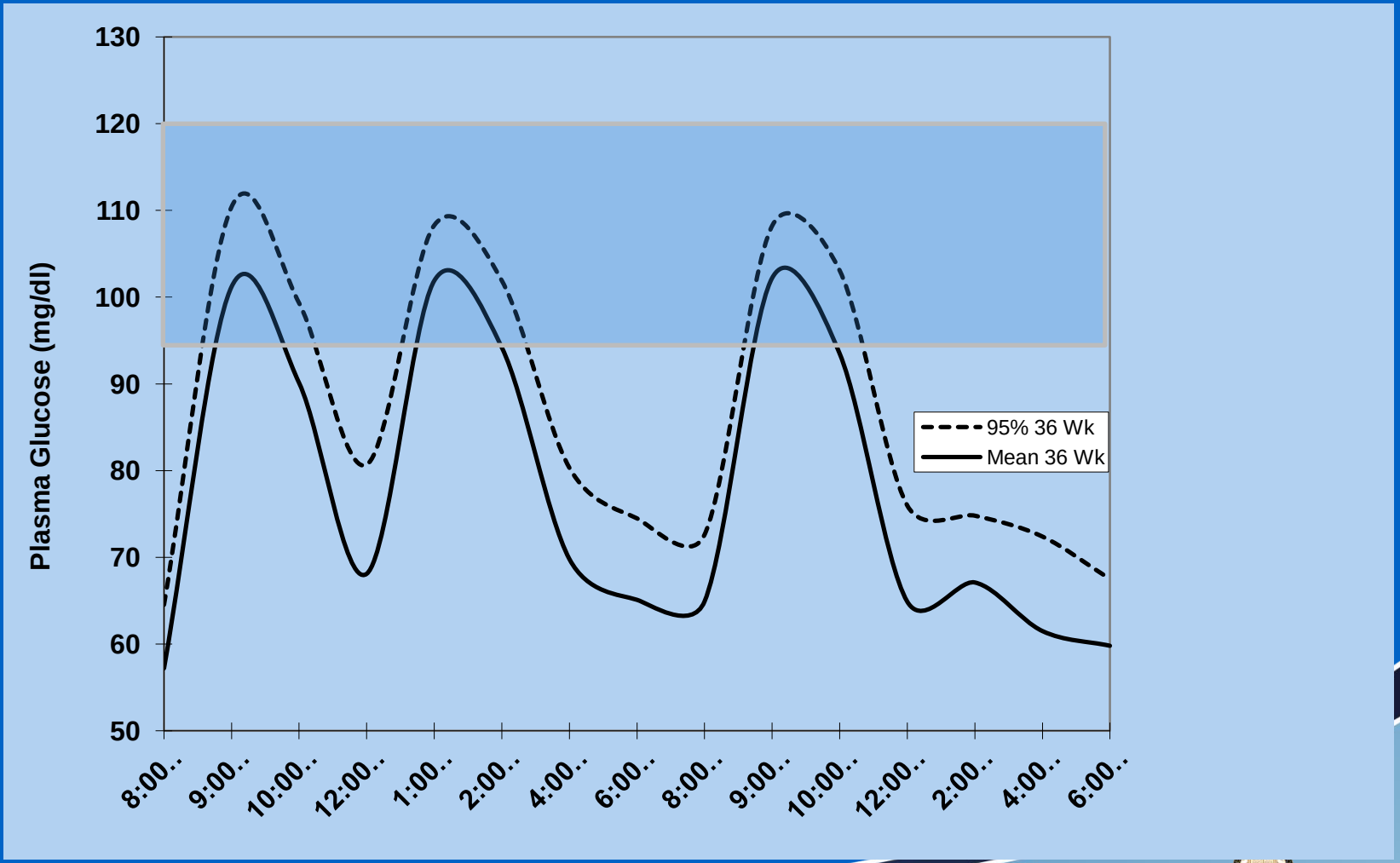
Treat GDM: What Glucose Targets?



Parretti, E., F. Mecacci, et al. (2001). Diabetes Care 24(8): 1317-1318.

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What Should Be Done?

- **Pregnancy**
  - Diagnose GDM, IGT
  - ***Optimize*** glycemic control
  - Diagnose fetal obesity
  - *Limit pregnancy weight gain?*

- **Well Woman Care**
  - Measure and report BMI
  - Counsel regarding obesity
  - Offer interventions (lifestyle, medication)
  - Lose pregnancy weight gain!

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What Must Be Done

- Newborn and Childhood
  - Avoid overfeeding
  - Reduce insulin resistance
  - More research needed
- Between Pregnancies
  - Diagnose IGT/NIDDM
  - Lose pregnancy pounds
  - Return to ideal body weight

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