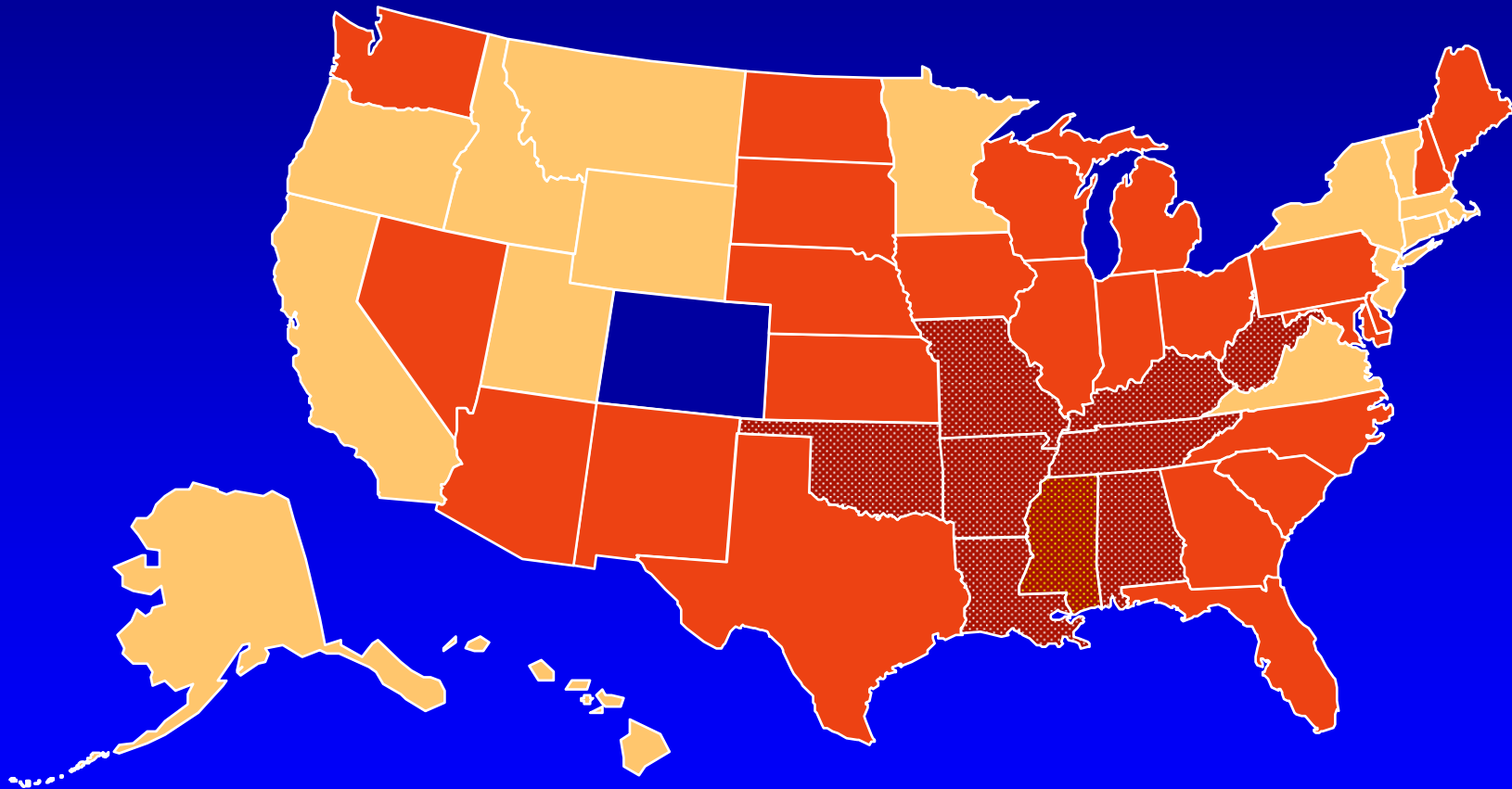


Preventing Obesity and Type 2 Diabetes in Youth



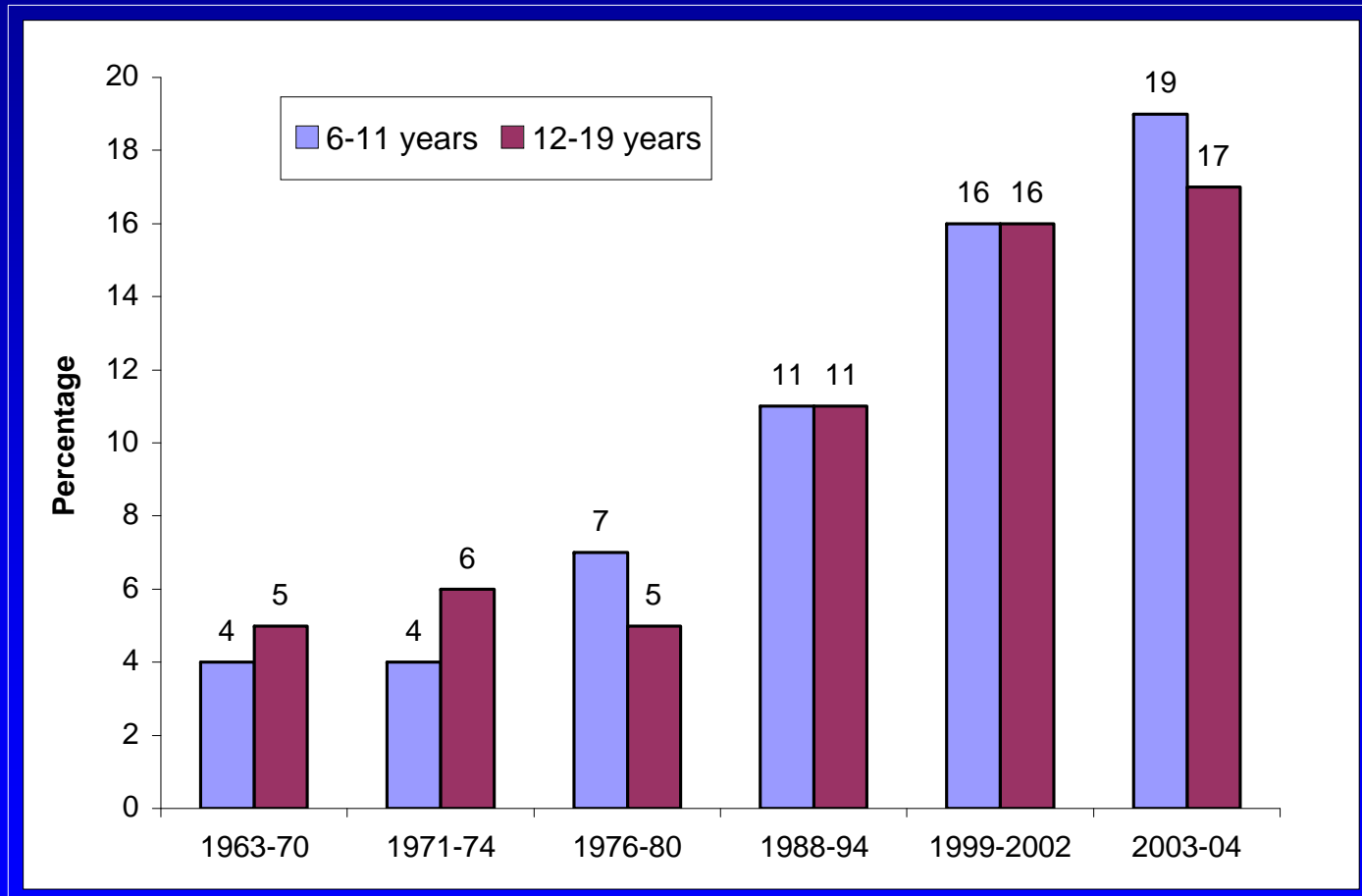
Phil Zeitler MD, PhD
University of Colorado Denver

Obesity Among U.S. Adults 2009

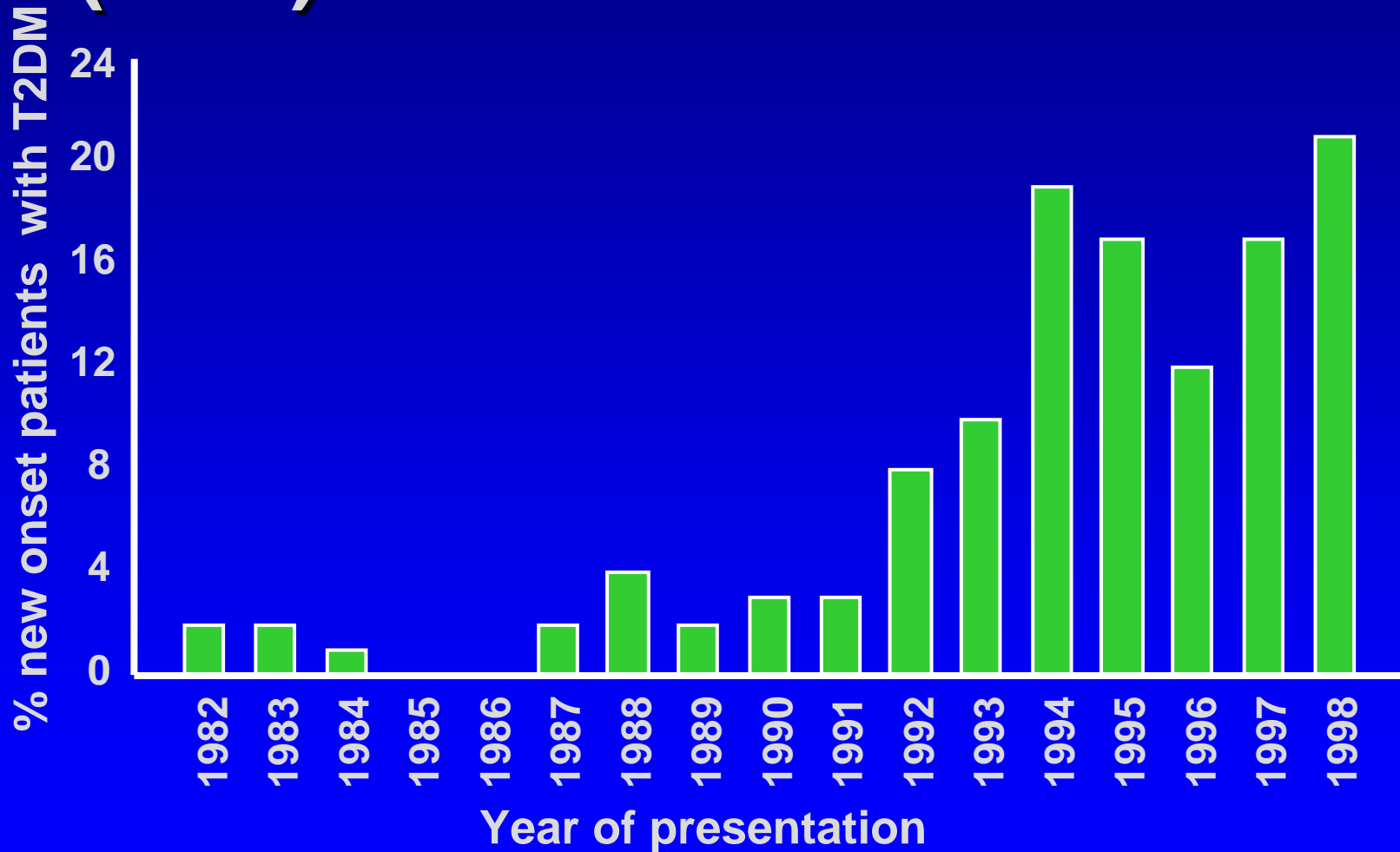


<10% **10%–14%** **15%–19%** **20%–24%** **25%–29%** **≥30%**

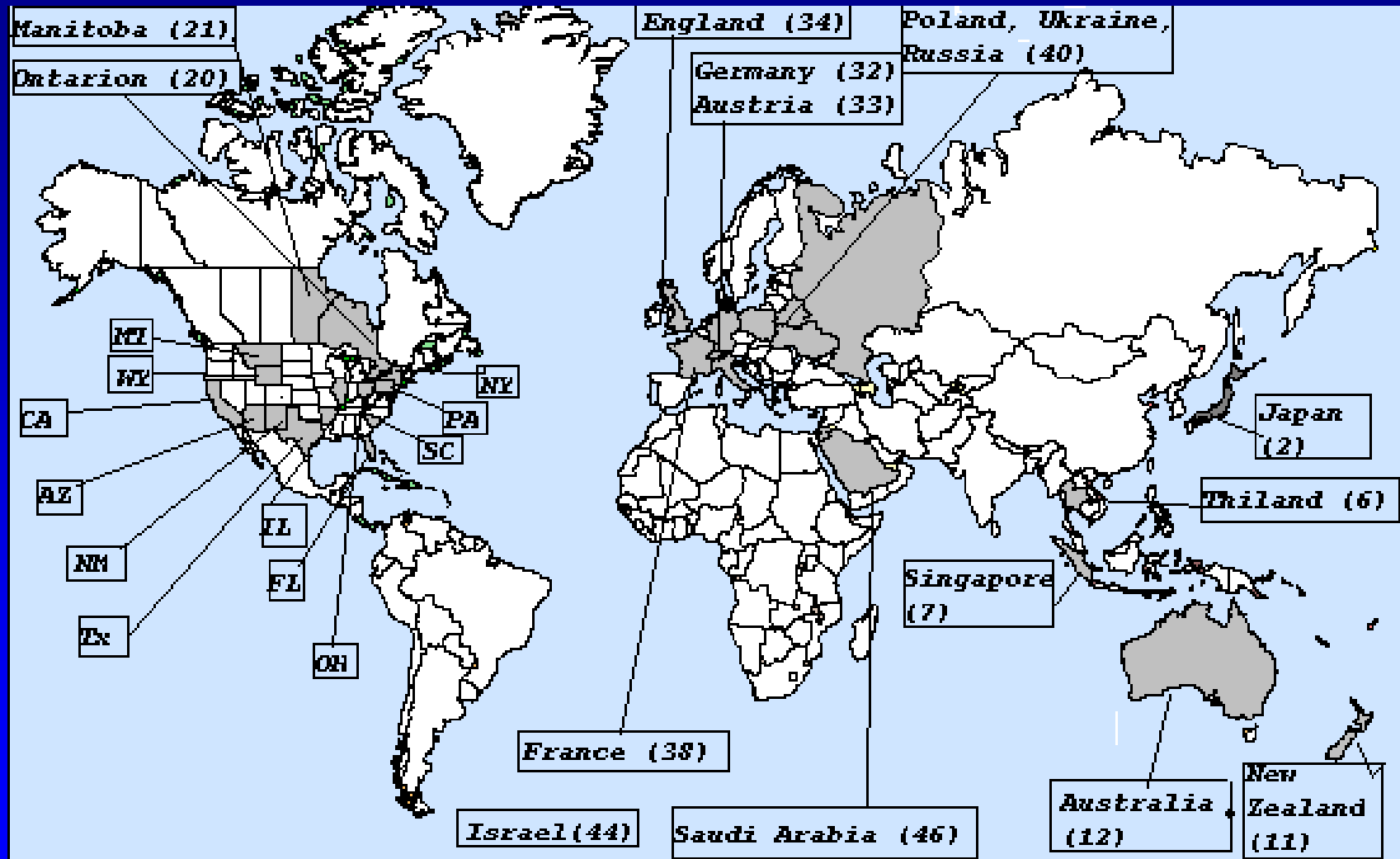
The Prevalence of Childhood Obesity Continues to rise in US



New Onset T2D in Youth (0-19)



A worldwide phenomenon



Who are these kids?



Is this environment?



Are they a genetic "extreme"?

If so, why now?



Unique aspects of type 2 in youth



Current US Demographics

- 1211 kids screened for a large study of T2D
 - Average age 14.2
 - 37% male
 - Average BMI 35
 - Ethnicity
 - 21% white
 - 34% Hispanic
 - 35% African-American
 - 5% American-Indian
 - 2% Asian



Current Incidence of T2D in Adolescents

- SEARCH for Diabetes in Youth
 - rare in children younger than 10 years of age, regardless of race or ethnicity.
 - after 10 years of age, newly diagnosed cases
 - 14.9% in non-Hispanic whites (NHW)
 - **0.19 cases per 1000 NHW youth**
 - 46.1% in Hispanic youth
 - 57.8% in non-Hispanic Blacks (NHB)
 - 69.7% in Asian/Pacific Islanders
 - 86.2% in American Indian (AI)
 - **1.74 cases per 1000 AI youth**
 - In total, approximately **3700** youth under 20 years of age are diagnosed with T2D in the US annually

The prevalence of undiagnosed diabetes is low

- NHANES 1999-2000 – 915 12-19 years
 - DM based on fasting criteria < 1%
- STOPP-T2D
 - 1750 8th graders, BMI > 85thile
 - 0.4% - DM – fasting criteria
 - 0.1% - DM - OGTT
 - 2% with IGT

The Prevalence of Impaired Fasting Glucose is high

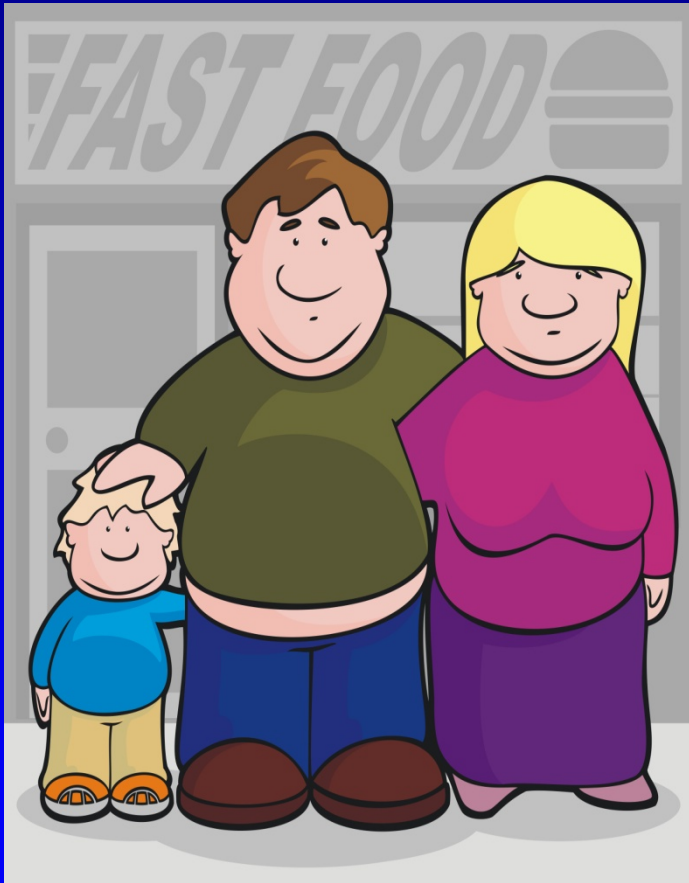
- NHANES 1999-2000 – 915 12-19 years
 - All adolescents IFG 7%,
 - 13% Mexican-Americans
 - 7% African-Americans
 - 4% NHW
 - Obese Adolescents 11.7%
- STOPP-T2D
 - 1750 8th graders , BMI > 85thile
 - 40.5% IFG
 - 2% IGT

The Type 2 Family



- n 45% of mothers and 40% of fathers with T2D
- n 27% both parents with T2D
 - 50% of the remaining fathers diagnosed with T2DM in the study
- Parents have poor DM control
 - mothers A1c: 13.4 ± 1.6 %
- Mothers, fathers AND siblings obese

The Type 2 Family



- n Diet high in fat, low in fiber
 - Doesn't make a difference if mother has T2D
- n Binge Eating prevalent
- n No routine activity
- n 3-5 hours/day TV
- n Insulin resistance prevalent among unaffected family members

The Type 2 Family – newer insights

- n Frequent family dysfunction
 - n Unstable residence and transportation
 - n Contact with justice system
 - n School absences or dropouts
 - n Poor communication
 - n Poor parenting
 - n Domestic violence
- n Increased family health burden
 - n diabetes and non-diabetes related disorders
 - n Psychological and psychiatric disorders in parents and family members.

Psychosocial Characteristics

	Non-Hispanic White	Hispanic	Non-Hispanic Black	American Indian
Lives with **				
Both parents	43%	43.2%	26.8%	46.5%
Mother only	40%	46.3%	58.2%	25.6%
Father only	11.1%	3.2%	3.8%	7.0%
Neither	5.9%	7.4%	11.3%	20.9%

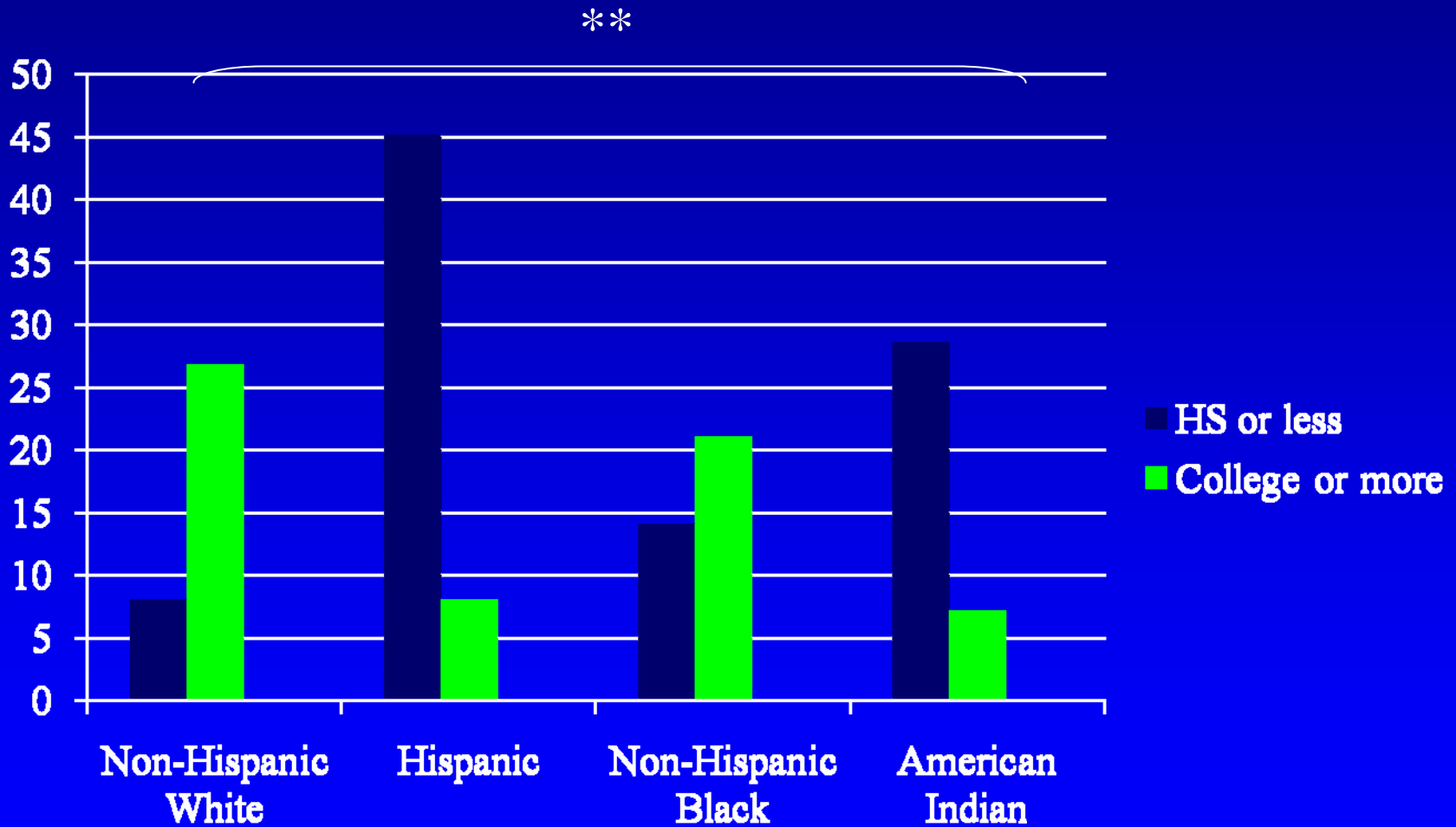
**** P < 0.01**

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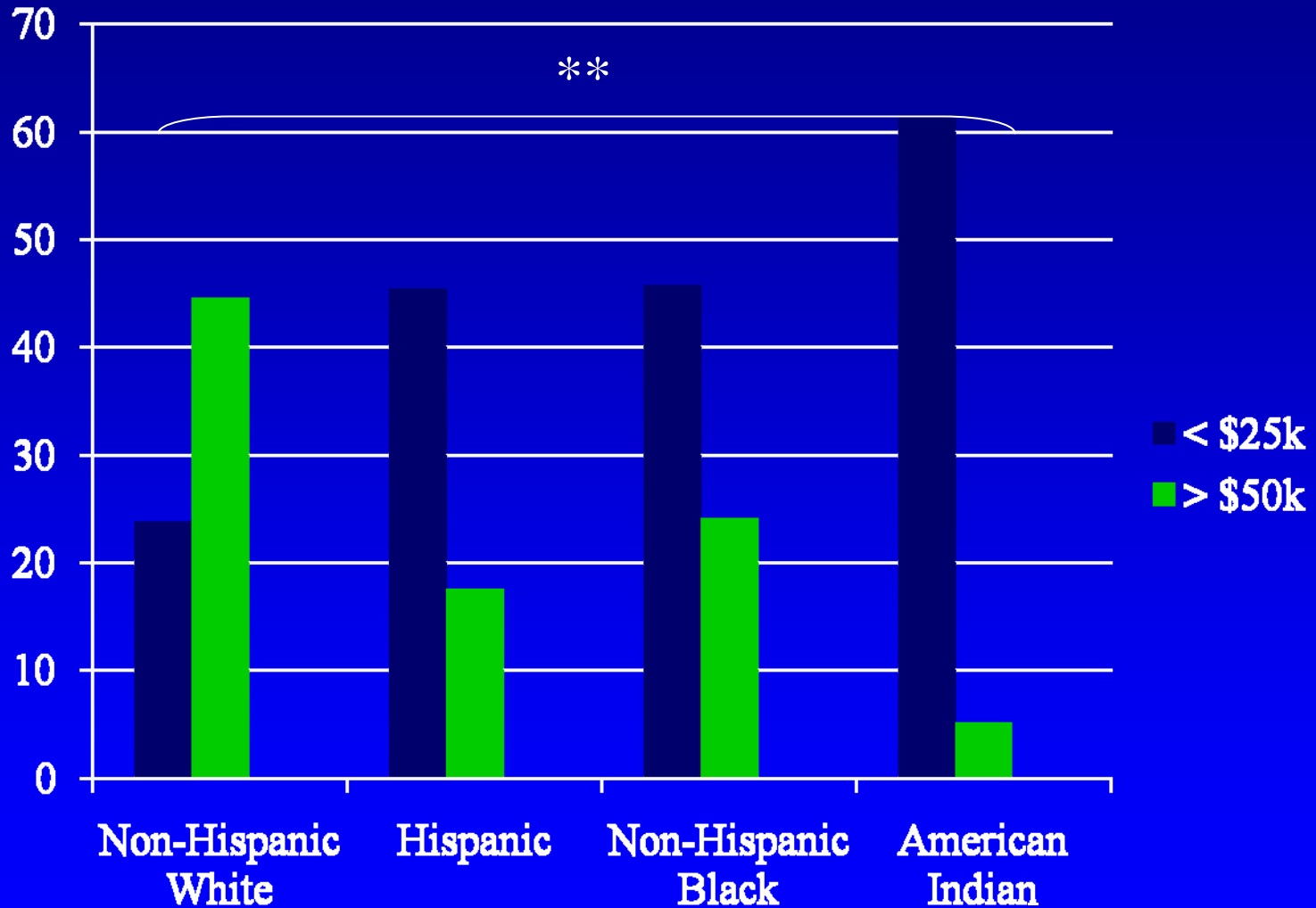
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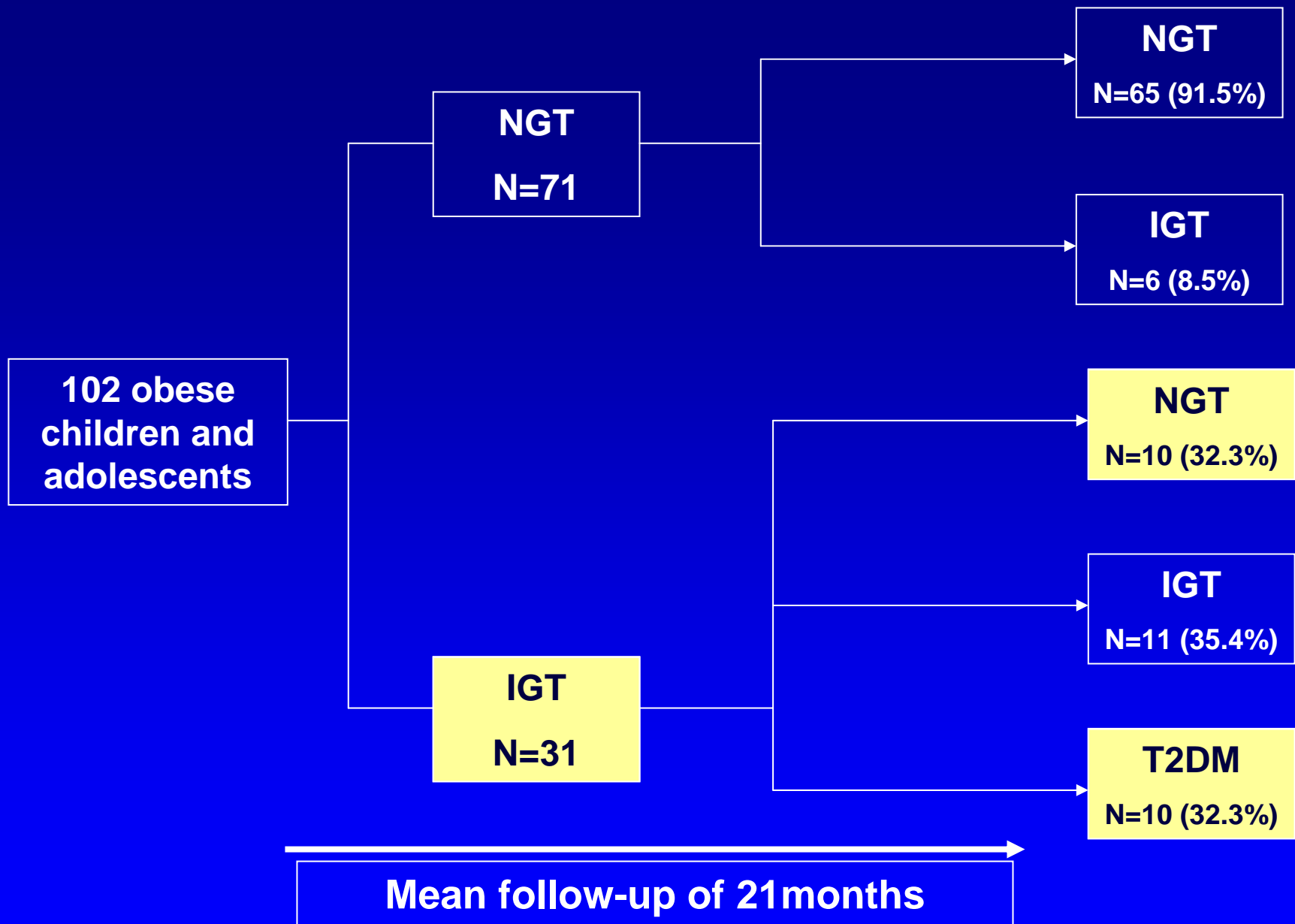
Parental Education Attainment



The Today Study Group
J Clin Endocrinol Metab *in press*

Family Income

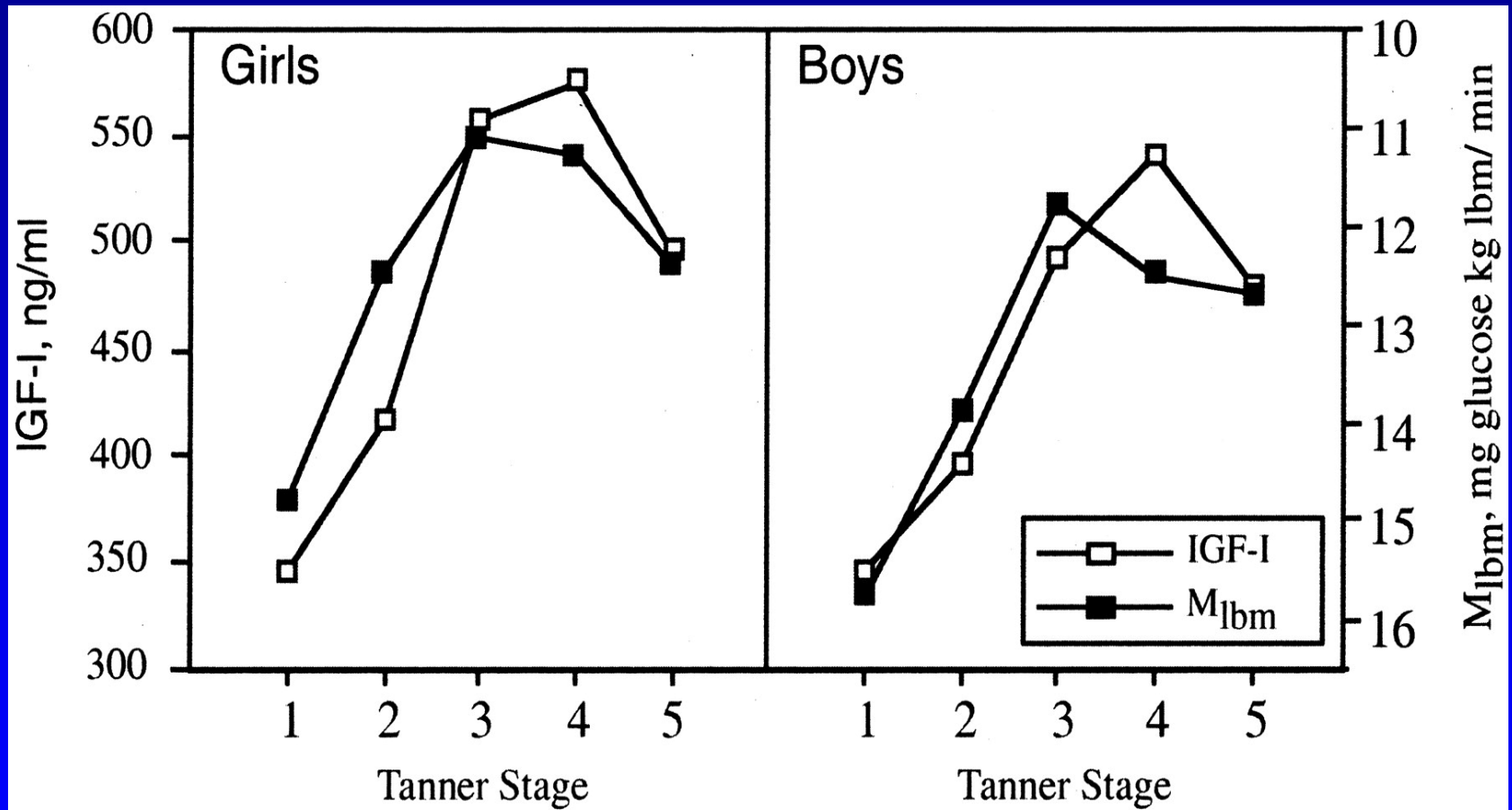




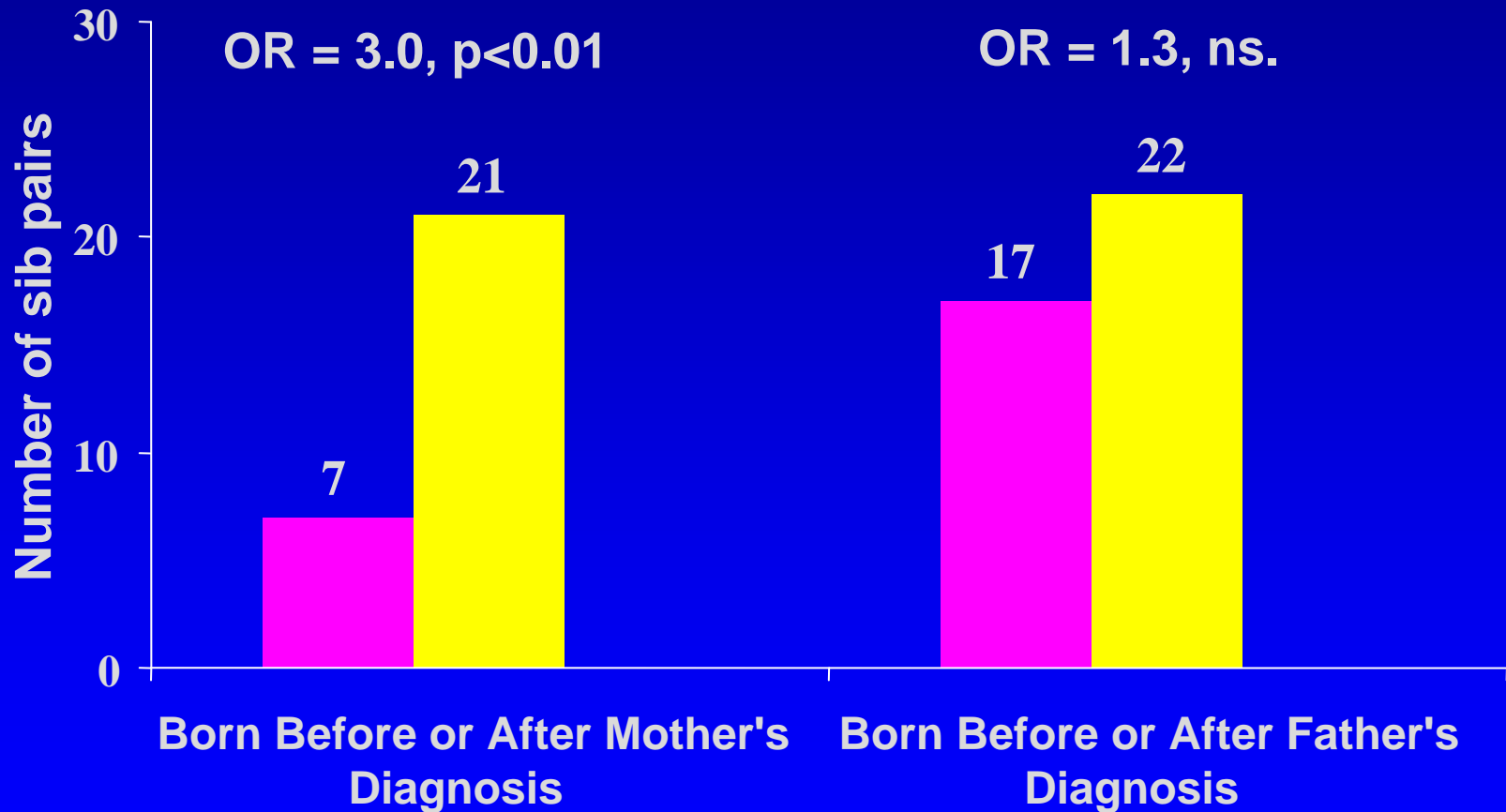
Factors Associated With The Transition Between Categories of Glucose Tolerance

- **Marked weight gain**
- **Profound insulin resistance at baseline**
- **Reduced first phase insulin secretion at baseline**

Insulin resistance and puberty



Pima Indian Sib Pairs Discordant for Diabetes and Exposure to Diabetes in Utero

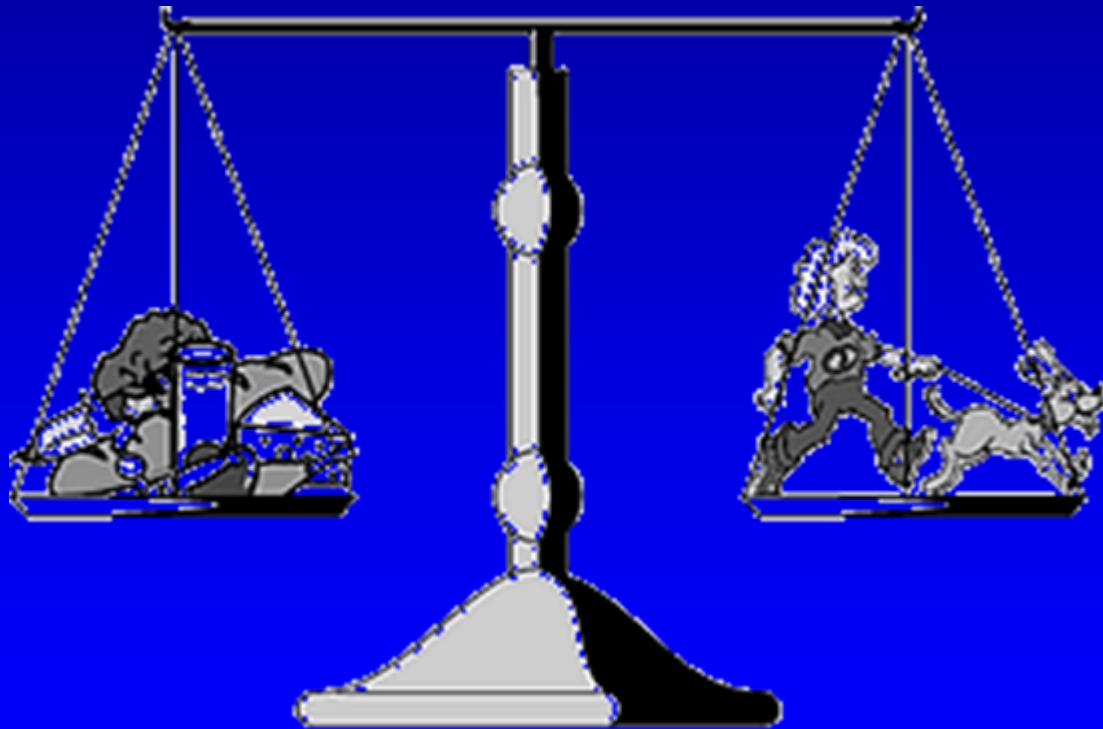


Preventing type 2 diabetes in youth

- Preventing development of insulin resistance
 - Prevention of visceral adiposity
 - Preventing worsening of the routine insulin resistance of puberty
- Preventing maternal obesity, weight gain, and gestational diabetes
- Accomplishing this in a setting of disrupted family structure and low socioeconomic status.



Energy Balance



A obesity culture for kids

- **dietary changes**
 - fast food
 - snacking
 - high caloric density
 - cheap
 - increased portion size
- **Cultural changes**
 - never hungry
 - Advertising assault
 - energy saving
 - automobiles vs. pedestrians
- **activity changes**
 - decreased active time
 - decreased school PE time
 - decreased play time at home
 - expenses associated with sports
 - emphasis on excellence
 - lack of supervision
- **increased sedentary time**
 - computers
 - video games
 - 64 channel TV
 - lack of supervision



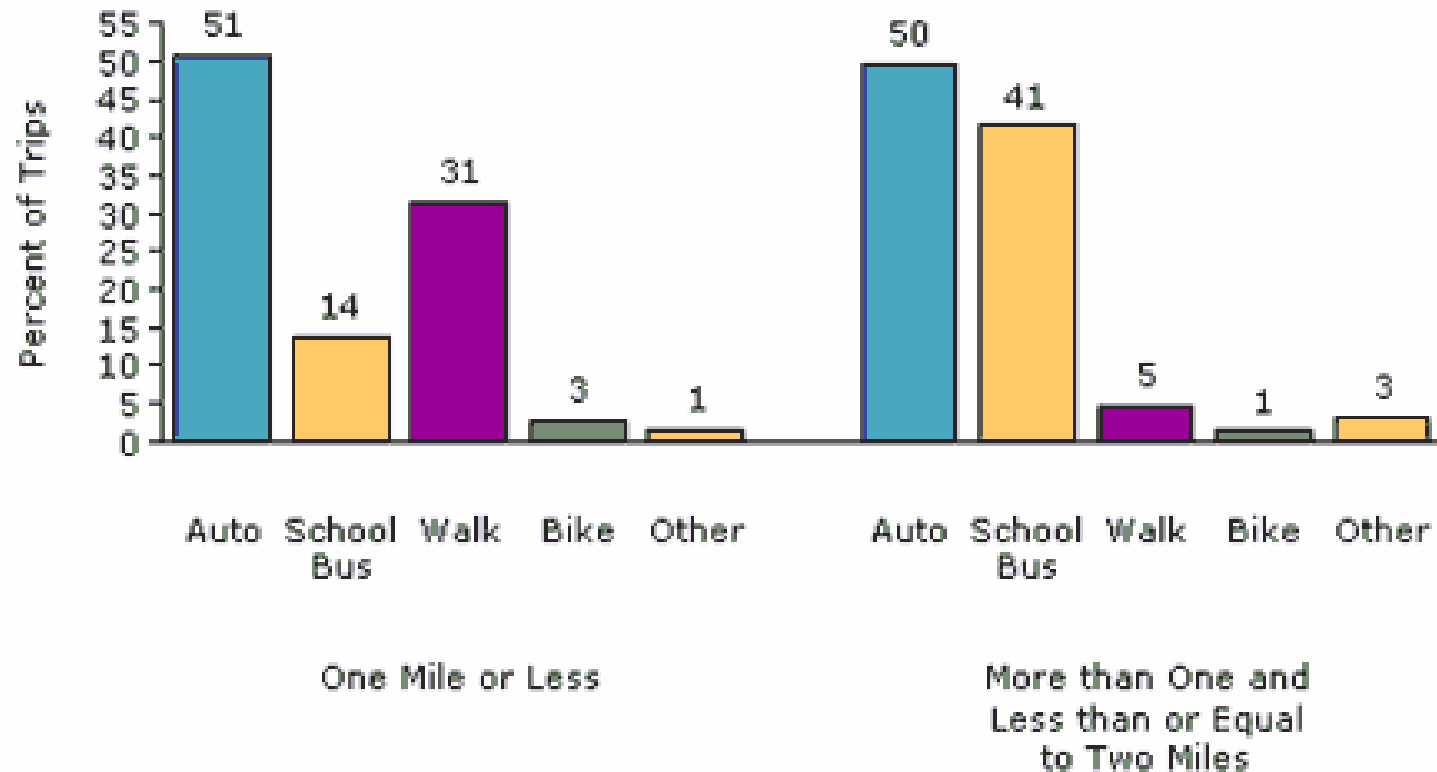
Energy Balance: Television

- Average # hrs/day a TV is on in an American household:
 - 6 hours, 45 minutes (405 minutes)
- Typical time spent in aerobic activity
 - 8 - 10 minutes
- 66% of Americans watch TV during dinner
- Hours/year in school: 900
- Hours/year watching TV: 1500
- Fast food is the #1 TV advertisement aimed at kids
- 4 hrs of Sat a.m. cartoons = 200 “junk food” ads

Energy Balance: Nutrition

- Consumption of sugar beverages
- Americans eat approximately 1/3 meals outside home
- Most of these meals are high fat, low nutrient
- High fat food intake leads to more high fat food intake
- Family eating practices are key
 - What are the parental eating practices?
 - Are meals eaten together?
 - Is there a “dinner table”?

Trips to School by Distance and Mode Youth Aged 5–15 Years





Behavior and Energy Balance

- INTAKE
- Burger King Meal
 - Triple Whopper w/Cheese
 - 1230 calories/82g fat
 - Large Fries
 - 600 calories/33g fat
 - Large Milkshake
 - 1236 calories/36g fat
- TOTAL
 - 3066 calories/233g fat
- EXPENDITURE
- Burning 3066 calories
 - Run 30 miles

Lifestyle Modification



In principle, it's easy!

- Reduce the accretion of visceral fat through lifestyle modification
- Reverse the trends in the toxic environment through thermodynamics
 - Reduce caloric intake
 - Increase caloric expenditure

Lifestyle Modification

- AAP Expert Committee:
 - Evidence based dietary interventions
 - Eliminate liquid calories
 - Reduce or eliminate eating out
 - Reduce portion sizes
 - Evidence based activity interventions
 - Reduce sedentary time/screen time
 - Encourage attainment of recommended activity goals.

In practice, it's difficult!

- Individual medical
 - Limited evidence for effectiveness
 - Labor intensive and low yield
- Home-based intervention
 - Limited research
- School-based intervention
- Change in the social and built environment

Individual interventions

- Diet change is key to successful weight loss
- Exercise required to maintain loss
- Increasing daily activity better than “formal” exercise
- Parents are critical
 - Parental obesity is a predictive factor
 - Parent/child >> Child alone
 - Parent >> child
- Caveat: all studies done on families presenting for weight loss!
 - Relevance to children referred for health problems?

School Interventions



Cochrane Meta-analyses

- Summerbell 2007 – No evidence for effectiveness of school-based interventions for the prevention of obesity
 - Some evidence for reported changes in dietary habits
- Summerbell 2007 – No evidence for effectiveness of school-based interventions for the treatment of obesity

Medications?

- Diabetes Prevention Program
 - Lifestyle intervention and metformin, effective in reducing progression of IGT to T2DM in adults
 - Lifestyle more effective in older participants
 - Metformin equally effective in younger participants
 - No youth involved
 - All participants had IGT
 - What is the evidence that metformin is useful in youth

Metformin

- Non-controlled case studies
- Freemark and Bursey
 - 29 mixed white and black boys and girls
 - BMI > 30 kg/m², Fasting insulin > 15
 - At least 1 1st or 2nd degree relative with T2DM
 - Metformin 500 mg BID or placebo for 6 months
 - BMI decreased 0.12 SD (1%) vs. increase of 0.23 SD (2%)
 - Decreased fasting glucose (all normal) and insulin

Metformin

– Love-Osborne et al.

- 58 kids 12-19
 - BMI > 95%ile
 - Fasting insulin > 15 or HOMA > 2.5
- Randomized to metformin or placebo for 6 months
- No difference in weight loss between groups overall
- No significant change in glucose, insulin, lipids, HOMA

DPP for Youth?

- Progression to diabetes is ~ 7% in 8 years with NGT among insulin-resistant Hispanic adolescents
- Assume metformin reduces progression by the same order of magnitude as in IGT adults (~0.3% progression vs ~0.5% every 6 months)
- Assume 5% dropout every 6 months
- Study would need 5000 kids and last 6 years to get 80% power to see the difference.

Summary

- Insulin resistance is the underlying defect in risk for type 2 diabetes
- The development of Type 2 diabetes reflects the progressive loss of compensation for insulin resistance due to β -cell failure
- Fat depots play an important role in insulin resistance and β -cell failure
- Prevention of type 2 diabetes in youth will require reversal of fat accumulation through reduction in caloric intake and increase in caloric expenditure
- We do not yet know how to accomplish this given the complex social and cultural factors involved

Thank you for your attention



The Big Texan – Amarillo, Texas