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University of Auckland

The Fetal Footprint - Is There a Link between Fetal and Adult Health - Main Session
(Workshop options scheduled)

Sunday, 23 June 2013

Start 9:45am

Duration: 25mins

Baytrust



 
Rotorua GP CME 2013

General Practice Conference & Medical Exhibition

20-23 June 2013 | Energy Events Centre | Rotorua

The fetal footprint: Is there a link between fetal and adult health



Wayne Cutfield
2013



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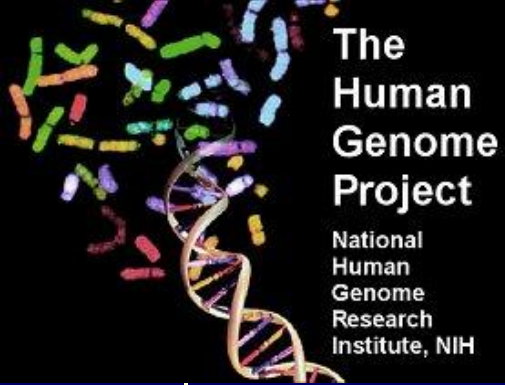
Declaration

Pfizer sponsored speaker

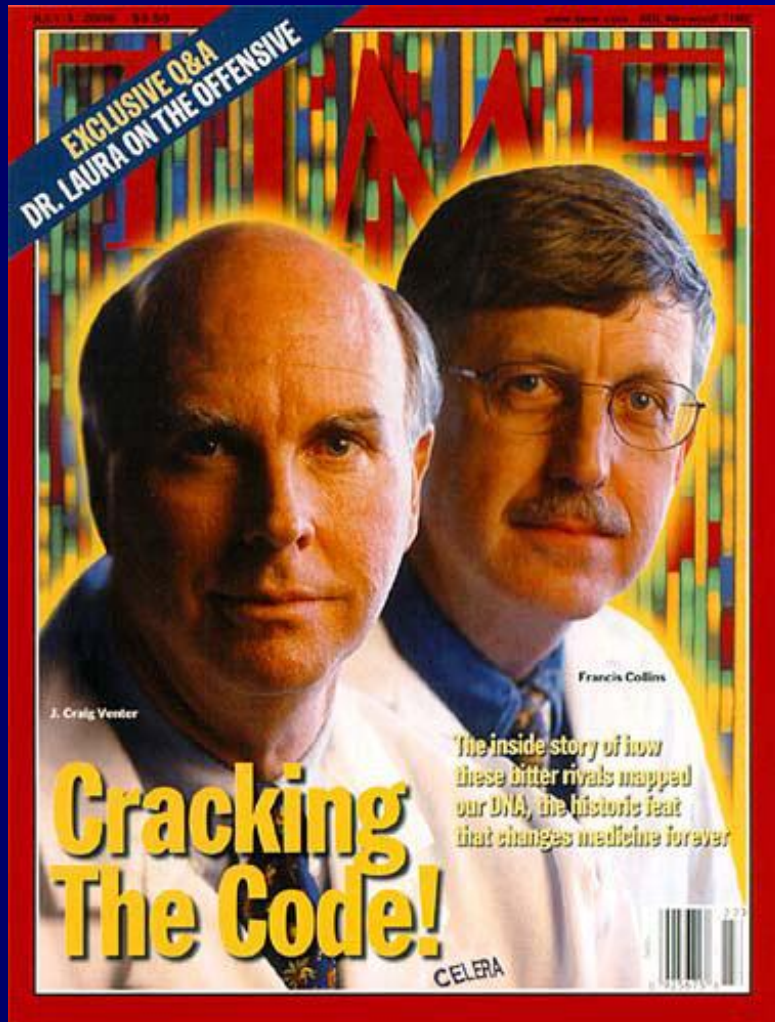
Nutrition and health common misperception

Your health depends entirely on your lifestyle and your genes





Human Genome Project: Failed promise?

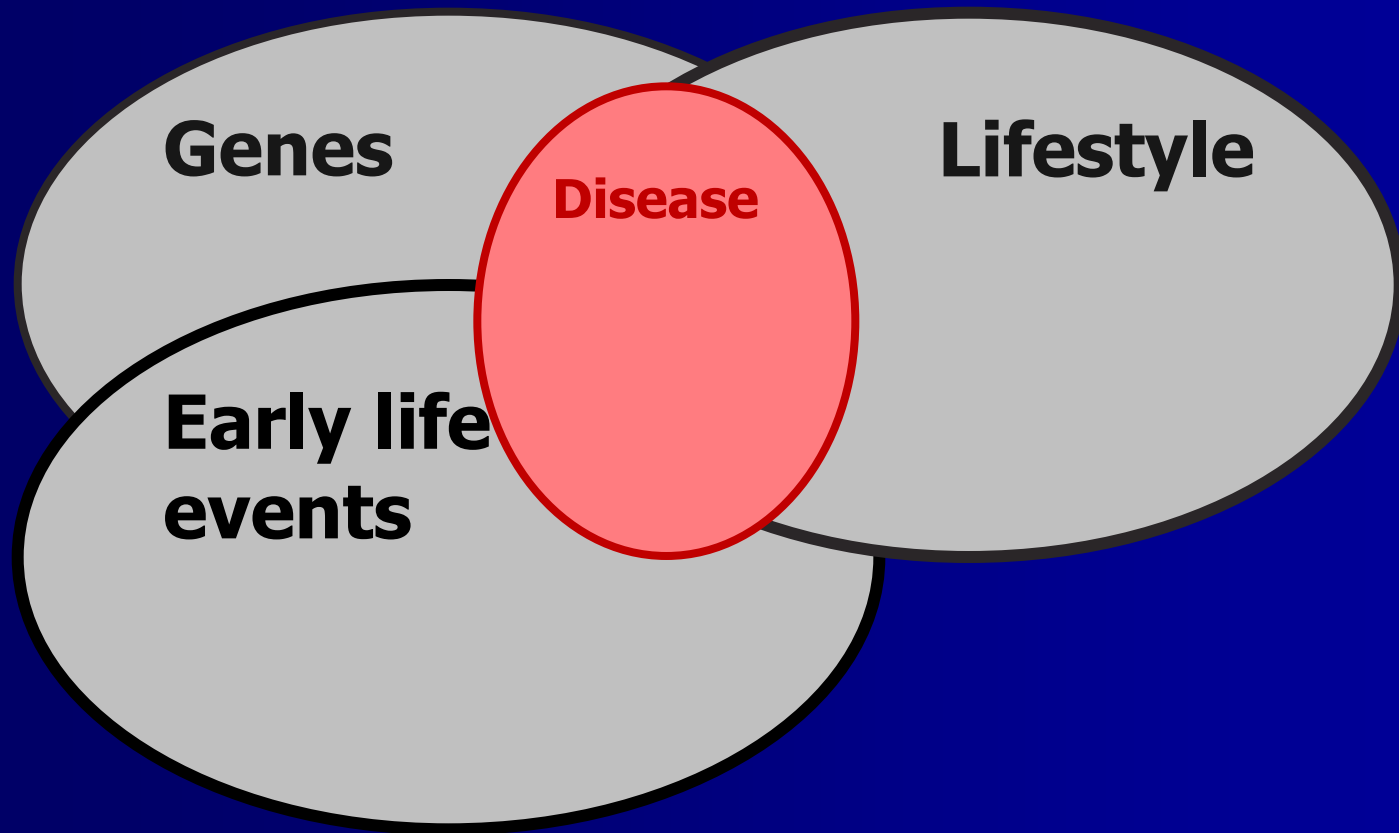


Common variations
in genes
account for <10% of
common diseases
such as
obesity
diabetes
heart disease
cancer



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Determinants of adult disease



As birth weight falls type 2 diabetes risk increases

B Wt (gm) ratio	N	%	Odds
<2500 SGA	20	30	6.6
-2900	54	19	4.8
- 3400	114	17	4.6
- 3900	123	12	2.6
- 4300	64	6	1.4
>4300	32	6	1.0

Fetal Origins (The Barker) Hypothesis

The origins of adult disease begin in utero. Fetal malnutrition is proposed as the cause of small birth size and programmed later adult disease.

Barker D et al. BMJ 1989; 298:564-7.

Birth Weight and Type 2 Diabetes Risk in Twins

Lifespan Twin study (Sweden)
2,888 monozygotic adult twins
185 with type 2 DM

Odds Ratio of 1 kg decrease in birth weight
and type 2 diabetes

Between twin pairs	2.23
Within twin pairs	2.03

Iliadou et al. Intl J Epidemiol 2004; 33: 948-53

Maternal famine affects the health of offspring

1st trimester famine:

Heart disease

Lipid problems

Obesity

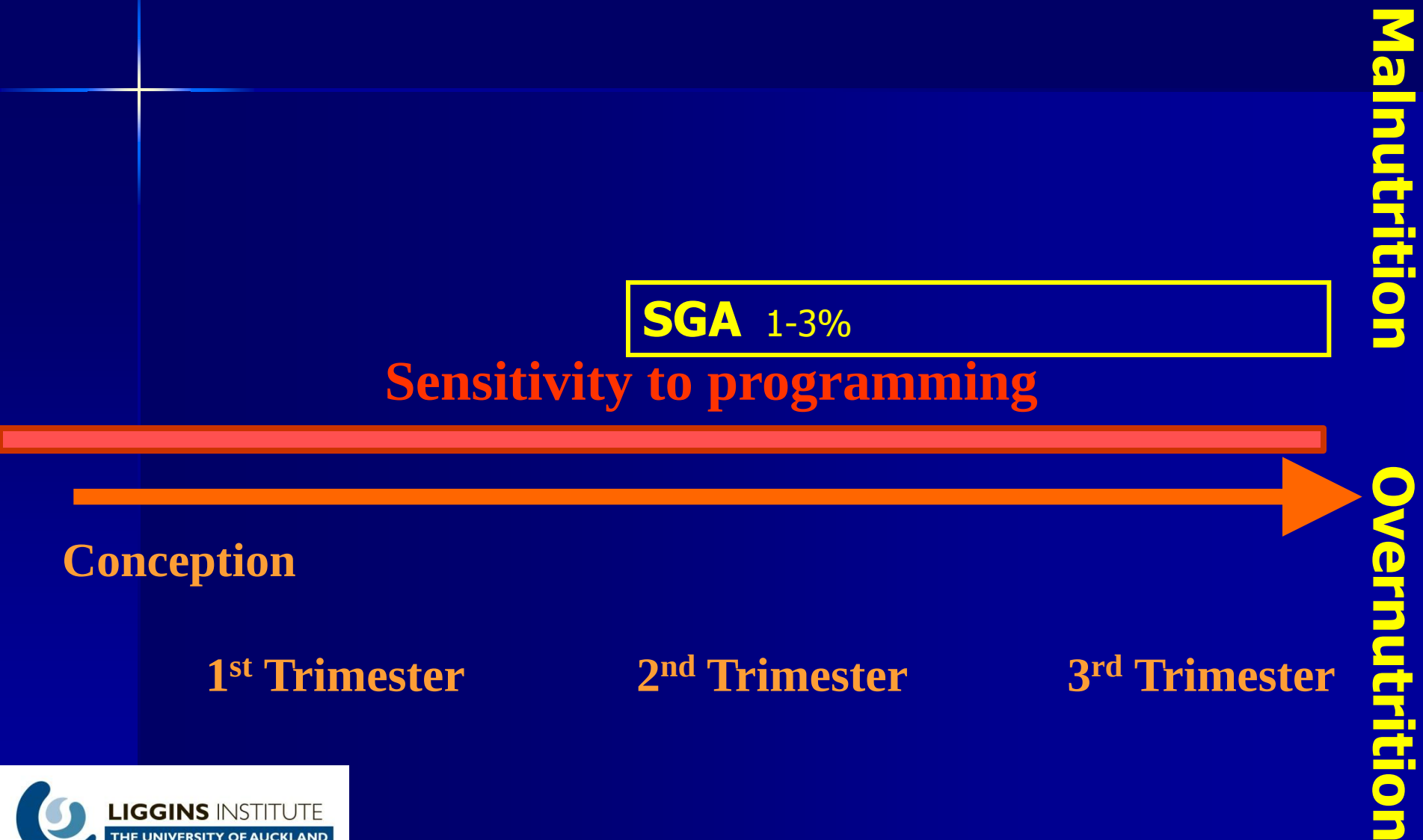
2nd trimester famine:

Chronic lung disease

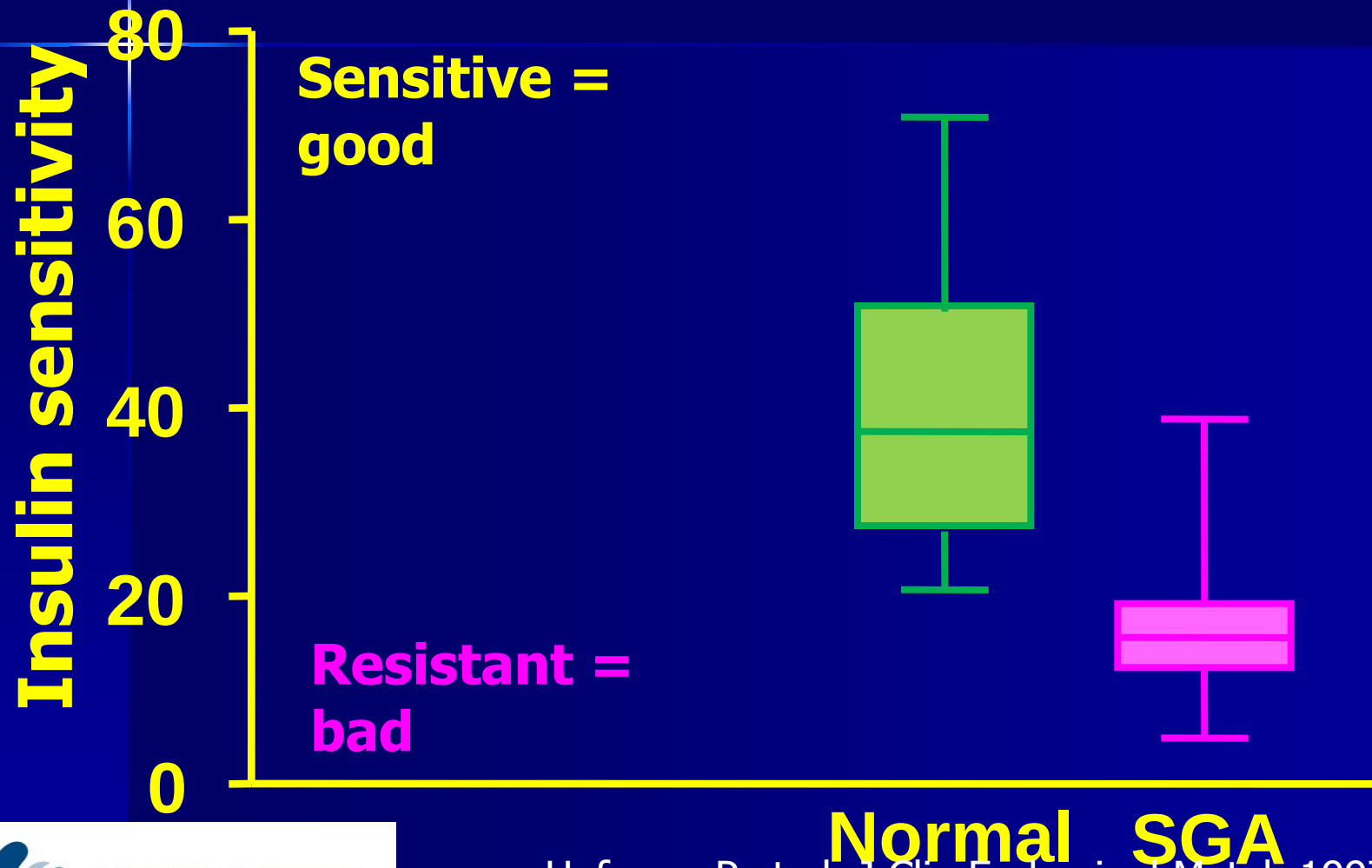
3rd trimester famine:

Diabetes risk

Programming Sensitivity

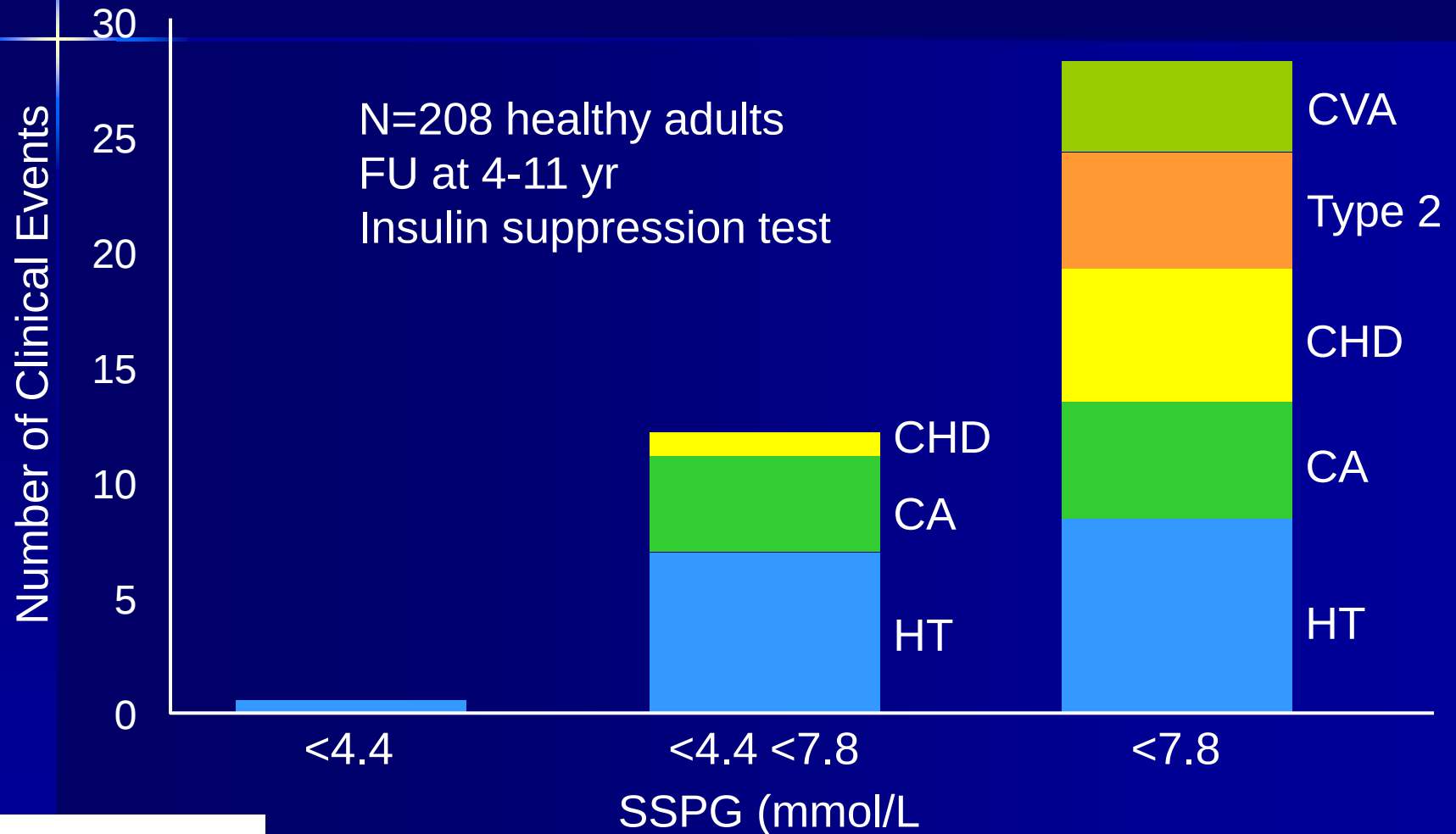


Small at birth (SGA) children are insulin resistant

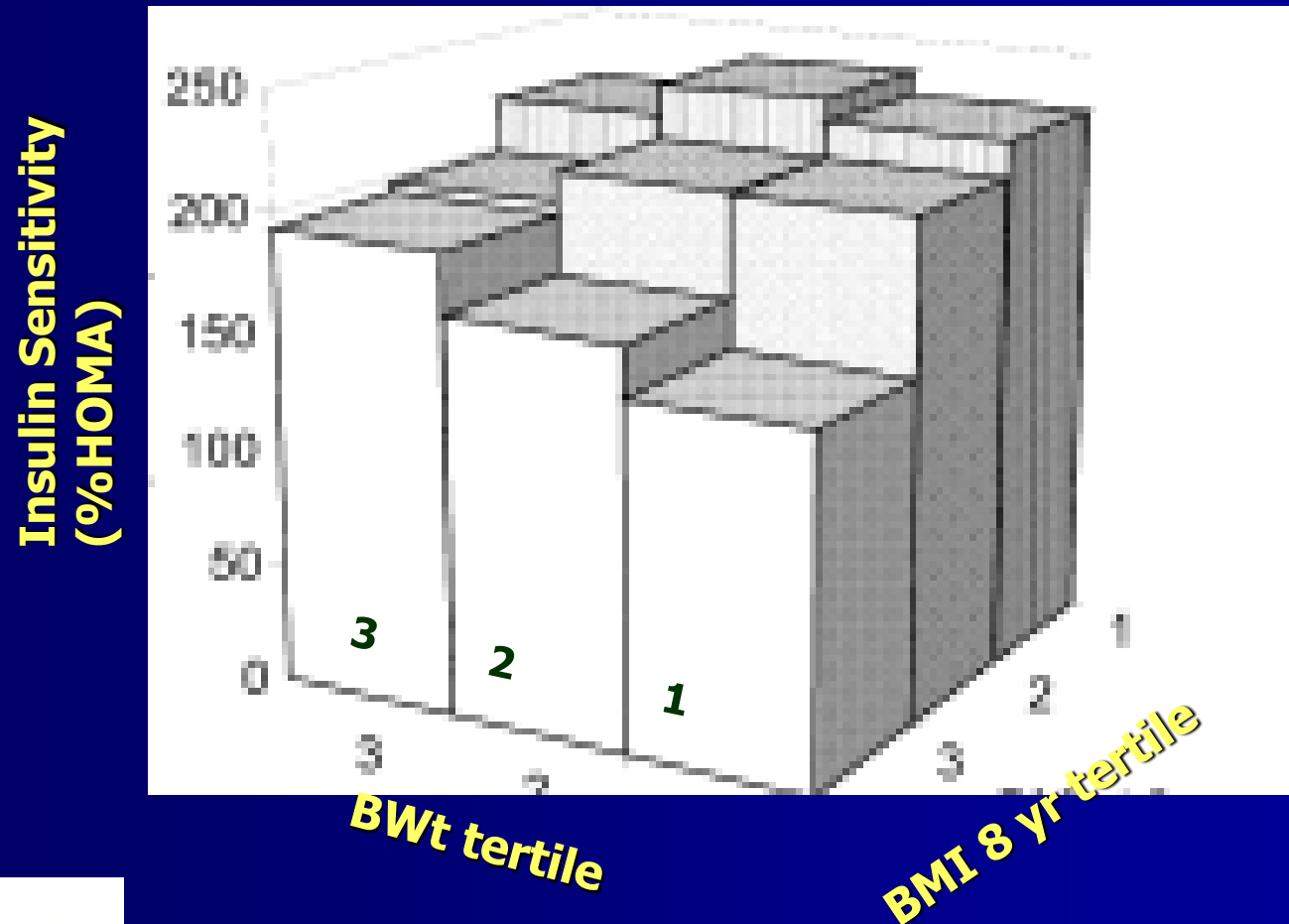


Hofman P et al J Clin Endocrinol Metab 1997; 82:402-6

Long Term Risks of Insulin Resistance



Birth Weight, BMI and Insulin Sensitivity



Metabolic Changes in SGA Children

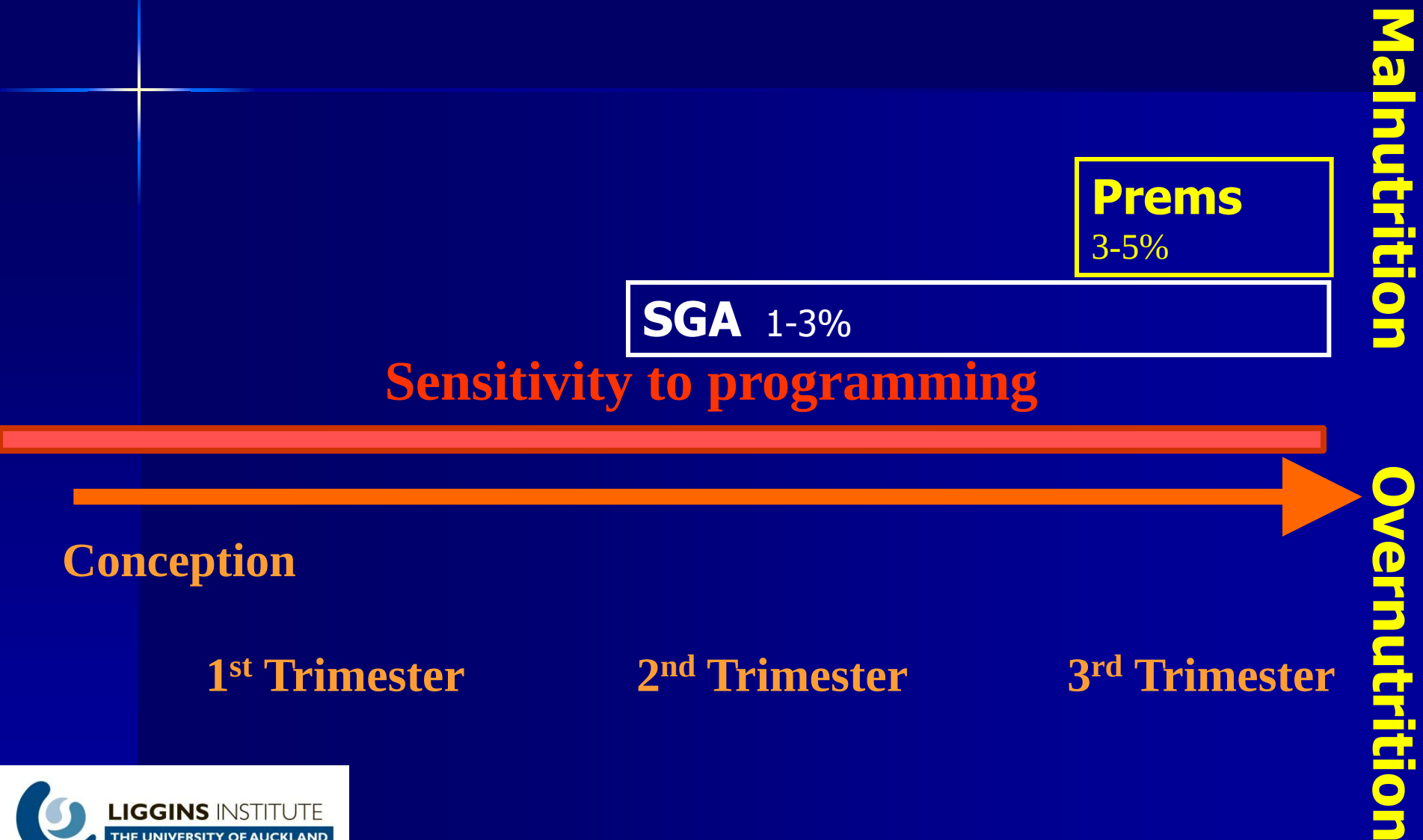
Fasting lipids:

- Increasing cholesterol in late childhood
- Dyslipidemia beginning to occur in young adulthood.

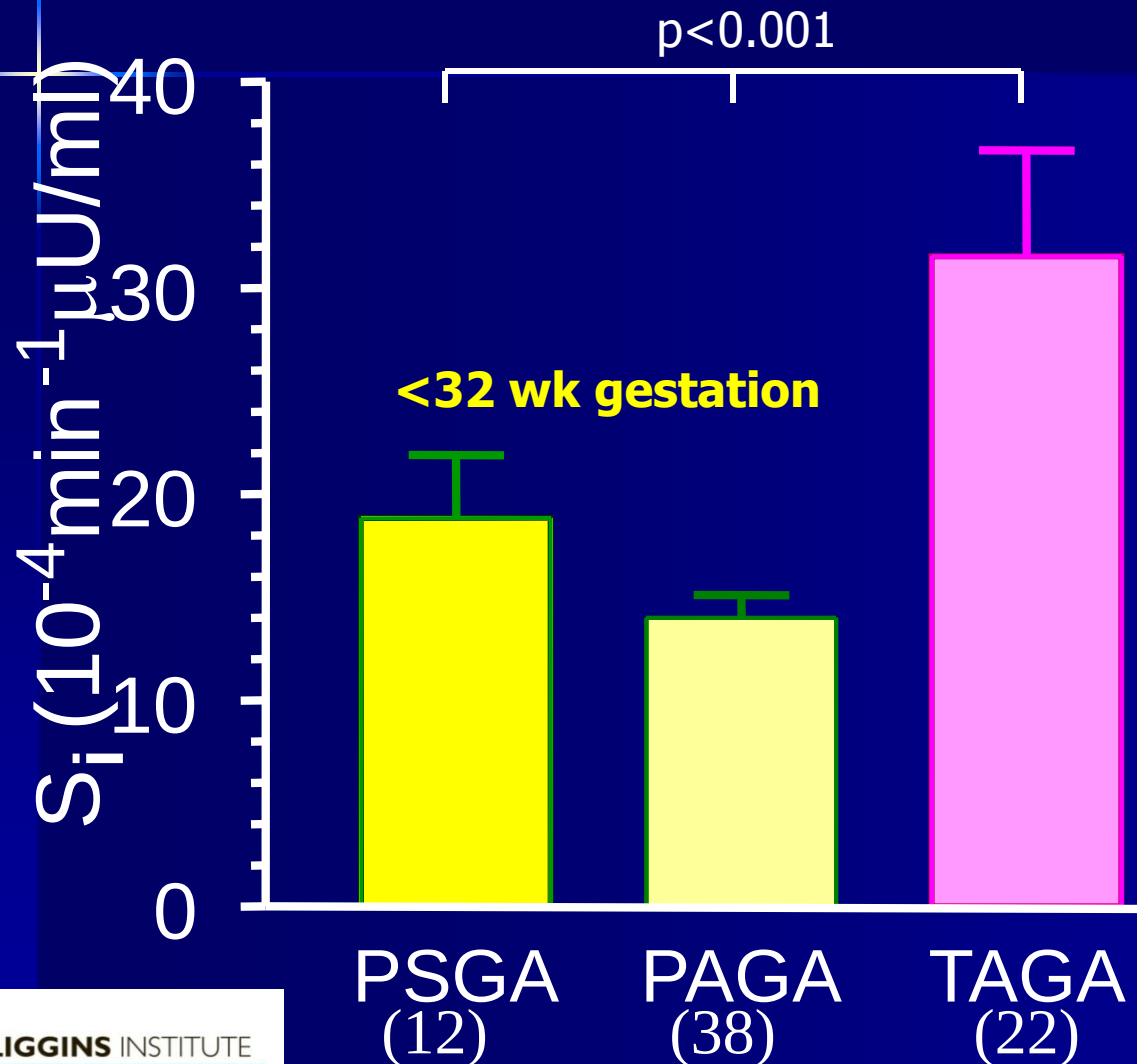
Blood pressure:

- Small increase in daytime systolic BP
- ↓ in normal night-time BP dipping (ABPM)

Programming Sensitivity



Insulin Sensitivity



Hofman P et al N Engl J Med.
2004 8; 351: 2179-86.
Hofman et al. J Clin Endocrinol
Metab 1997; 82; 402-6

Early Nutrition in Auckland VLBW infants

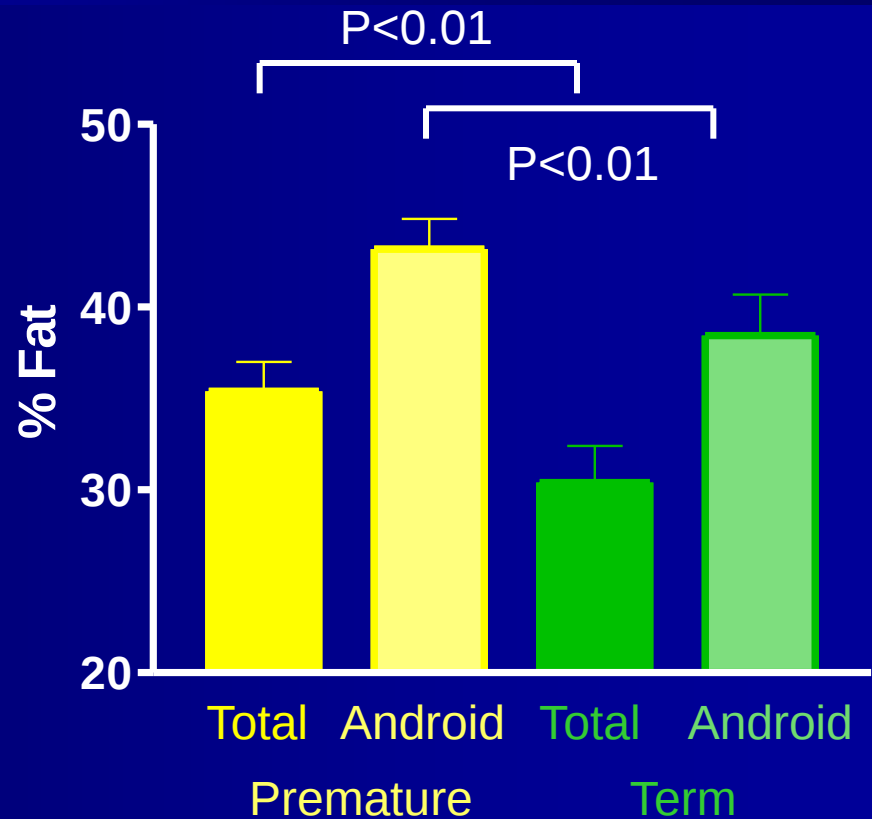
Low protein intake 0-4, 4-8, 8-12 wks

High lipid intake 4-8, 8-12 wks

High carbohydrate intake 4-8, 8-12 wks

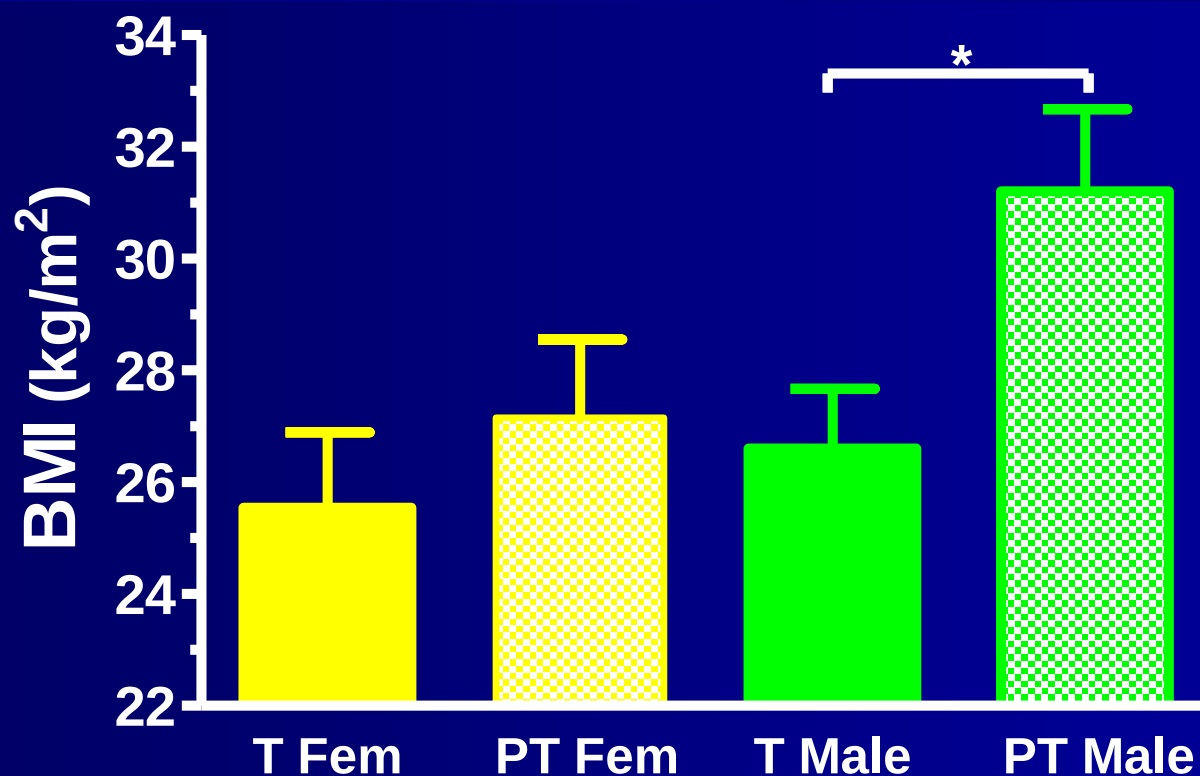
Higher carbohydrate intake in the first month of life was associated with greater current BMI SDS ($p < 0.05$).

Prematurely born adults are insulin resistant and overweight



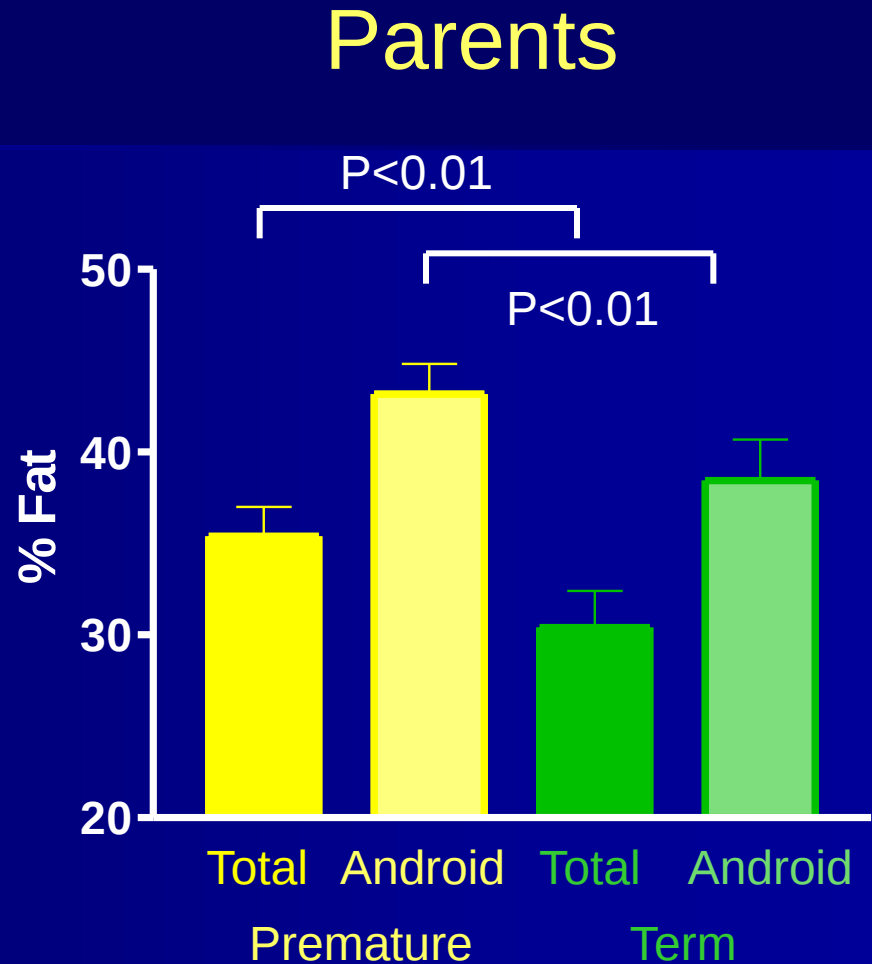
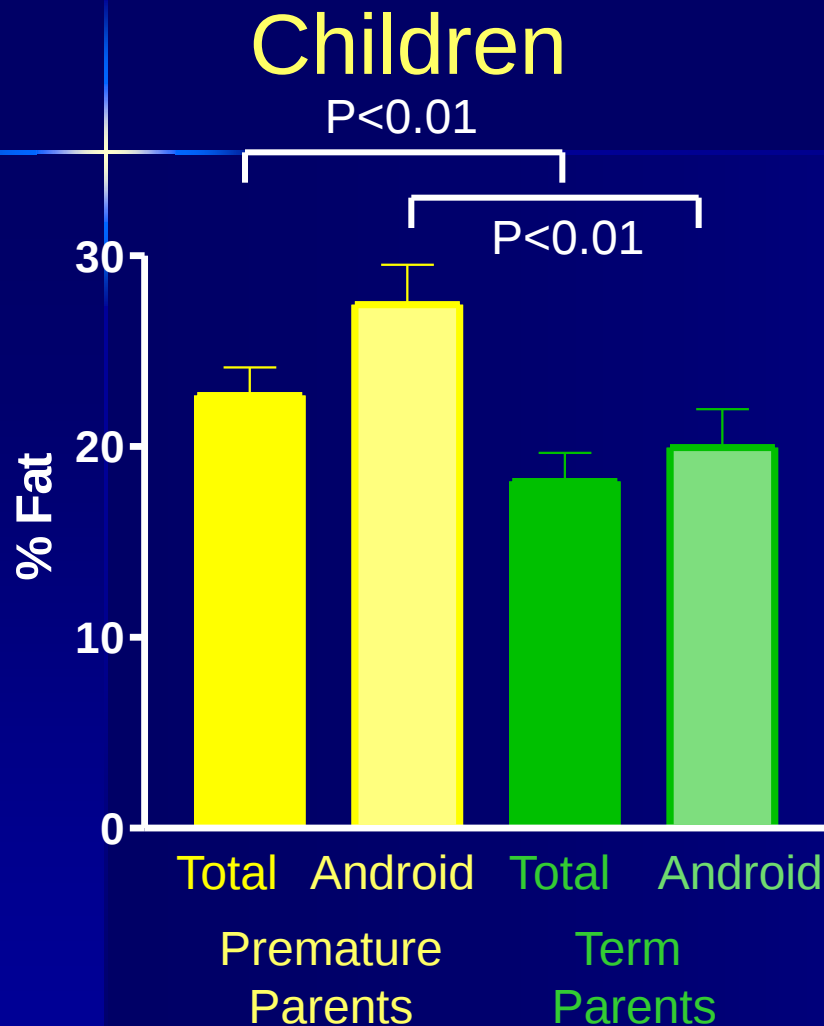
Mathai S et al Diabetes 2012; 61: 2479-83

Prematurity and adult male adiposity

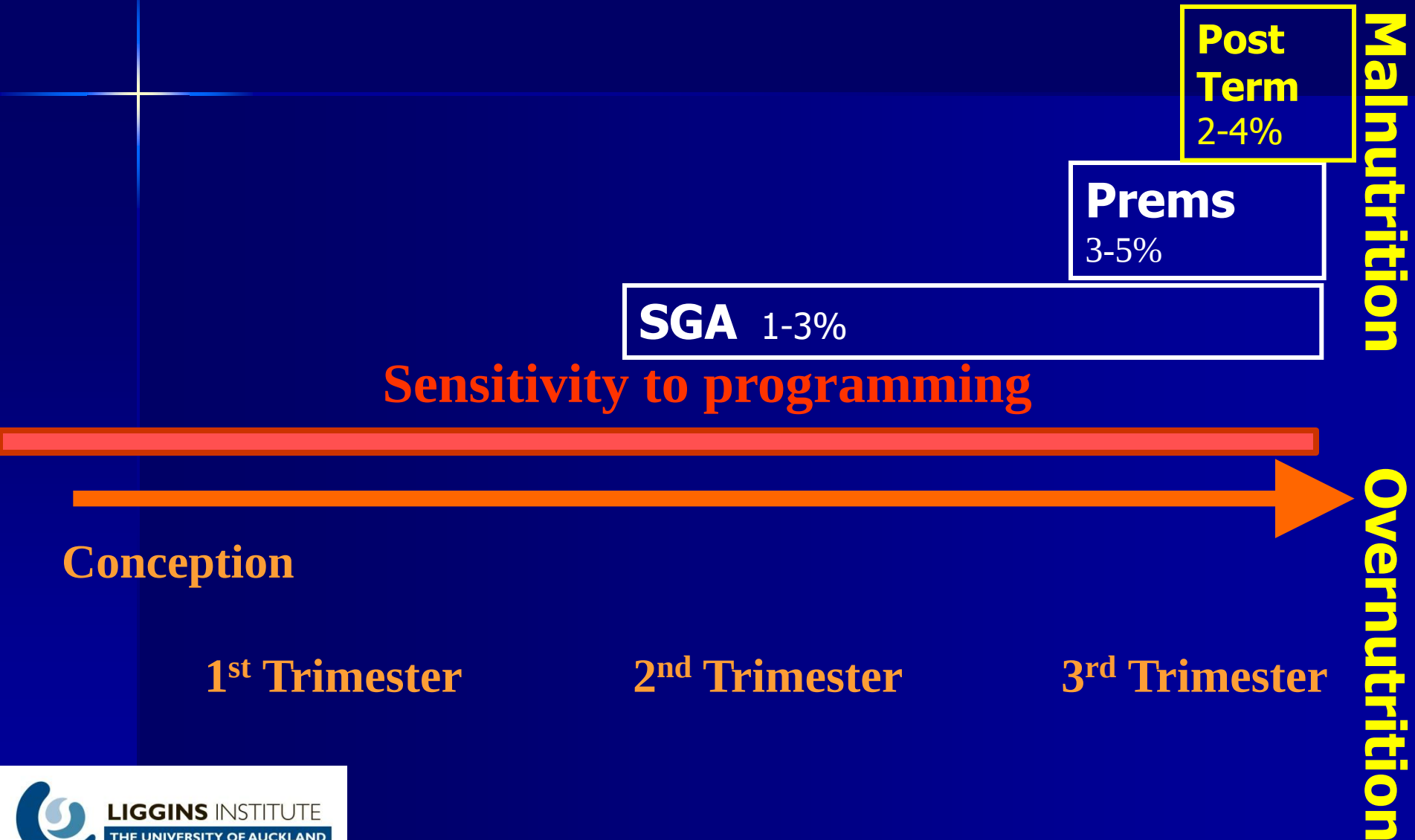


Mathai S et al Diabetes 2012; 61: 2479-83

Prematurity affects the next generation!



Programming Sensitivity



Background

Post-term children: born after 42 weeks of gestation

Incidence of post-terms highly variable:
0.4 – 12%

In Auckland 2009-10:

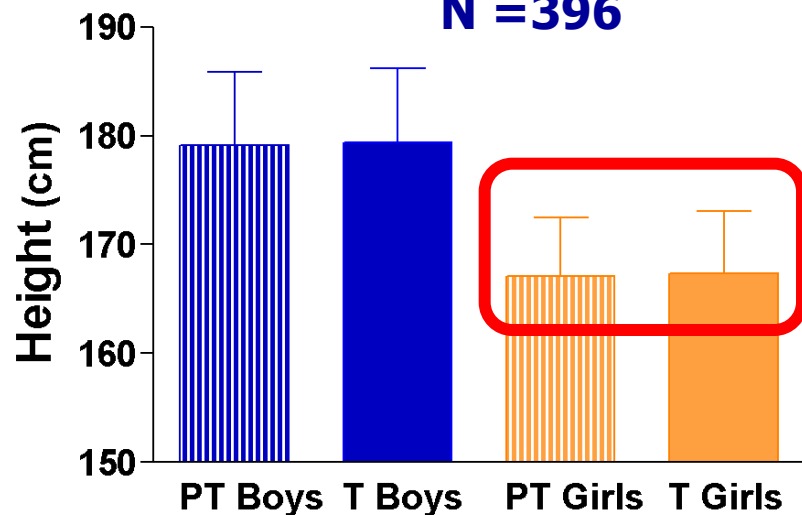
1.8% European, 2.5% Maori and PI



Post term children at 16 yrs

** $p < 0.01$ * $p < 0.05$

N = 396



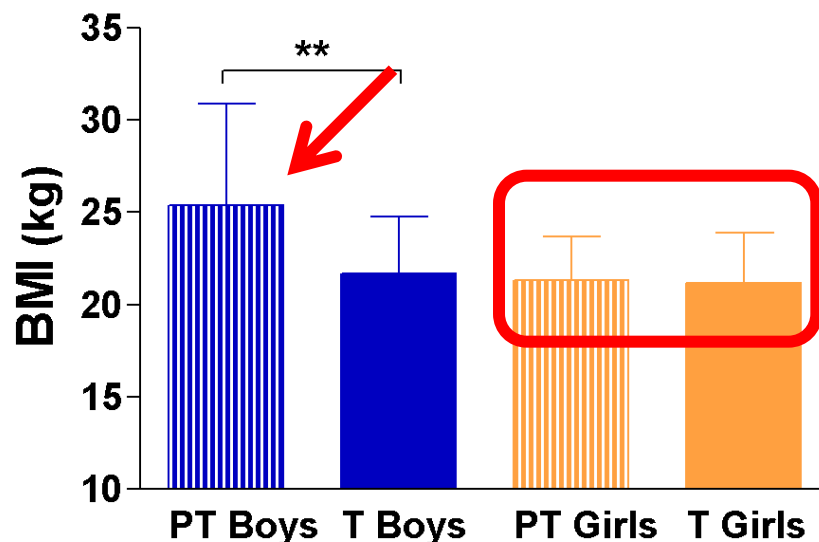
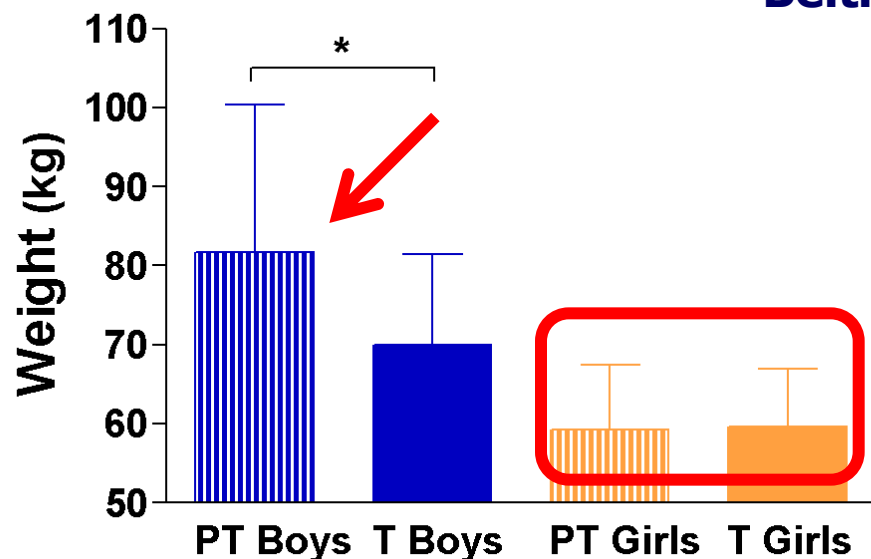
Females

- Same weight, height and BMI

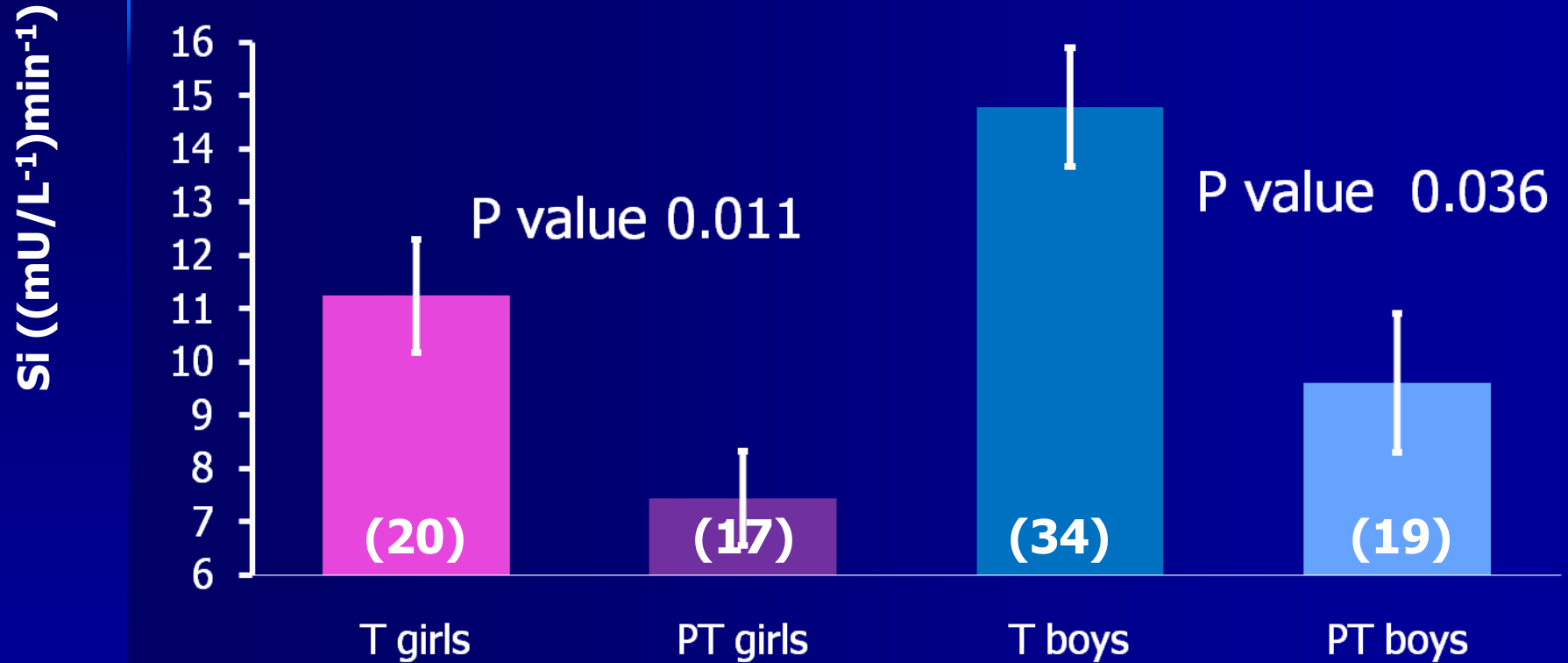
Males

- Same height but higher weight
- Greater BMI
- 8/17 obese

Beltrand J et al J Pediatr 2011; 160: 769-773



Insulin sensitivity



T= Term **PT= Post-term**
Adjusted for age and DEXA fat mass

Post term children

Lower insulin sensitivity

Higher cholesterol

Greater abdominal fat

Reduced nocturnal BP dipping

At risk of the Metabolic Syndrome
(diabetes, high blood pressure, greater abdominal fat and high lipids)

Programming Sensitivity

First born children 60%

Post Term
2-4%

Premis
3-5%

SGA 1-3%

Sensitivity to programming

Conception

1st Trimester

2nd Trimester

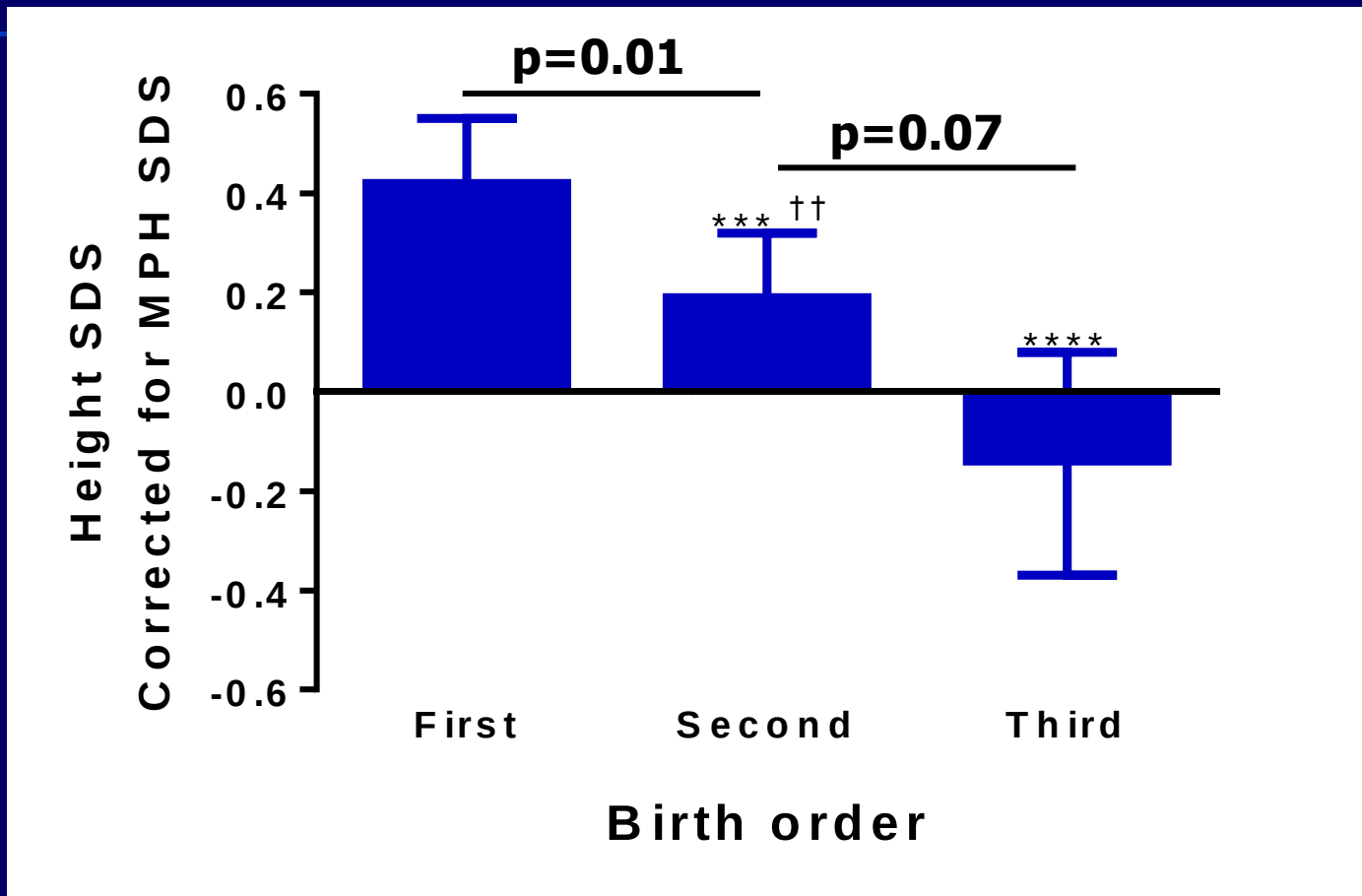
3rd Trimester

Malnutrition

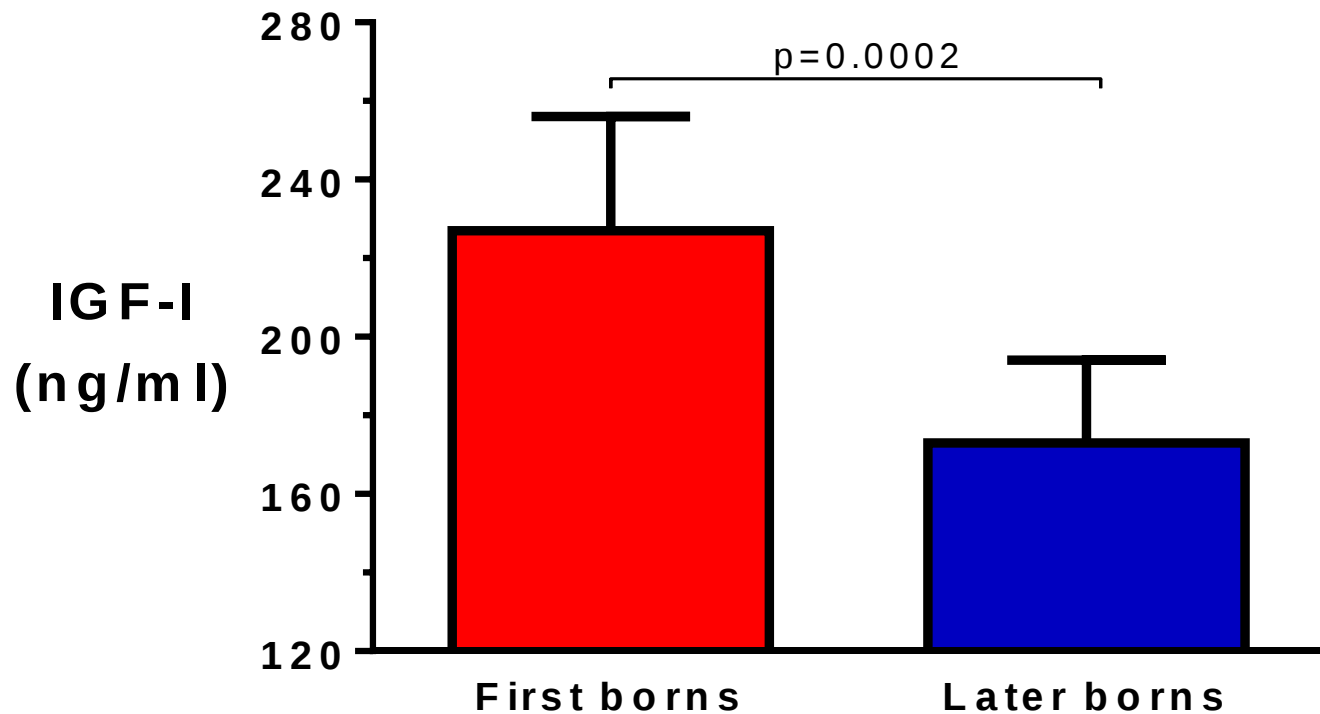
Overnutrition

Height

(1st vs 2nd vs 3rd borns)

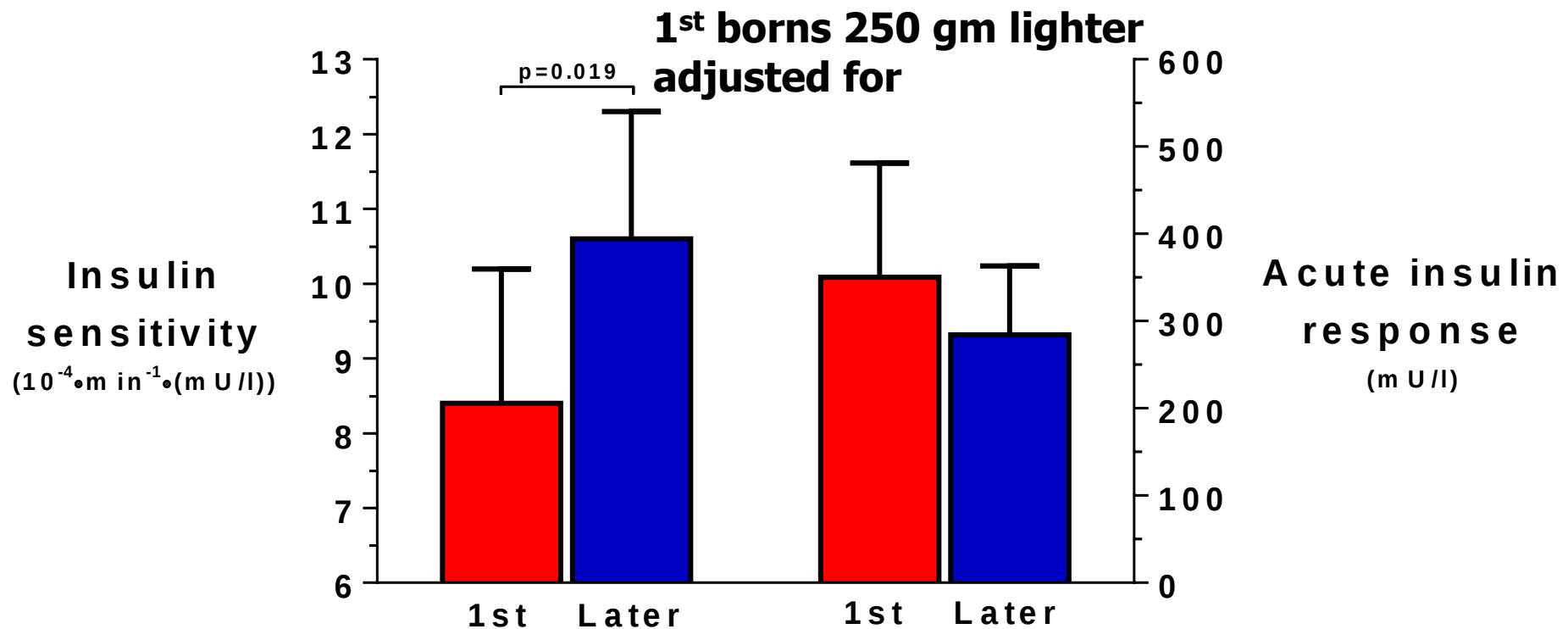


IGF-I

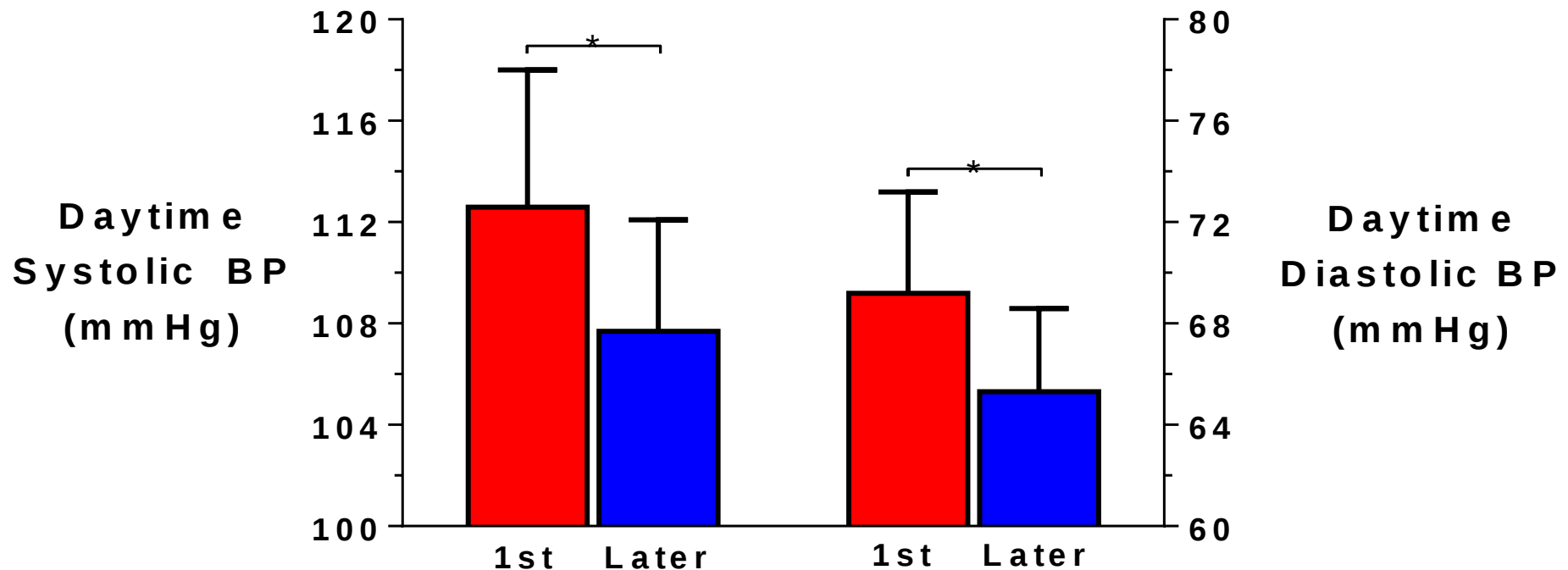


Savage T et al Clin Endocrinol 2013; Jan 24 epub

First born children are different to later born children



First born children are different to later born children





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First-born children are more likely to get diabetes... but they are taller and slimmer too

- First-born children found to have greater difficulty in absorbing sugars into the body
- Physical changes in the mother's womb during her first pregnancy may help nutrient flow to future children

By CLAIRE BATES

PUBLISHED: 17:18 GMT, 13 February 2013 | UPDATED: 17:18 GMT, 13 February 2013

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Being the eldest child has many advantages, such as having your parents full attention and avoiding cast-off clothes.



© Murray Sanders

First-borns like HRH The Duchess of Cambridge (right) are more likely to be taller and slimmer than their siblings (Pippa, left). But scientists suggest they may also have a higher risk of diabetes, at least during childhood

Conclusions

First borns are taller, insulin resistant with higher blood pressure.

We speculate that reduce placental vascularisation in first pregnancies leads to nutritional compromise and adverse metabolic programming

Programming Sensitivity

First born children 60%

Hyperemesis 2%

Post Term
2-4%

Twins 2%

Older maternal age/older paternal age

Prem
3-5%

IVF
2-4%

SGA 1-3%

Sensitivity to programming

Conception

1st Trimester

2nd Trimester

3rd Trimester

Malnutrition

Overnutrition

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Programming Sensitivity

First born children 60%

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Older maternal age/older paternal age

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IVF
2-4%

SGA 1-3%

Sensitivity to programming

Malnutrition

Conception

Maternal/fetal obesity 27% / **maternal gest. Diabetes** 4-15%

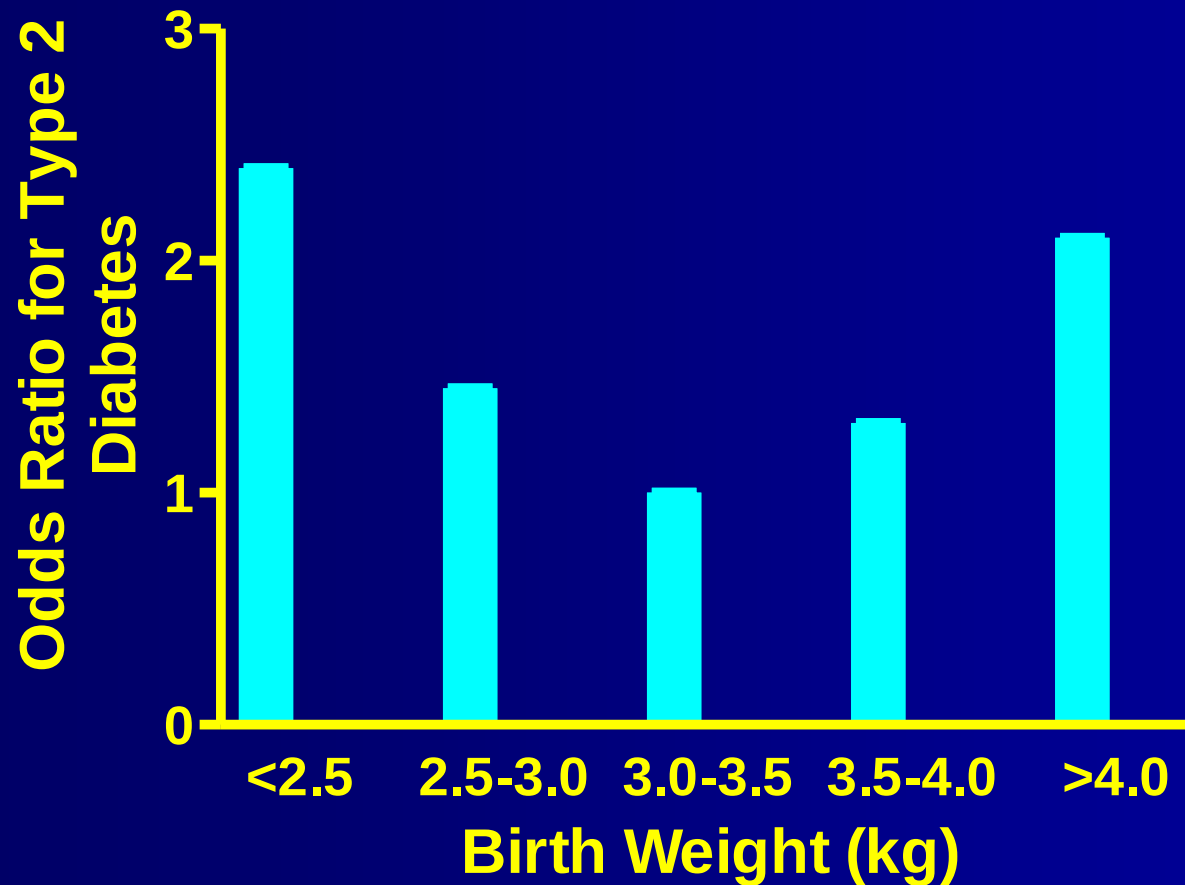
1st Trimester

2nd Trimester

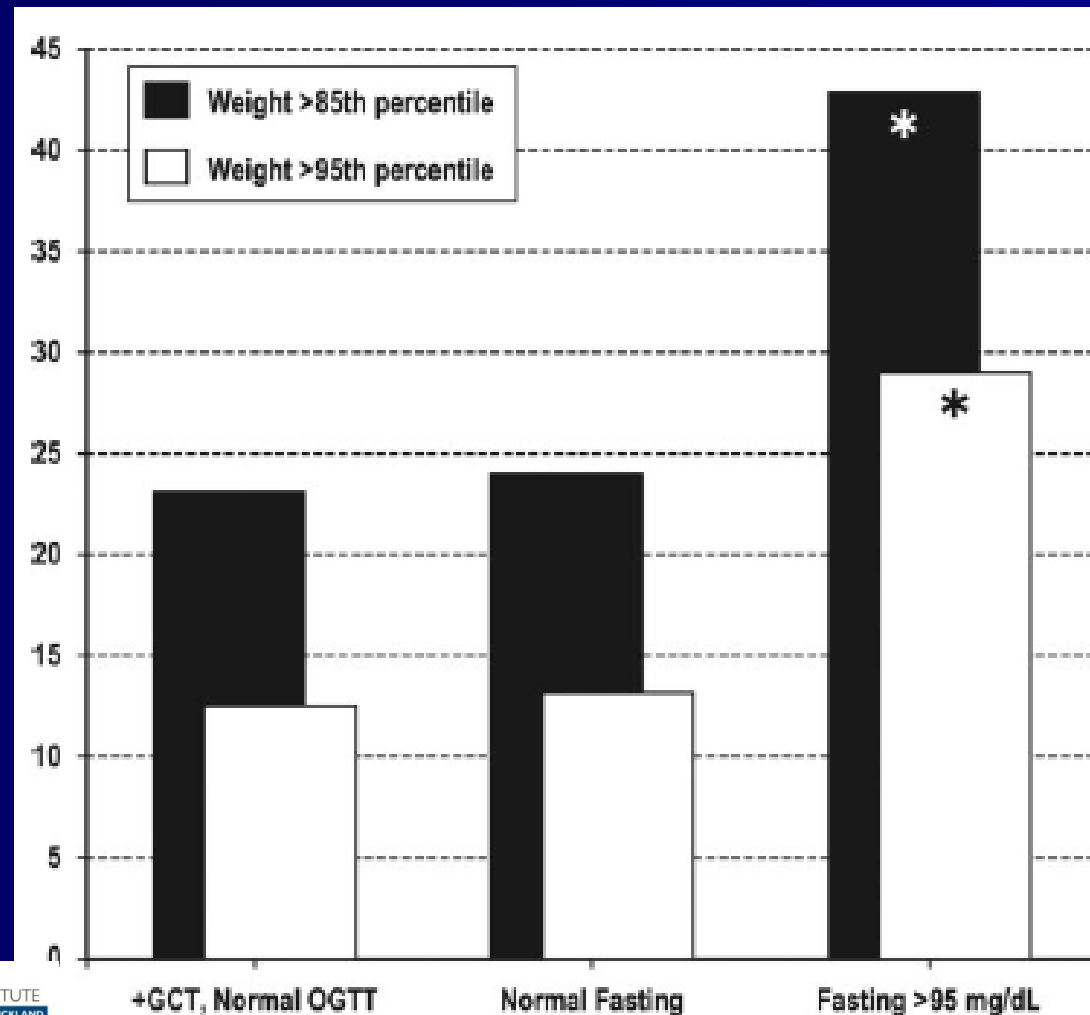
3rd Trimester

Overnutrition

Birth Weight and Type 2 Diabetes Risk in Taiwanese Children



Gestational diabetes leads to offspring obesity



Mothers with glucose screening in pregnancy

9,439 offspring

GCT: 1 hr 50 gm glucose challenge test

Hillier TA et al Diab Care 2007; 30: 2287-92

Fasting >5.3 mmol/l

Conclusions

The optimal fetal environment is delicately poised.

Deviation away from average progressively increases risks of obesity, diabetes and cardiovascular disease.

Conclusions

Nutrition prior to and during pregnancy affects the health of offspring lifelong

Excessive weight gain following fetal undernutrition or malnutrition amplifies programmed risks of metabolic disease

Conclusions

What more to do

The triggers and mechanisms of developmental programming remain elusive and unclear

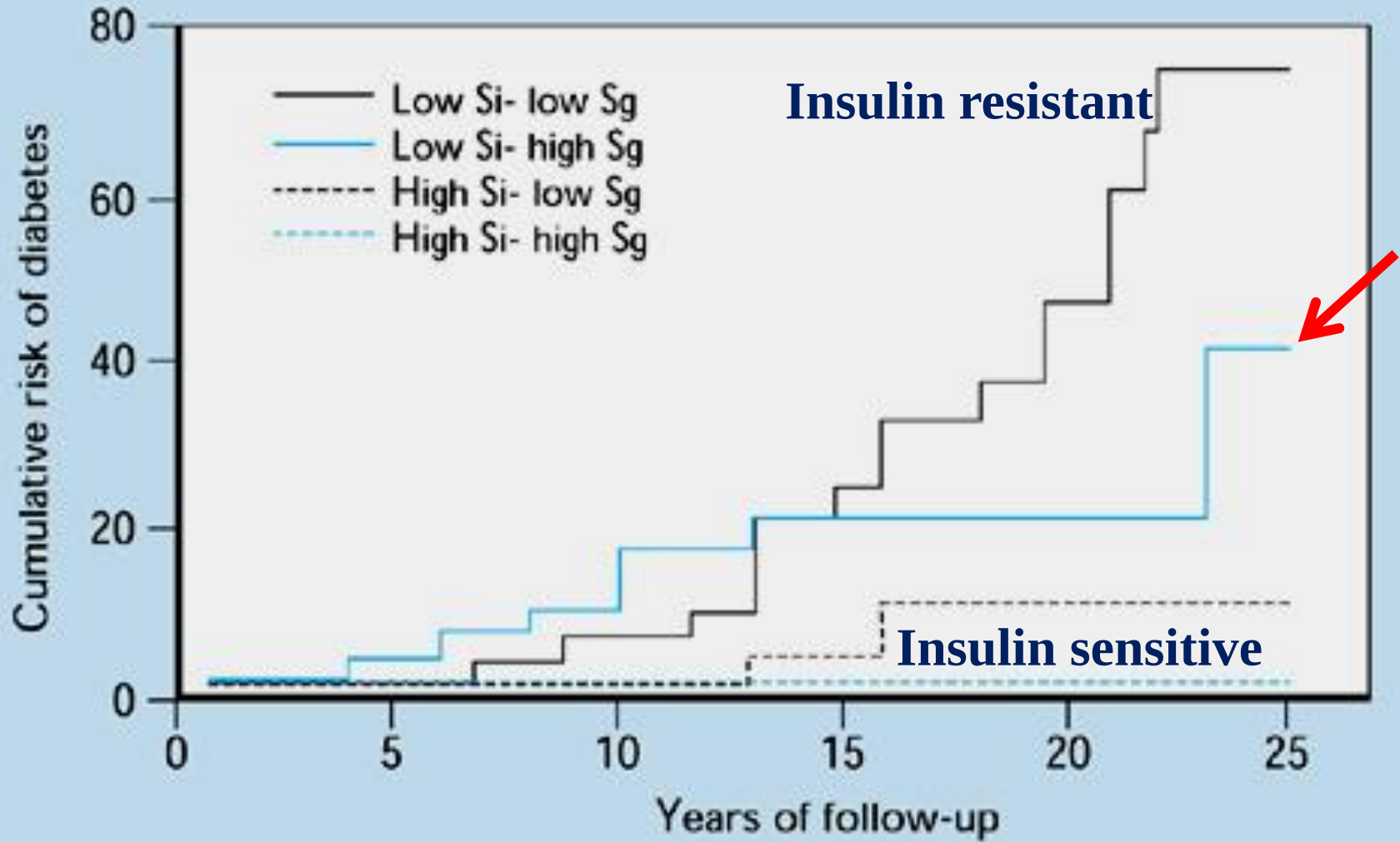
The contribution of early life events to adult metabolic disease need to be more accurately quantified

Acknowledgements

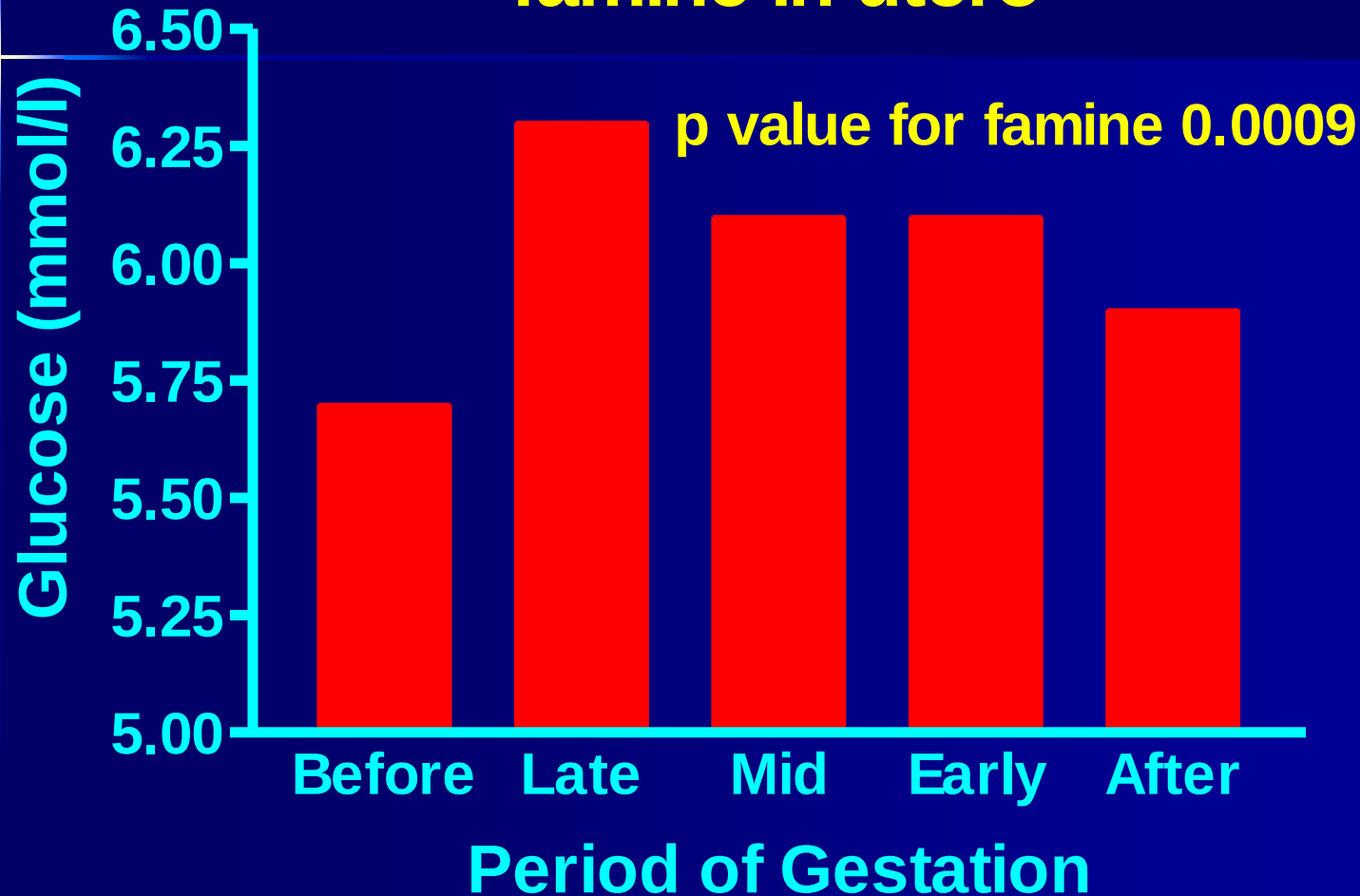
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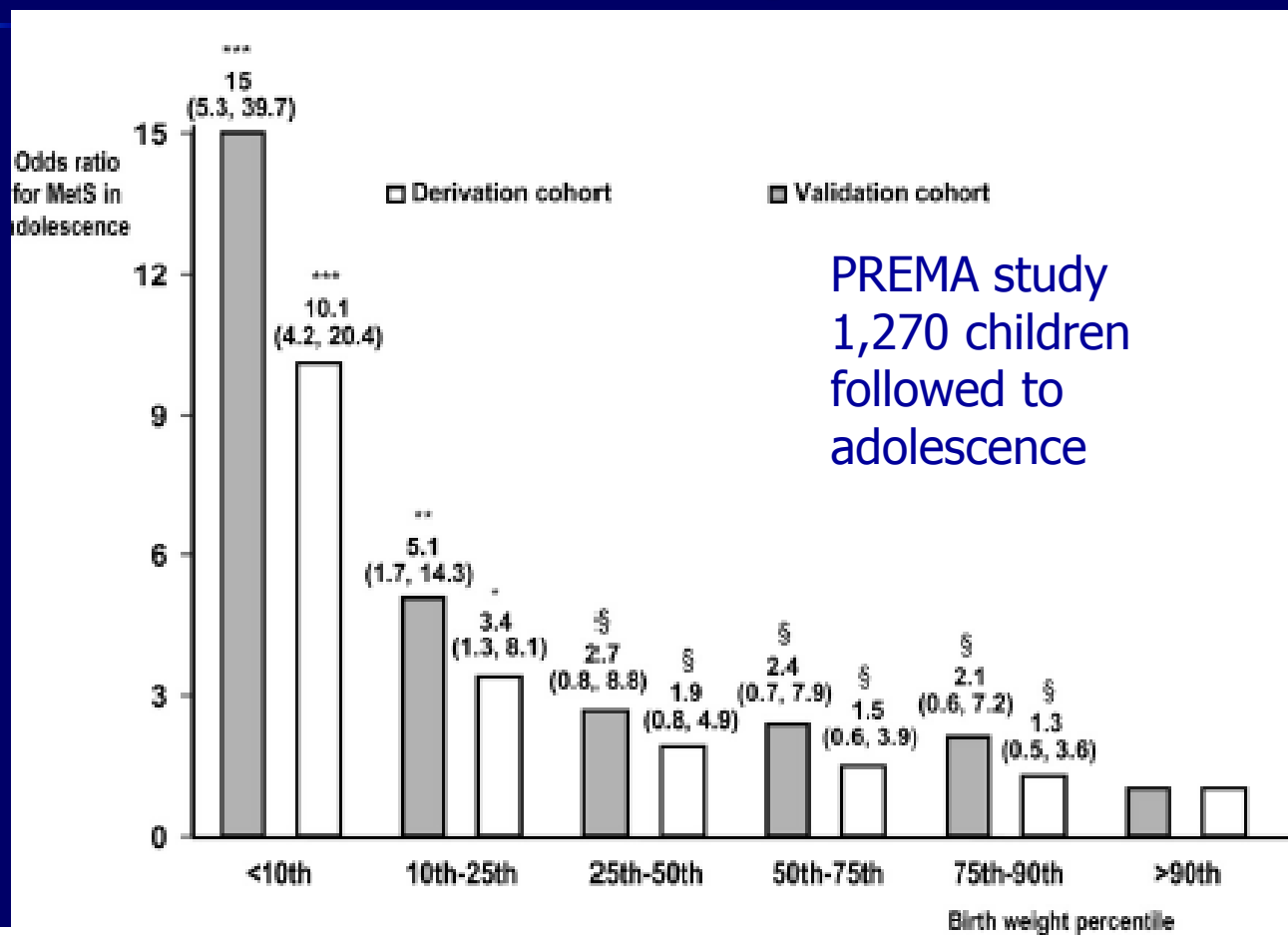
Long term diabetes risk of insulin resistance



2 hr glucose values in 702 50 yr old adults exposed to famine in utero

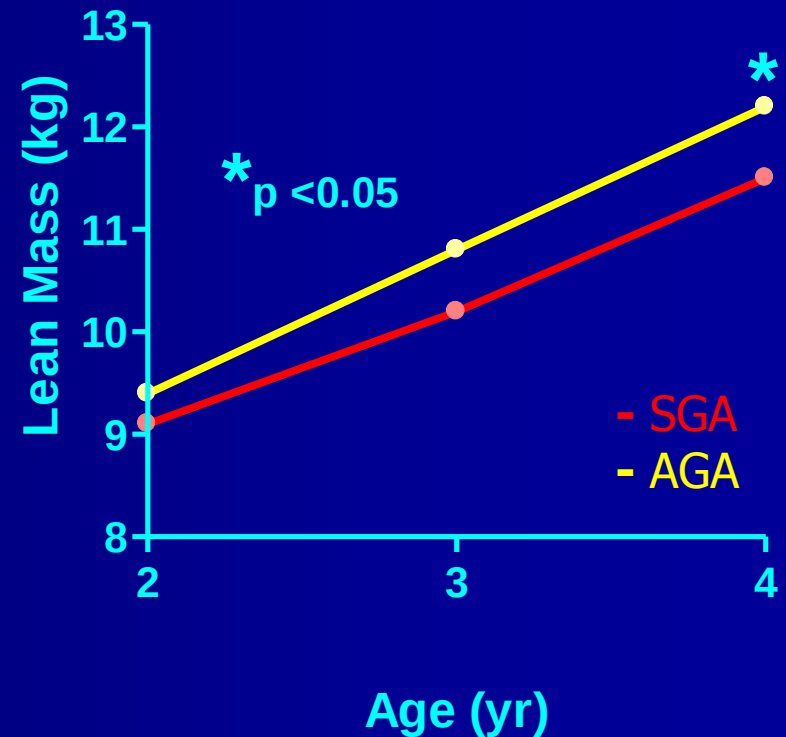
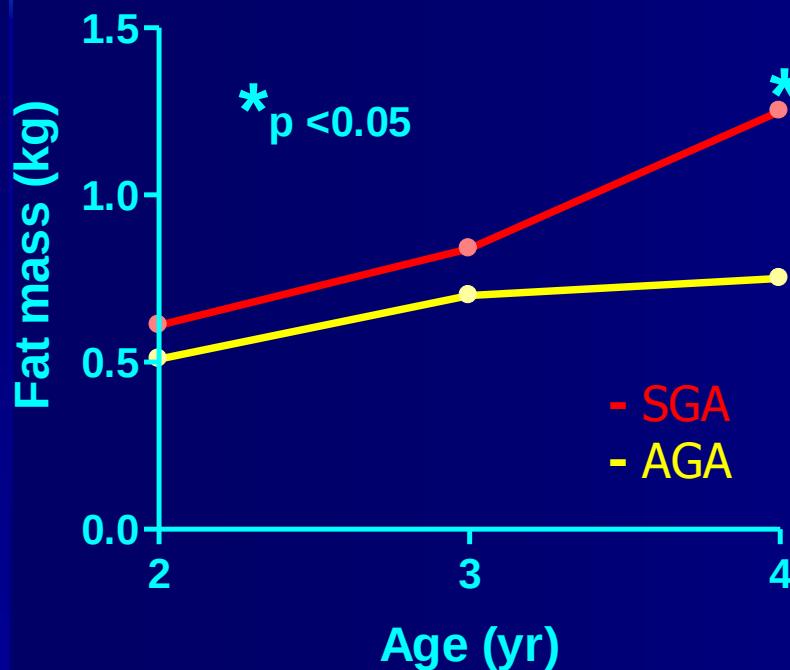


Low birth weight and metabolic syndrome



Body Composition in SGA Children

29 SGA, 22 AGA. No differences in Ht, Wt nor BMI at 2,3, or 4 yrs



Speculation

Double hit phenomenon:

Common gene variant leads to prolonged gestation and risk of metabolic syndrome

The nutritional and physiological stress of prolonged gestation amplifies metabolic syndrome risks