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Associate Professor at the Liggins

Being Born Too Large, Too Small, Too Early or Too Late – Main Session (Workshop options scheduled)

Sunday, 18 August 2013

Start 9:20am

Duration: 25mins

Plenary



South GP CME 2013

General Practice Conference & Medical Exhibition

15-18 August | Edgar Centre | Dunedin

Being born too large, too small, too early or too late – the link with later adult disease



Paul Hofman
2013



LIGGINS INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

Declaration

Pfizer sponsored speaker

Early life nutrition is a common factor altering later phenotype

Yellow dung fly – variation in size with dung scarcity or abundance.

J Evol Biol. 2007 Jan;20(1):87-103

Locusts – respond to overcrowding and food shortage by migration. This requires substantial phenotypic change which is determined in the larval stage.

Gene – environment interactions in development

Environmental changes early in life can create permanent phenotypic alterations that have their primary advantage in later life.

It is not the genome but the expression of the genome that determines our phenotype.

Cloning $\neq$ identical phenotype



Genome/ Nature

Environment/ Nurture

Phenotype



**We are born naked, wet and hungry
Then things get worse.....**

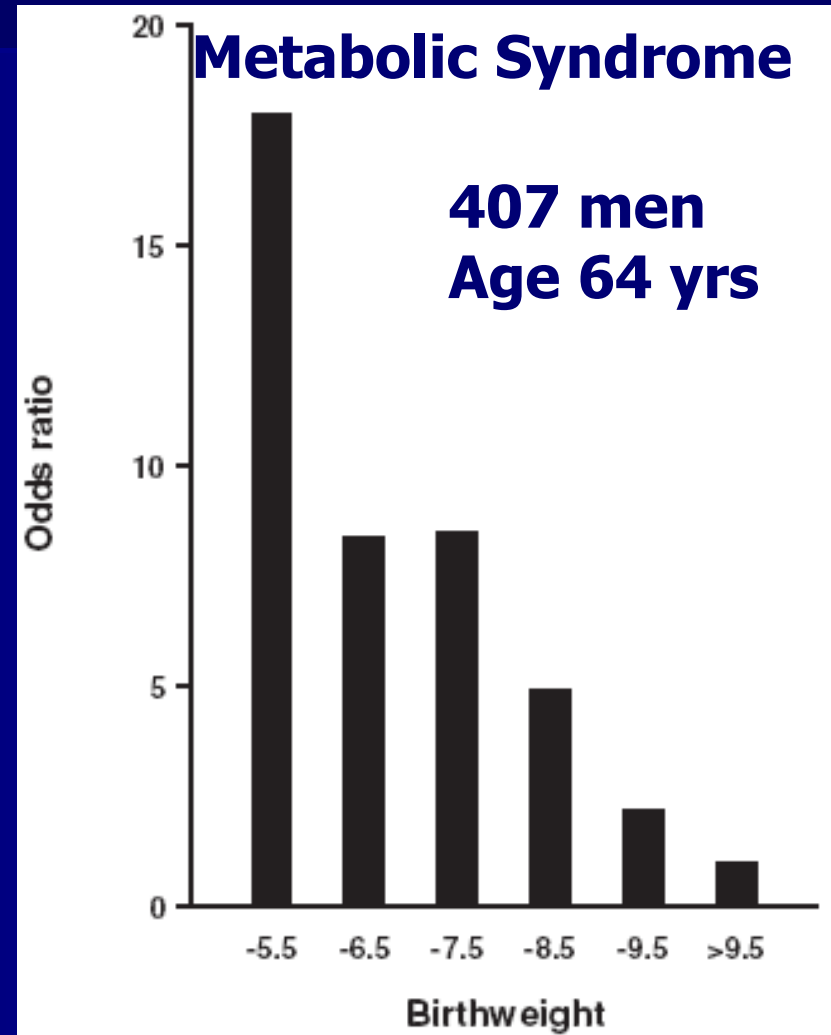
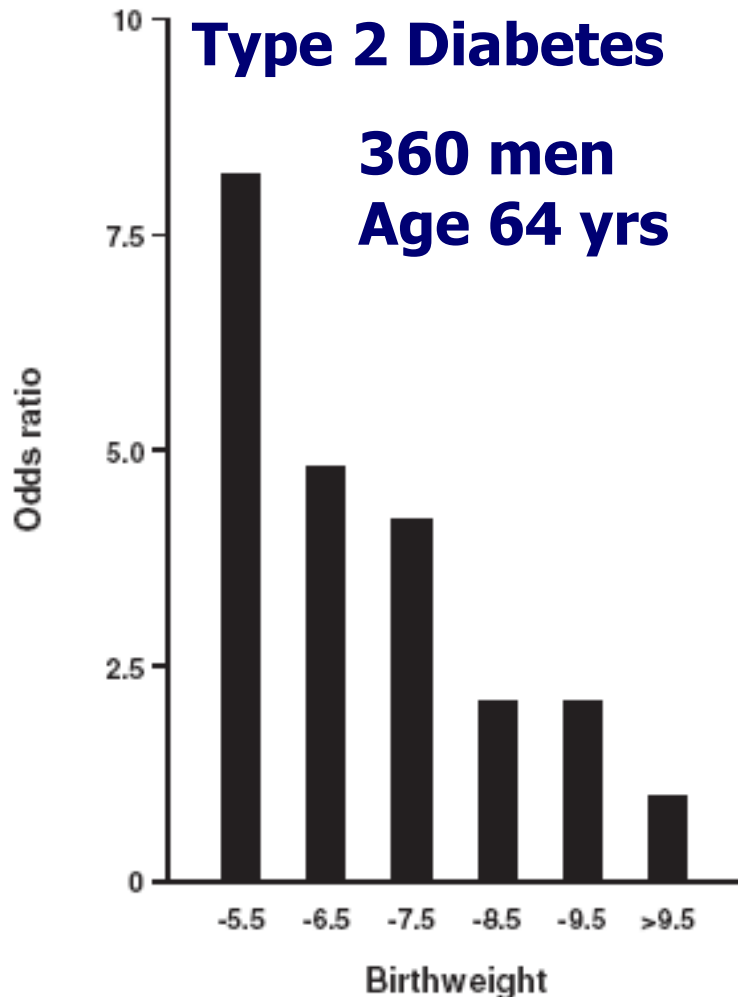
Fetal Origins (The Barker) Hypothesis

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 later disease

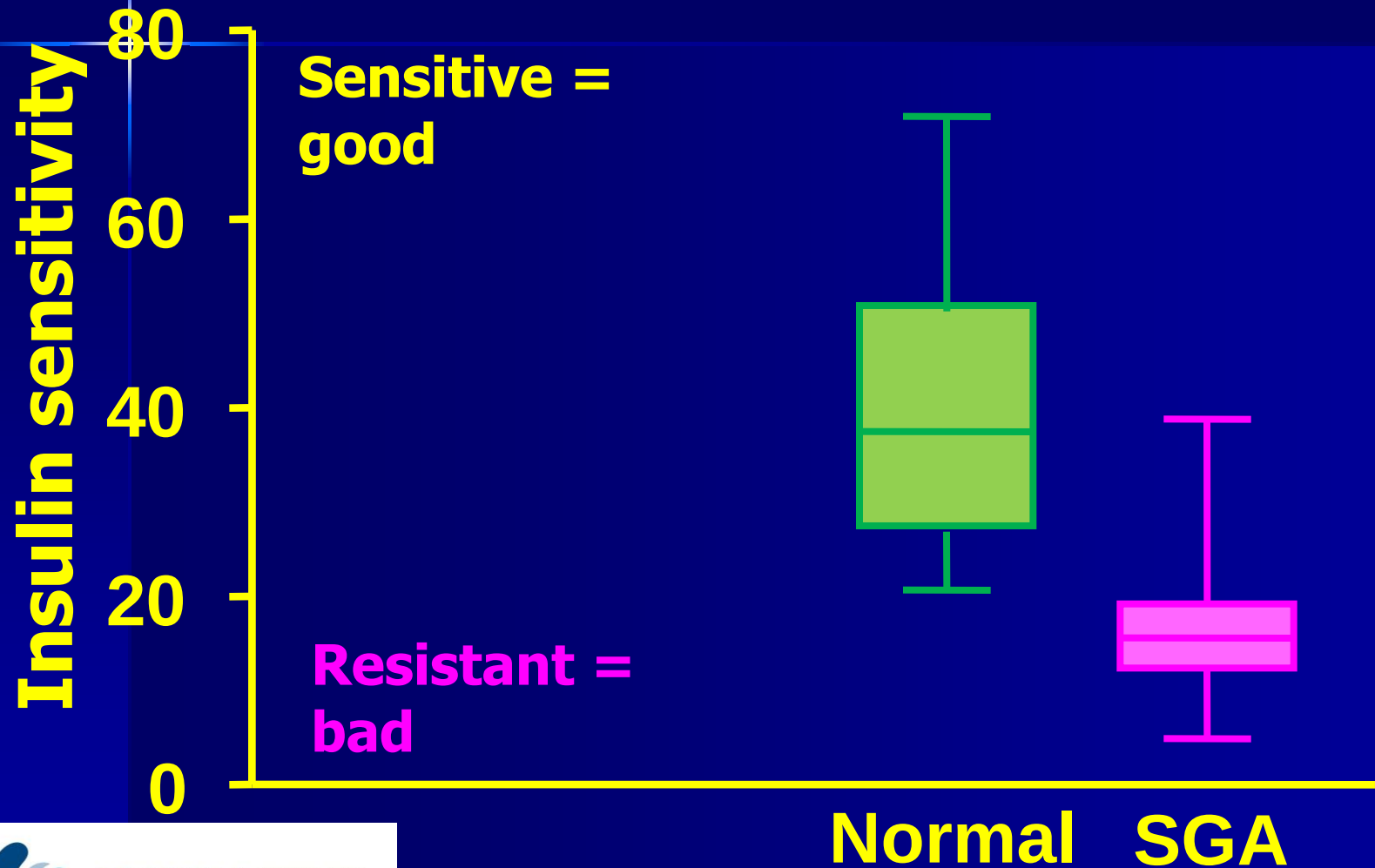
British Medical Bulletin 2001; 60: 5–20



Adult problems associated with low birth weight

- Metabolic Syndrome
- Obesity
- Coronary Heart Disease
- Type 2 diabetes mellitus
- Hypertension
- Insulin resistance

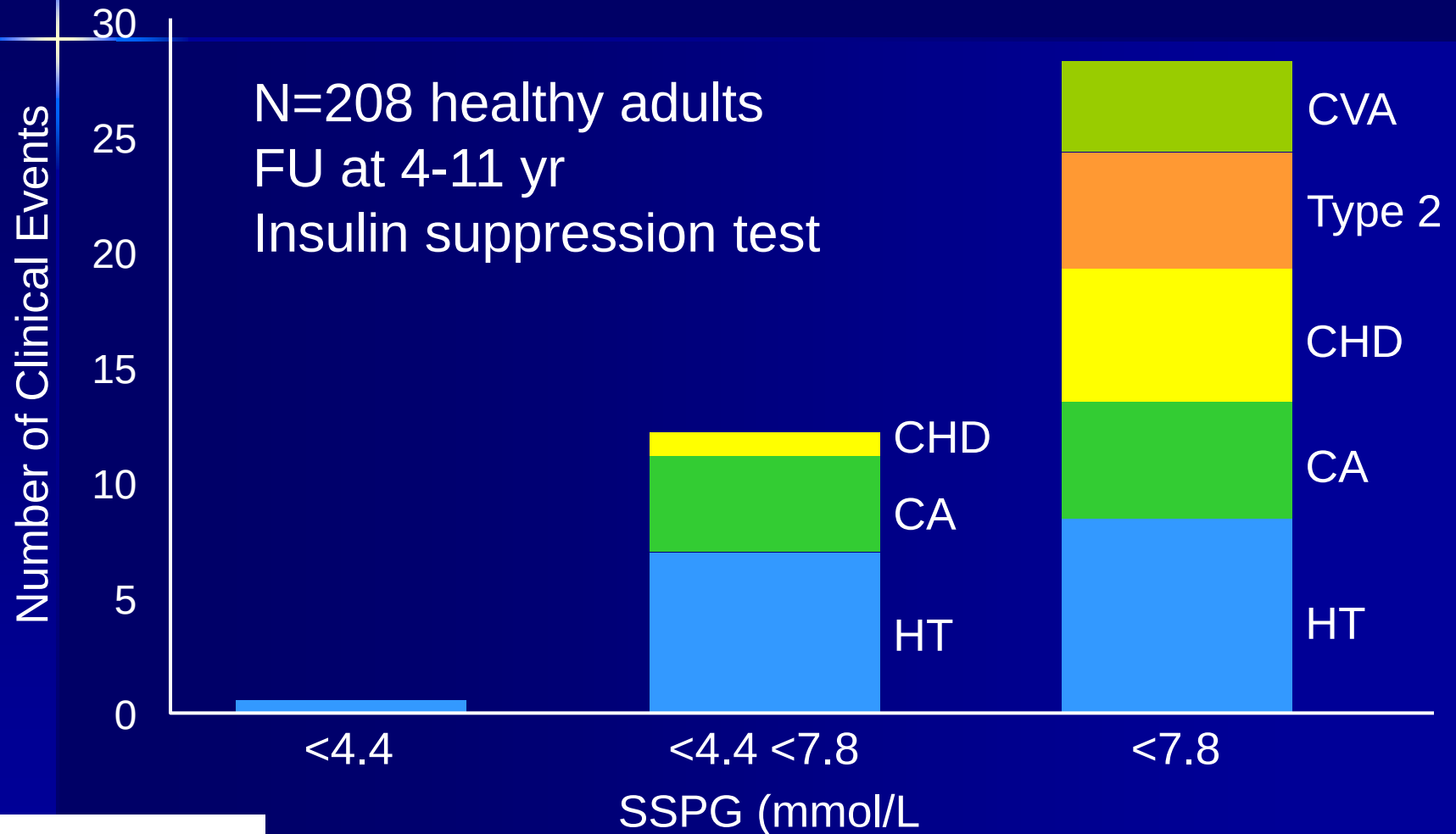
Small at birth (SGA) children are insulin resistant



What
happens if
you are
insulin
resistant?



Long Term Risks of Insulin Resistance



Which small babies at birth eventually get diabetes?

Those that rapidly gain weight from mid-childhood through early adult life.

Regular exercise is associated with a lower risk of type 2 diabetes in those of lower birth weight.

Who has low birth weight (LBW)?

LBW

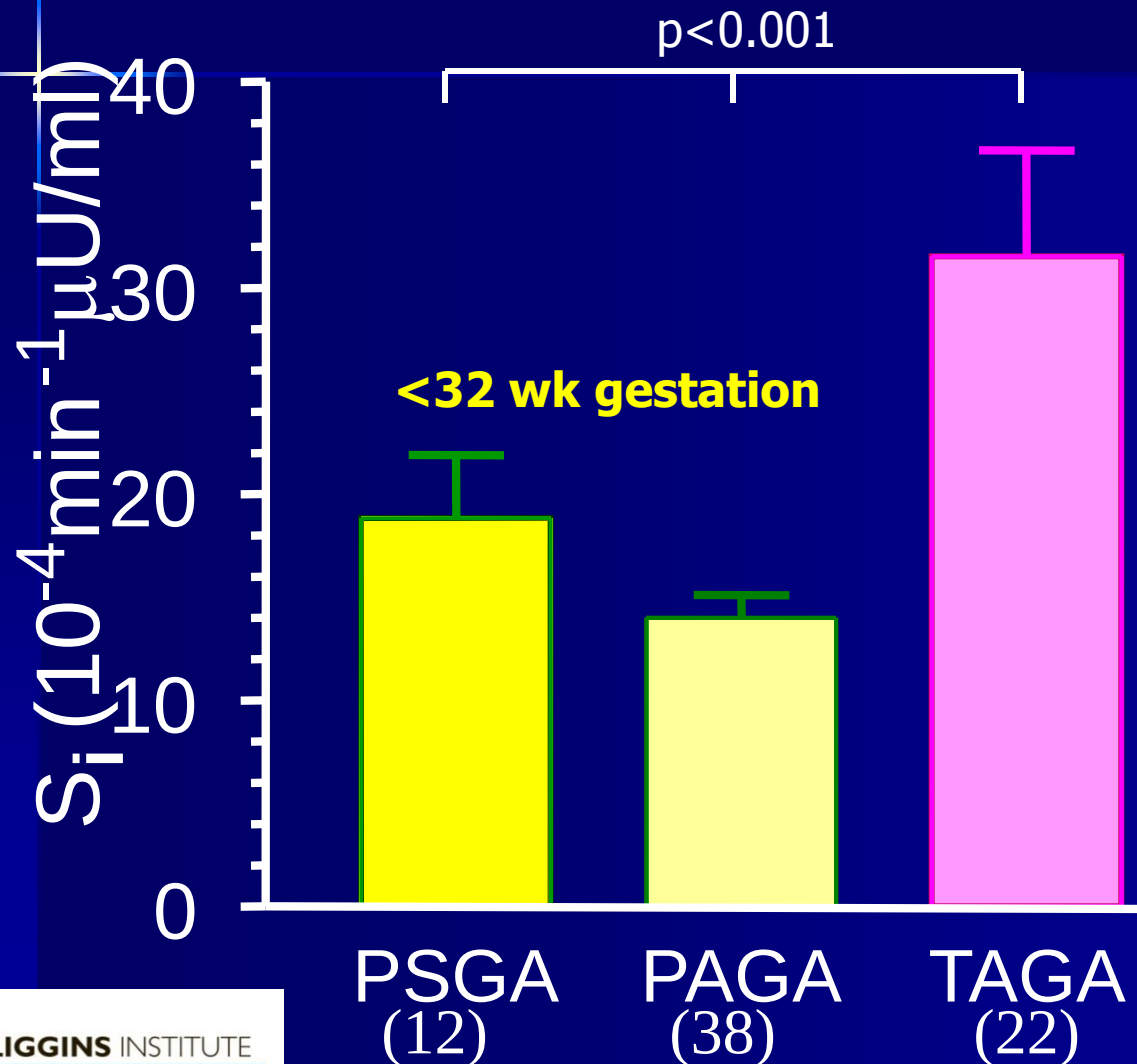
SGA



Prem



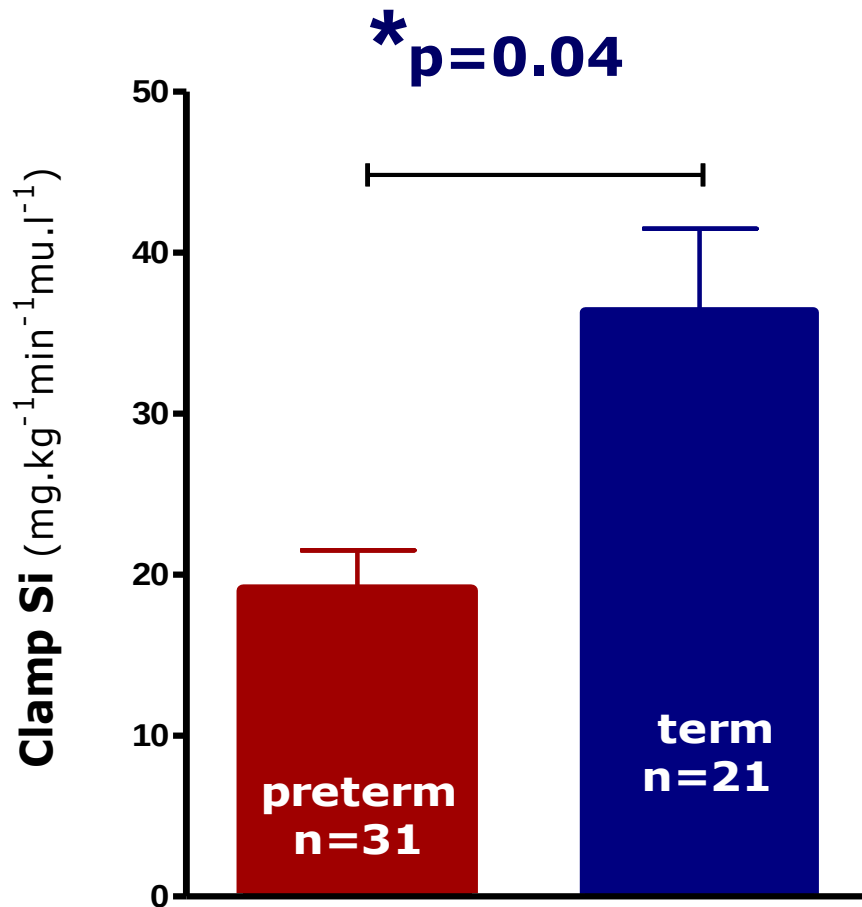
Insulin Sensitivity



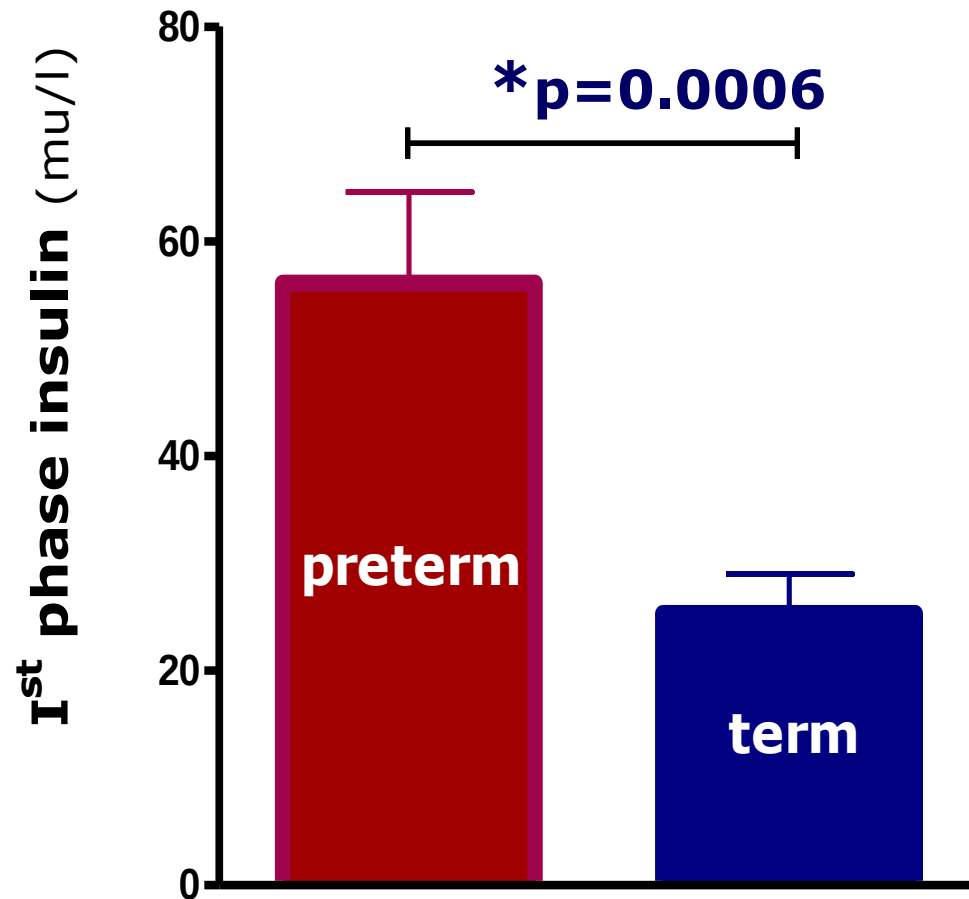
Hofman P et al N Engl J Med. 2004 8; 351: 2179-86.

Adult results

Insulin sensitivity



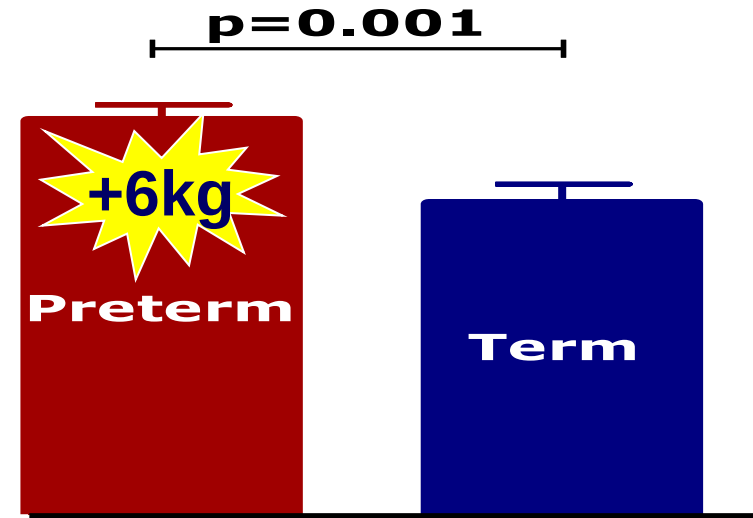
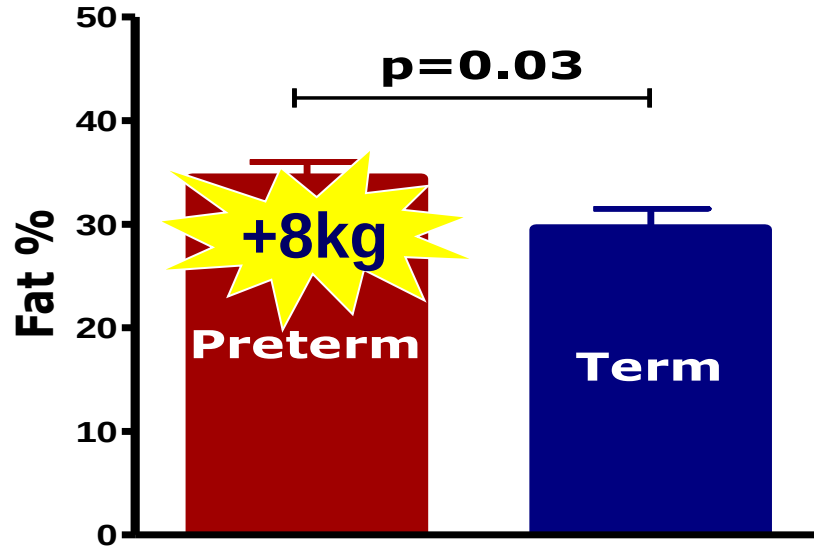
Insulin secretion



Mean Fg glucose: preterm 4.72 & term 4.65 mmol/l

Body composition

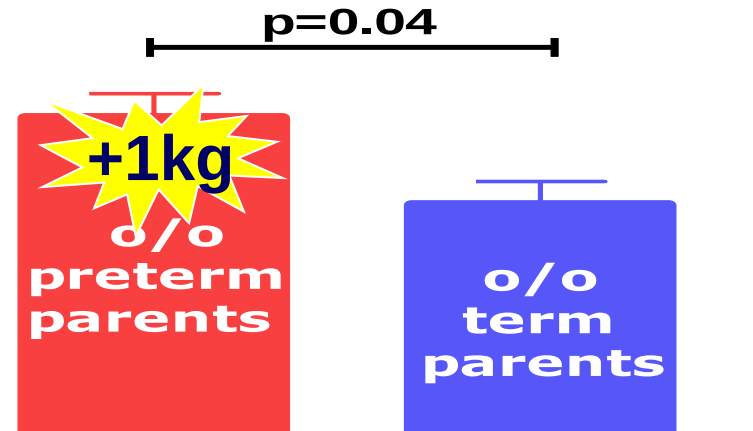
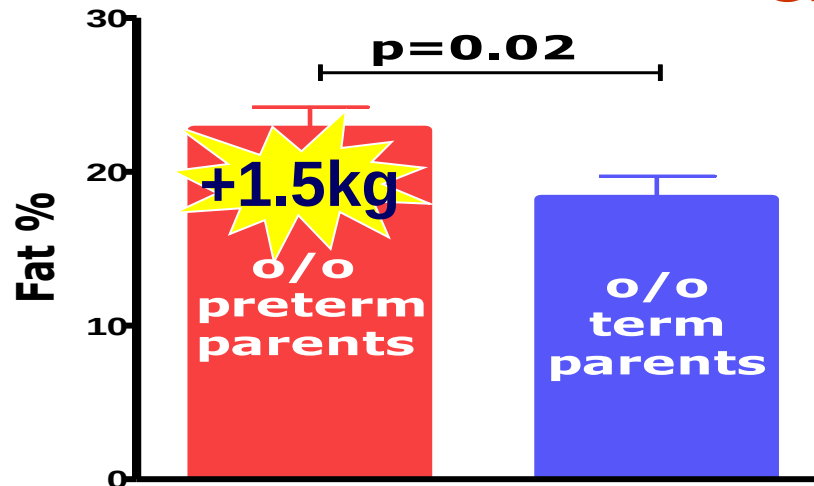
Adults



Total fat

Abdominal fat

Children



Preterm children are not obese
but become so as they enter
adolescence and adulthood.

Older premature adults are much
fatter - and
their children are too

What about post term births?

Post-term children: born after 42 weeks of gestation

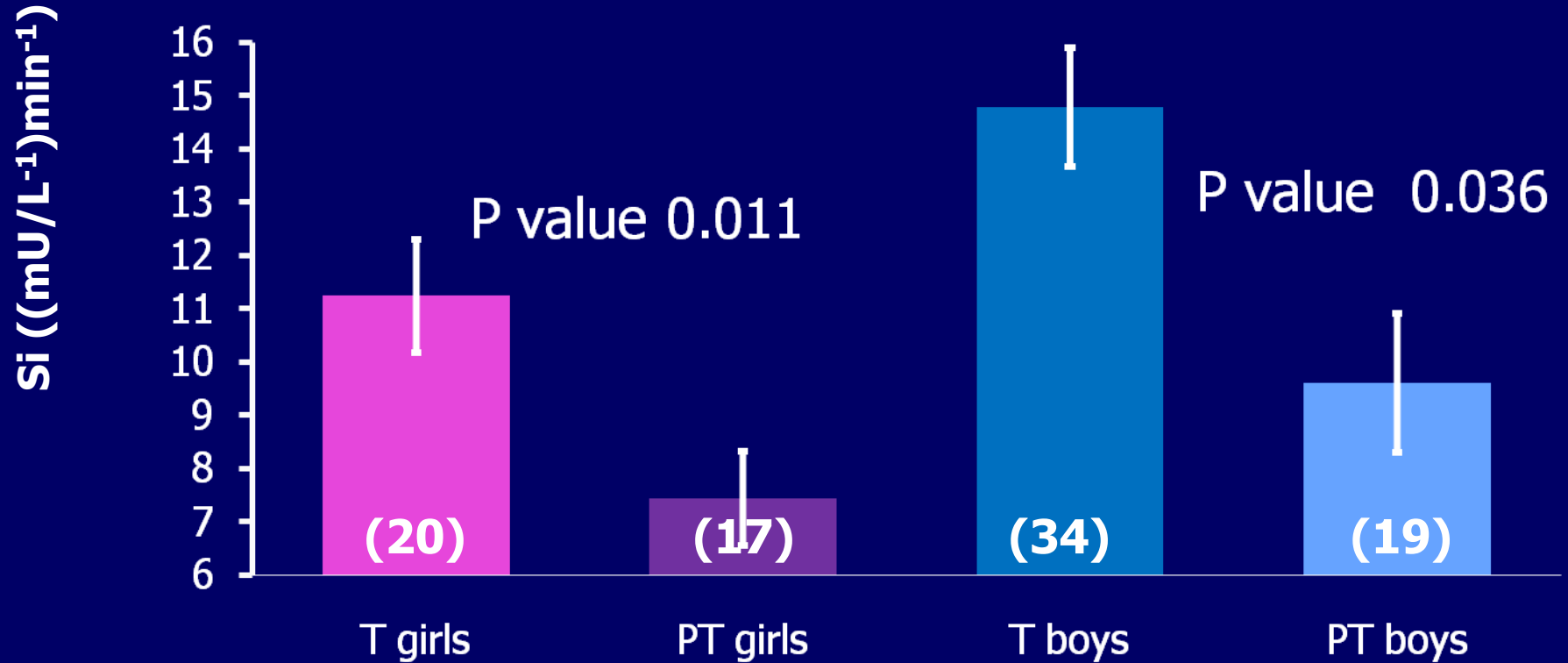
Incidence of post-terms highly variable:
0.4 – 12%

In Auckland 2009-10:

1.8% European, 2.5% Maori and PI



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)

What about First Borns?

Tend to be lightest child

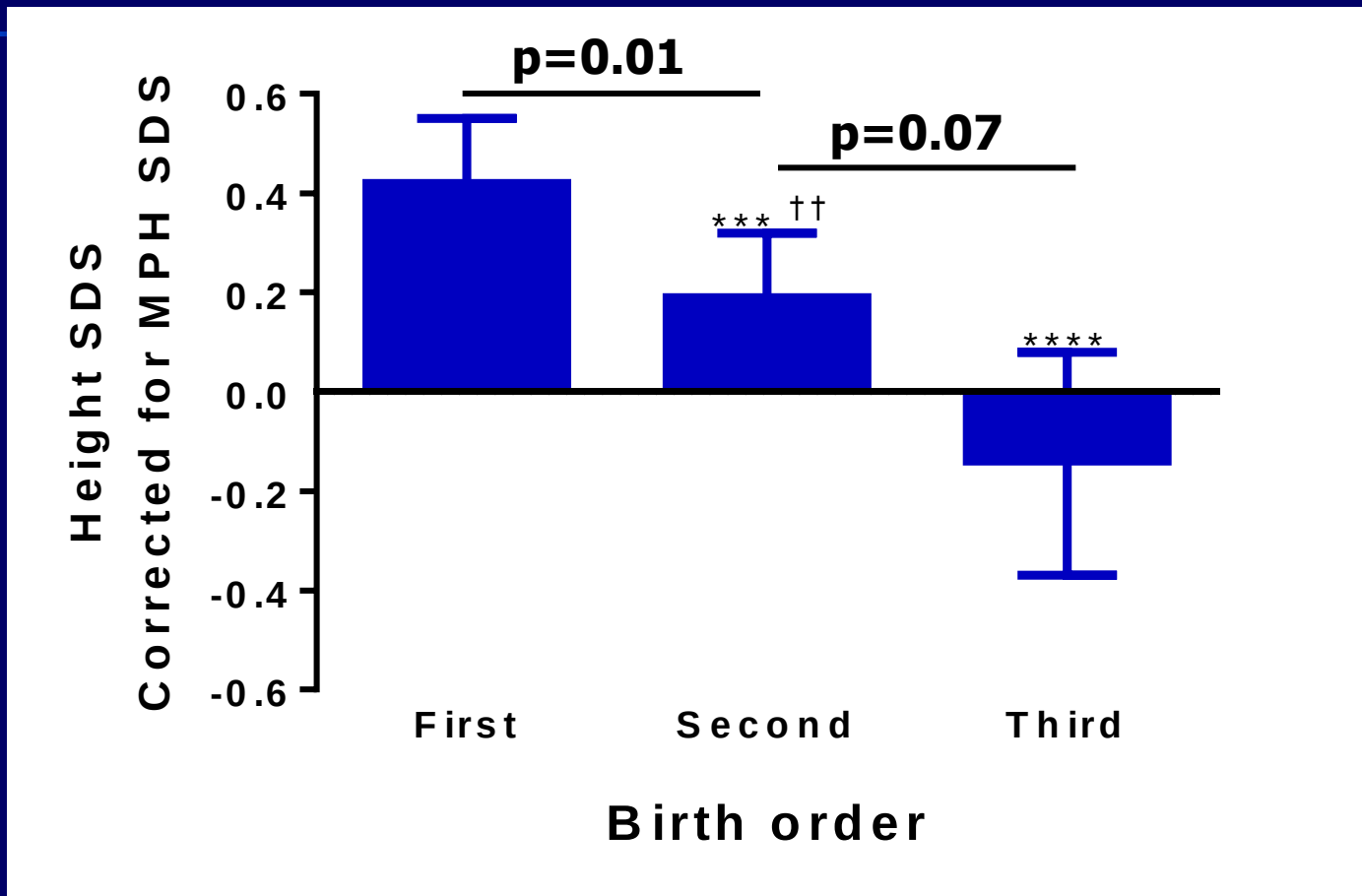
?Nutritionally compromised

Are they different from other siblings?



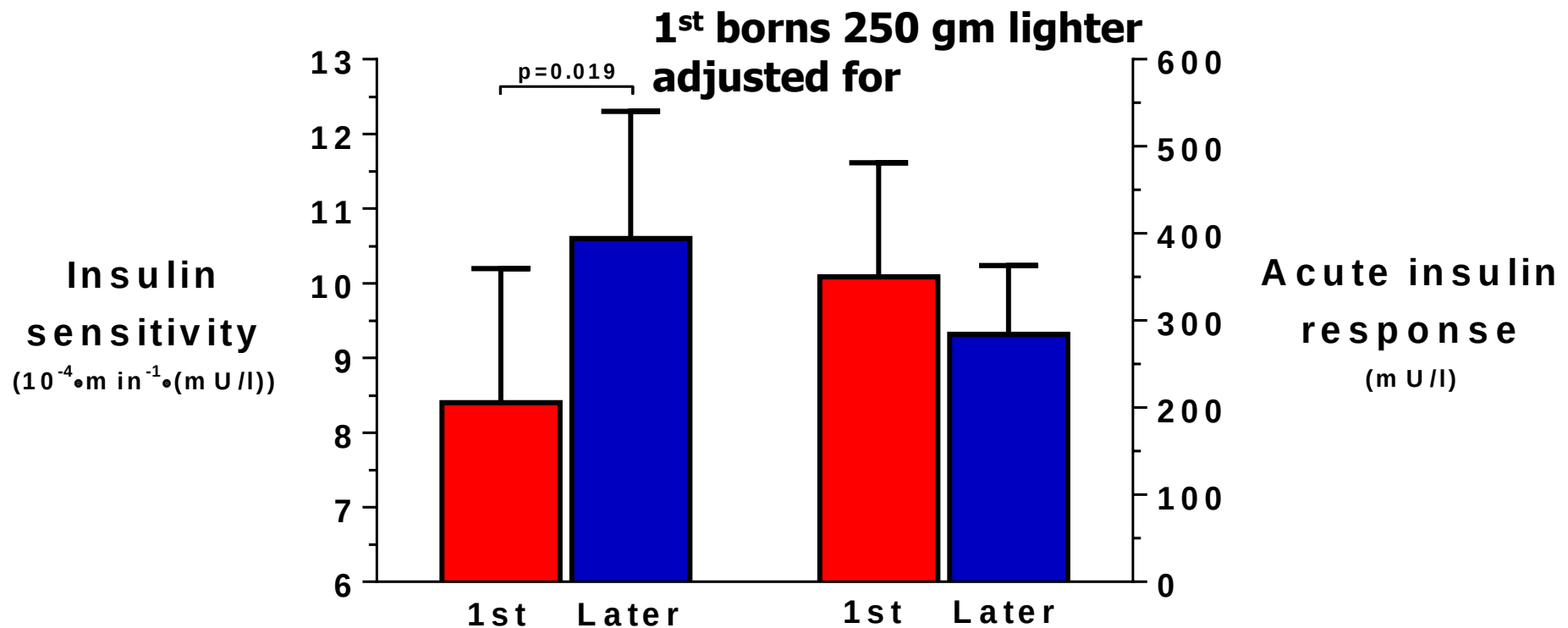
Height

(1st vs 2nd vs 3rd borns)

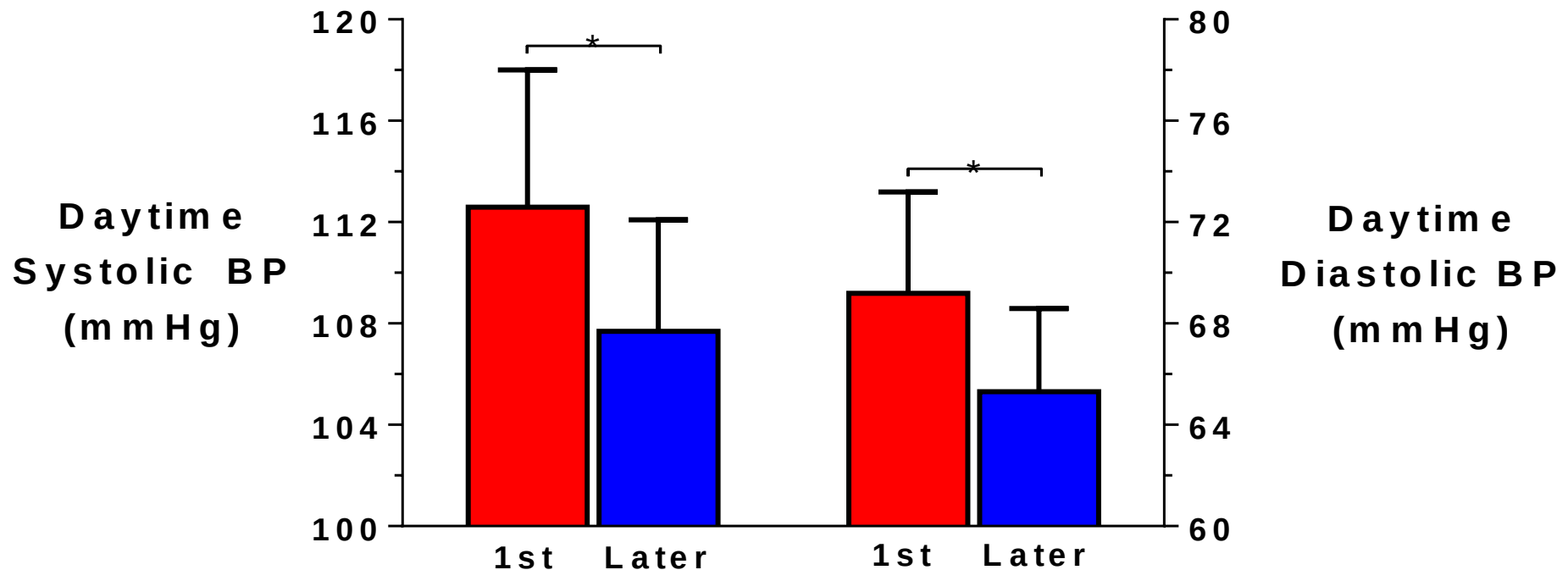


Savage T et al Clin Endocrinol 2013; Jan 24 epub

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

Summary

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

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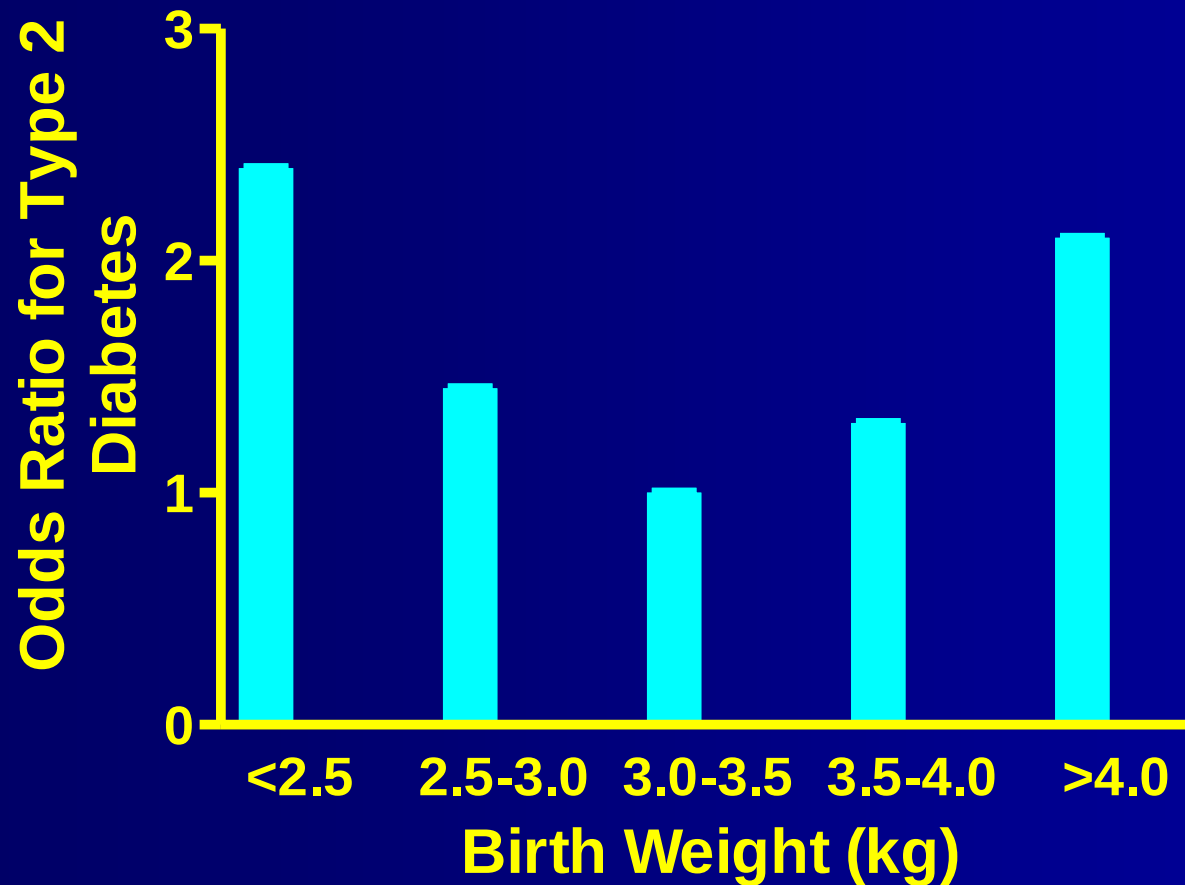
Hide Figures

Fetal Overnutrition versus Fetal malnutrition

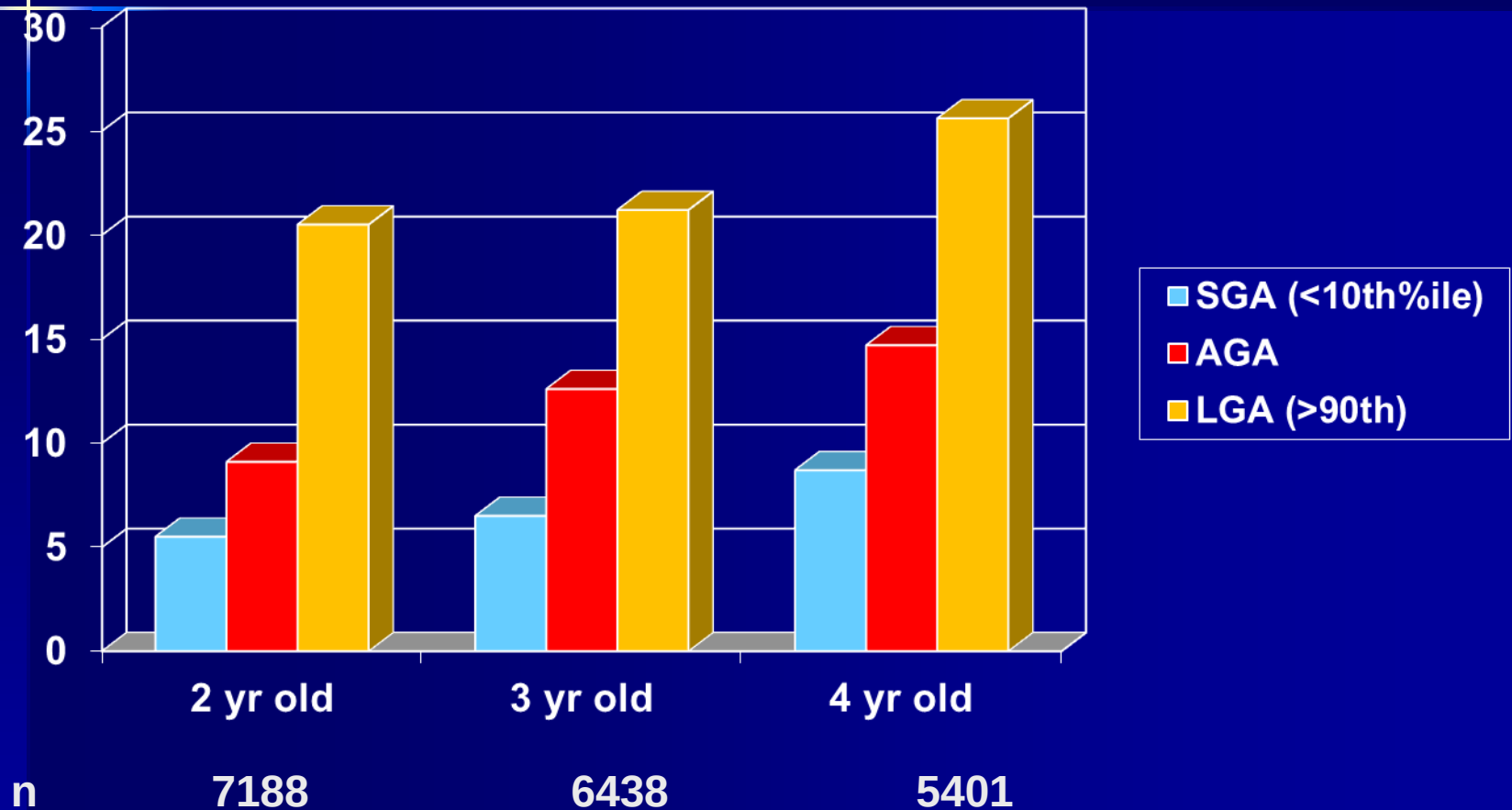
Large for gestational age babies at risk for similar problems seen in small for gestational age babies

However they are more prone to obesity at an earlier age which then tracts through life

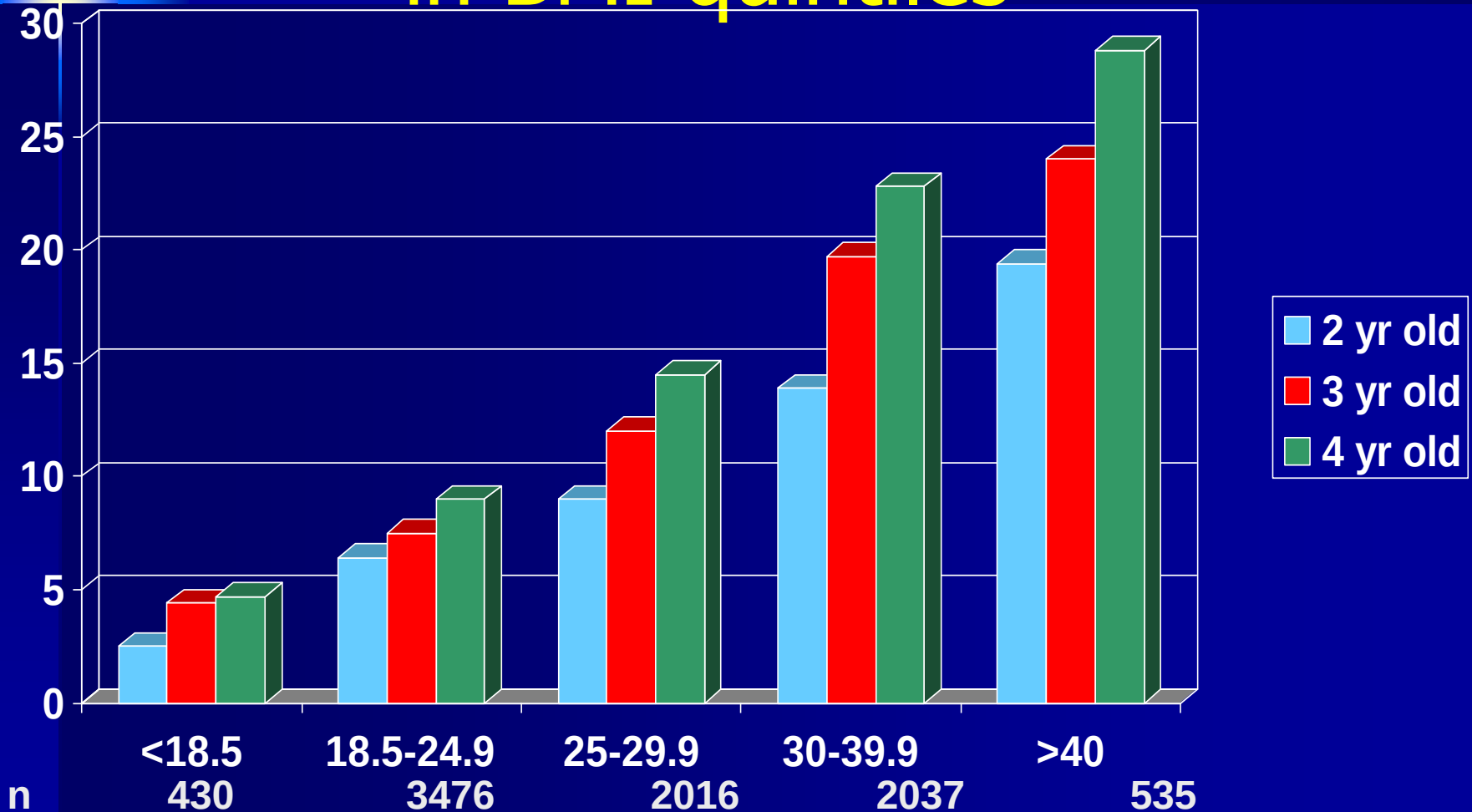
Birth Weight and Type 2 Diabetes Risk in Taiwanese Children



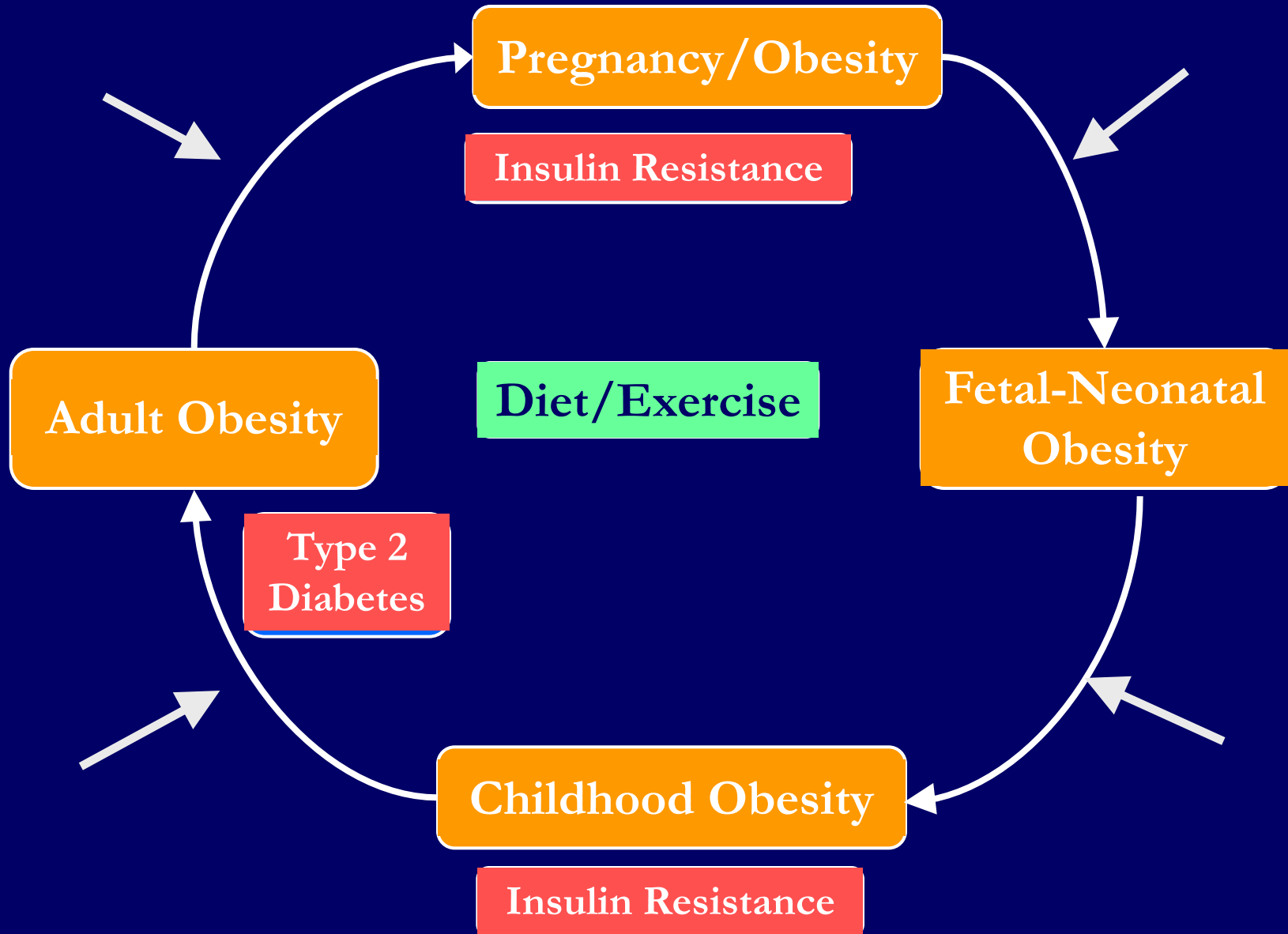
Percentage obesity (BMI > 95th PC) of children born at different birth weights



Childhood obesity (BMI < 95th PC) versus first trimester maternal weight in BMI quintiles



The Obesity Cycle



Conclusions

The optimal fetal environment is delicately poised.

Deviation away from the ideal 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

Acknowledgements

Wayne Cutfield

Craig Jefferies

Harriet Miles

Dyanne Wilson

Fiona Regan

Wendy Jackson

Fran Mouat

Sarah Mathai

Tim Savage

Deb Rowe

Martin DeBock

Ahila Ayyavoo

Ben Albert

Janene Biggs

Christine Brennan

