

# Reducing Obesity and Diabetes Risk

CHARLES PERKINS CENTRE



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## Structure of Talk

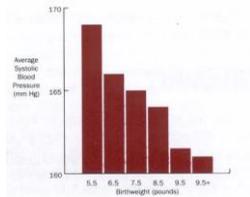
- › Obesity and Diabetes
  - Background
  - Relationship to fetal programming
  - Mechanisms
  - Potential interventions
  - What can be done now?

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## Developmental origins of health and disease

How during early life (the first 1,000 days) the environment induces changes in development that have a long-term impact on future health and disease risk



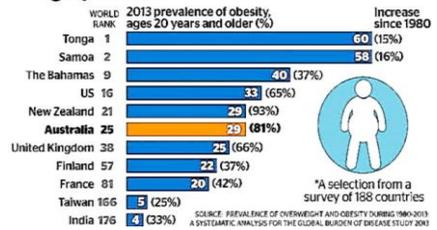
Systolic blood pressure



## Obesity is a global concern

- › Overweight and obesity rates in both women and men of reproductive age are increasing

### Weighty matters



Steel et al. Lancet, 2014.

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## Obesity in Australia

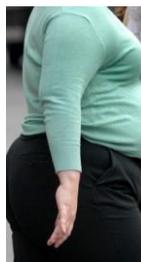


- › **Fourteen million** Australians are overweight or obese.
- › More than **five million** Australians are obese (BMI  $\geq 30$  kg/m<sup>2</sup>)
- › By 2025, close to 80% of all Australian adults and a third of all children will be overweight or obese
- › Obesity has overtaken smoking as the leading cause of premature death and illness in Australia

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## The effect of obesity on pregnancy



### Big Babies

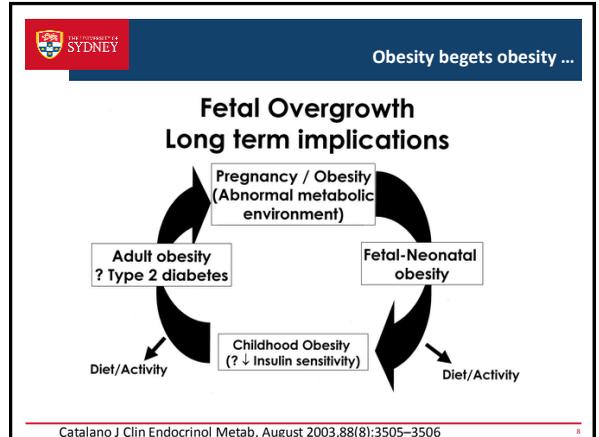
Mothers who gain more weight during pregnancy have heavier infants



Lancet 2010

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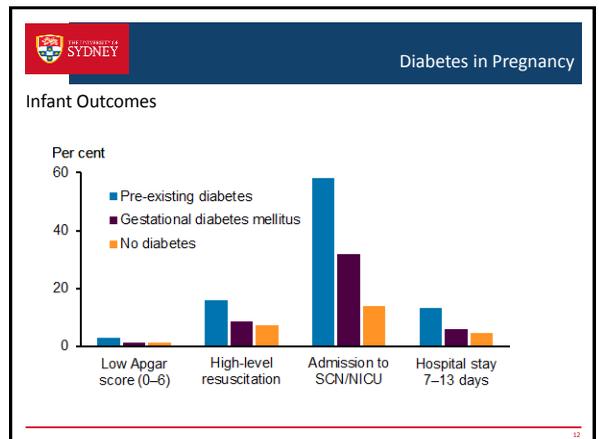
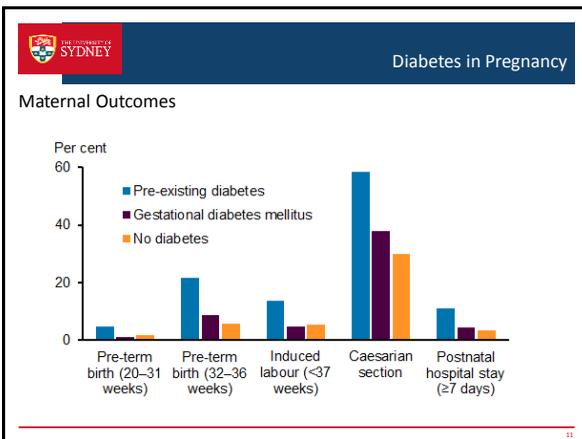
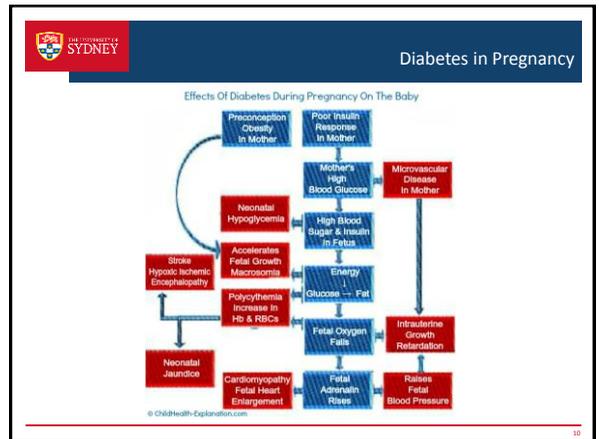
	Maternal complications	Paternal complications	Fetal complications
<b>Pre-pregnancy</b>	Menstrual disorders Infertility	Infertility	
<b>Early pregnancy</b>	Miscarriage		Intrauterine death Congenital anomalies
<b>Antepartum (During pregnancy)</b>	GDM Pregnancy-induced hypertension Pre-eclampsia Venous thromboembolism		Macrosomia
<b>Intrapartum (During labour)</b>	Induction of labour Caesarean section Emergency caesarean Anaesthetic problems		Fetal distress Birth injuries Shoulder dystocia Meconium aspiration
<b>Postpartum (After labour)</b>	Haemorrhage Anaemia Infections (UTI,Wound) Venous thromboembolism Lactation problems Maternal morbidity/mortality		Perinatal morbidity/mortality Higher risk of adult obesity

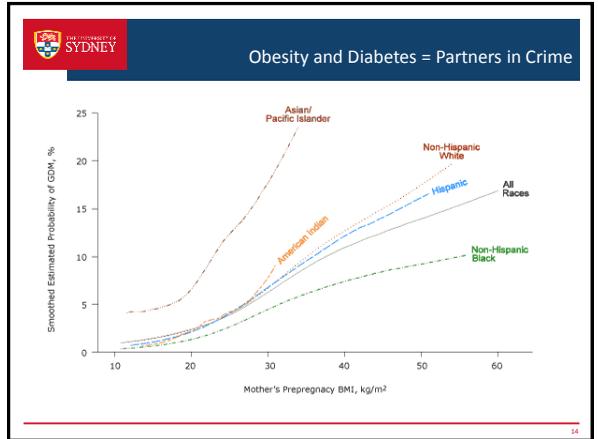
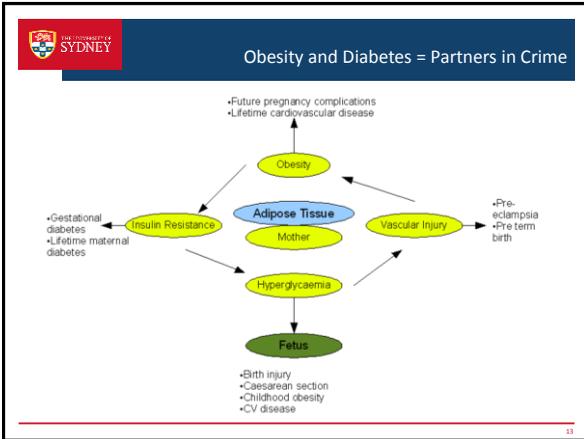


### Diabetes in Australia

- > **4%** of Australians (999,000 people) have diabetes. This rate was 1.5% in 1989.
- > **1 in 20** pregnancies are affected by diabetes
- > **3 to 1** = diabetes in the Indigenous population compared to the diabetes in the non-Indigenous population.
- > **Over half** of adults are overweight or obese, which puts them at greater risk for diabetes.
- > **Three in five** people with diabetes also have cardiovascular disease.
- > **8.2 million** pharmaceutical scripts were claimed for diabetes medicines in 2012.
- > **\$1,507 million** was spent on treating diabetes in 2008-9 = 2.3% of all health expenditure.

<http://aihw.gov.au/diabetes/>





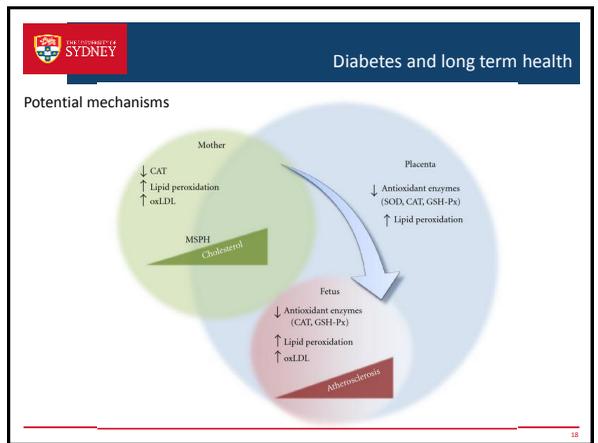
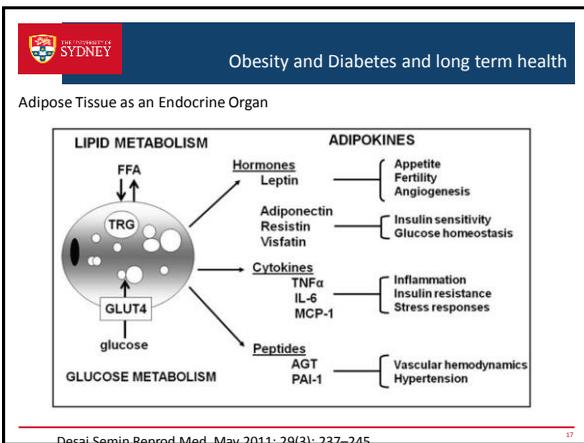
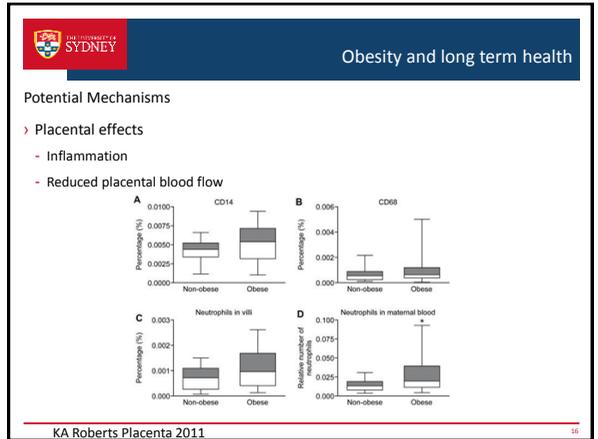
### Obesity and long term Health

**Potential Mechanisms**

- Metabolic and Hormonal Theories
  - Obesogenic maternal diet directly contribute to total body adiposity, adipose tissue dysfunction, central fat accumulation and adult disease
  - Increase in gluconeogenic enzyme expression
  - Reduction in liver insulin signalling

} Insulin resistance

- Epigenetic Theories
  - Increased insulin receptor promoter methylation
  - Glucose positively associated with methylation
  - Histone modification of liver genes that assist with gluconeogenesis



**Where to Intervene?**

International Journal of Obesity 34, S44-S52 (December 2010) | doi:10.1038/ijo.2010.239 K Melzer and Y Schutz

**What actually works?**

**Preconception Care**

- More likely to change risk behaviours
  - quit smoking before pregnancy OR 2.94,
  - decrease alcohol consumption from 5.4 to 0.8%
  - 5 times more likely to use folic acid before pregnancy
  - 39% more likely to seek antenatal care
- Better Outcomes
  - neonatal mortality 24% risk reduction
  - 20% more likely to breastfeed.

Recent Sydney LHD study shows 2/3 of pregnancies are intended<sup>2</sup>

Bhutta Systematic Review of Preconception Risks and Interventions *Rassi Aust NZ J Public Health*, 2013

**What actually works?**

**Pre pregnancy Obesity**

- Interventions that combine
  - calorie restriction and physical activity
  - a support system and monitoring
  - sustained over longer periods

**Table 3** Pregnancy rate, fertility treatment and obstetric-related outcomes at 12 months by treatment group

	Intervention (n=22)	Control (n=202)	Odds ratio of mean difference (95% CI)	P value
Clinical pregnancy rate	48.1%	13.6%	5.88 (1.40 to 24.46)	0.007
Assisted pregnancy	10	3	3.73 (0.89 to 15.53)	0.06
Natural conception	3	0	–	0.11
Number of assisted conception cycles undertaken	31	33	0.9 (0.0 to 1.2)	0.04
Fresh transfer (IVF or ICSI)	17	11	0.2 (-0.3 to 0.48)	0.43
Cryopreserved embryo transfer	14	2	0.4 (0.1 to 0.68)	0.01
Miscarriage rate, %	29.4%	25.0%	–	0.91
<6 weeks	4	1	–	–
Weeks 6-12	1	0	–	–
Live birth, n (%)	12 (54.5%)	3 (1.5%)	–	0.02
Gestational diabetes	0	1	–	0.12
Hypertensive disorders of pregnancy	0	1	–	0.12
Preeclampsia	1	0	–	0.92

*doi:10.1038/ijo.2010.239*

**What actually works?**

**Pregnancy care - diabetes**

- Low risk** – screen at 24 – 28 weeks
- Moderate risk** – random or a fasting glucose test in early pregnancy +/- OGTT
- High risk - 75 g pregnancy OGTT at the first opportunity after conception**
  - Previous GDM
  - Previously elevated blood glucose level
  - Maternal age ≥40 years
  - Family history DM (1st degree relative with diabetes or a sister with GDM)
  - BMI > 35 kg/m<sup>2</sup>
  - Previous macrosomia (baby with birth weight > 4500 g or > 90th centile)
  - Polycystic ovarian syndrome
  - Medications: corticosteroids, antipsychotics
- Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African,
- BMI 25 – 35 kg/m<sup>2</sup>

ADIPS Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia (modified June 2014)

**What actually works?**

**Pregnancy Care**

- Multidisciplinary
  - Dietician
  - Diabetes Educator
  - Diabetologist or Endocrinologist
  - Obstetrician

**Consider hypoglycaemic therapy for women with gestational diabetes:**

- if lifestyle changes do not maintain blood glucose targets over 1–2 weeks
- if ultrasound shows incipient fetal macrosomia (AC > 70th percentile)

Crowther *ACHOIS NEJM* 2008

**What actually works?**

**Inter Pregnancy Care**

- Multidisciplinary care
- Preconception folic acid supplementation
- Post partum screening for type 2 diabetes
  - Gestational Diabetes should be considered a pre-diabetes condition
  - Women with GDM 7-fold future risk of type 2 diabetes vs. women with normoglycemic pregnancy
  - Blood glucose testing in first few days after delivery

Bellamy *Lancet*, 2009, 373(9677): 1773-9

- › Identify obesity at pre-conception appointments
  - monitor weight and encourage lifestyle (nutrition and exercise) changes
  - appropriate referral to a dietitian/exercise specialist
- › Discuss risks of obesity on both fertility and pregnancy outcomes.
- › Inform women that even gains of 1–2 BMI units (kg/m<sup>2</sup>) **between** pregnancies can increase the risk of gestational hypertension, macrosomia and gestational diabetes <sup>1</sup>.
- › Encourage daily exercise as per national guidelines.



<sup>1</sup> RANZCOG Sept 2013 1 – Villamor Lancet 2006

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- › Institute of Medicine

BMI (kg/m <sup>2</sup> ) (WHO) <sup>19</sup>	Classification	Singleton pregnancy total weight gain range	Rates of weight gain in 2 <sup>nd</sup> and 3 <sup>rd</sup> Trimester
<18.5	Underweight	12.5-18kg	0.51 (0.44- 0.58)
18.5-24.9	Normal	11.5-16kg	0.42 (0.35- 0.50)
25-29.9	Overweight	7-11.5kg	0.28 (0.23-0.33)
≥30	Obese (includes all Obesity classes 1, 2 and 3); Obesity Class 1: BMI 30-34.9 Obesity Class 2: BMI 35-39.9 Obesity Class 3: BMI >40	5-9kg	0.22 (0.17-0.27)

- › 1 out of 6 women classified differently compared with 1990
- › 17% of appropriate gainers in 1990 now classified as “overgainers”.

Weight Gain During Pregnancy: Reexamining the Guidelines. National Academy of Sciences 2009.

- › Safe for mothers and developing child <sup>1</sup>
  - Reduced caesarean sections
  - Reduced pregnancy related hypertension
  - No increase in low birth weight infants
- › But...
  - Many women unaware of gestational weight gain guidelines<sup>2</sup>
  - 40 % of normal weight women exceed the IOM recommendations
  - > 60% of overweight/obese women exceed the IOM recommendations<sup>3</sup>



<sup>1</sup> - Finerson Obesity 2011, <sup>2</sup> - de Jersey ANZJOG 2012, <sup>3</sup> - Weisman Womens Health Issues 2010

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### Postnatal

- › Breastfeeding
  - Early and exclusive
  - 13 – 22% reduced risk of obesity in later life
  - each additional month associated with a 4% lower risk of obesity later in life
- › Limiting catch up weight gain
  - Rapid early growth in first weeks or months associated with later obesity
- › Infant sleep
  - Infants who slept < 12 hours 2 x more likely to be overweight at 3 years of age

Harder Am J Epi 2005, Aranz IUQ 2005, Baird BMI 2005, Nevarez acta paediatrica 2010

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- › Maria is a 28-year-old G2P1
- › Attends your practice at 8 weeks' gestation
- › She is 1.68 cm tall and weighs 74 kg
- › She works as a lawyer full time in a busy firm
- › In her first pregnancy, she gained 15 kg and delivered a healthy infant at 39 weeks weighing 3.95 kg
- › How should you counsel the patient regarding nutrition and weight gain in this pregnancy?

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# QUESTIONS?

› *The doctor of the future will give no medicine, but will interest her or his patients in the care of the human frame, in a proper diet, and in the cause and prevention of disease.*

› **Thomas Edison**  
*US inventor (1847-1931)*

## Aim

› To develop a flagship study to investigate novel scientific questions focused on gaining a greater understanding of the mechanisms

to

ar

### Epigenetics and Fetal Metabolic Programming: A Call for Integrated Research on Larger Cohorts

› Luigi Bonchard

- Recombination/Environment of both men and women
- Will assess stimuli within appropriate critical windows
- Will nest interventional studies into the cohort
- Will translate evidence into practice