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?

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

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Systolic blood pressure

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

Steel et al. Lancet; 2014

Obesity in Australia

› Fourteen million Australians are overweight or obese.
› More than five million Australians are obese (BMI ≥ 30 kg/m²)
› 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

The effect of obesity on pregnancy

Lancet 2010

› Mothers who gain more weight during pregnancy have heavier infants

Steel et al. Lancet; 2014
### Maternal complications

<table>
<thead>
<tr>
<th>Period</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-pregnancy</td>
<td>Menstrual disorders, Infertility</td>
</tr>
<tr>
<td>Early pregnancy</td>
<td>Miscarriage, Intrauterine death</td>
</tr>
<tr>
<td>Antepartum</td>
<td>Gestational diabetes, Hypertension, Pre-eclampsia, Venous thromboembolism</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>Induction of labour, Caesarean section, Emergency caesarean Anaesthetic problems</td>
</tr>
<tr>
<td>Postpartum</td>
<td>Haemorrhage, Anaemia, Infections (UTI,Wound), Venous thromboembolism, Lactation problems, Maternal morbidity/mortality</td>
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### Fetal complications

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<tr>
<td>Early pregnancy</td>
<td>Intrauterine death, Congenital anomalies</td>
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<tr>
<td>Antepartum</td>
<td>Macrosomia</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>Fetal distress, Birth injuries, Shoulder dystocia, Meconium aspiration</td>
</tr>
<tr>
<td>Postpartum</td>
<td>Perinatal morbidity/mortality, Higher risk of adult obesity</td>
</tr>
</tbody>
</table>

### Fetal Overgrowth

**Long term implications**

- [Birth weight](#)
- [Adult obesity](#)
- [Type 2 diabetes](#)
- [Fetal-Neonatal morbidity](#)
- [Abnormal metabolic environment](#)
- [Diet/Activity](#)
- [Childhood Obesity](#)
- [Type 1 insulin sensitivity](#)

**Catalano J Clin Endocrinol Metab, August 2003, 88(8):3505–3506**

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### 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.


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### Diabetes in Pregnancy

#### Maternal Outcomes

![Maternal Outcomes Graph](#)

#### Infant Outcomes

![Infant Outcomes Graph](#)
Obesity and Diabetes = Partners in Crime

Potential Mechanisms

- **Obeseogenic 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

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

- **Potential Mechanisms**
  - Insulin resistance

Adipose Tissue as an Endocrine Organ

Potential mechanisms

- **LIPID METABOLISM**
  - FFA
  - TRO
  - GLUT4

- **GLUCOSE METABOLISM**
  - glucose

Adipokines

- **Hormones**
  - Leptin
  - Adiponectin

- **Resistin**

- **TNFα**

- **IL-6**

- **BCP-1**

- **Peptides**
  - AGT
  - PAI-1

Potential mechanisms

- **Insulin sensitivity**
  - Glucose homeostasis

- **Inflammation**
  - Insulin resistance

- **Stress responses**

- **Vascular hemodynamics**
  - Hypertension

- **Appetite**
  - Perity

- **Argiogenesis**

- **Glucose homeostasis**

- **Insulin sensitivity**

- **Stress responses**

- **Vascular hemodynamics**
  - Hypertension

KA Roberts Placenta 2011
Where to Intervene?

**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 take 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

**Pregnancy care - diabetes**
- **Low risk** - screen at 24 – 28 weeks
- **Moderate risk** – random or a fasting glucose test in early pregnancy +/- OGTT
- Ethnicity: Asian, Indian subcontinent, Aboriginal, Torres Strait Islander, Pacific Islander, Maori, Middle Eastern, non-white African,
  - BMI 25 – 35 kg/m²
- **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/m²
  - Previous macrosomia (baby with birth weight > 4500 g or > 90th centile)
  - Polycystic ovarian syndrome
  - Medications: corticosteroids, antipsychotics

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]

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

What actually works?
Current Australian Guidelines

- 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/m²) between pregnancies can increase the risk of gestational hypertension, macrosomia and gestational diabetes.

- Encourage daily exercise as per national guidelines.

Institute of Medicine

<table>
<thead>
<tr>
<th>BMI (kg/m²) (WHO)</th>
<th>Classification</th>
<th>Single pregnancy total weight gain range</th>
<th>Rates of weight gain in 2nd and 3rd Trimester</th>
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</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
<td>12.5-18kg</td>
<td>0.51 (0.44-0.56)</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>Normal</td>
<td>11.5-18kg</td>
<td>0.42 (0.36-0.50)</td>
</tr>
<tr>
<td>25-29.9</td>
<td>Overweight</td>
<td>7-11.5kg</td>
<td>0.28 (0.23-0.33)</td>
</tr>
<tr>
<td>≥30</td>
<td>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 &gt;40</td>
<td>5-8kg</td>
<td>0.22 (0.17-0.27)</td>
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- 1 out of 6 women classified differently compared with 1990
- 17% of appropriate gainers in 1990 now classified as "obergainers".

Gestational weight gain

- Institute of Medicine
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- 17% of appropriate gainers in 1990 now classified as "obergainers".

Do the Guidelines Work?

- Safe for mothers and developing child
  - Reduced caesarean sections
  - Reduced pregnancy related hypertension
  - No increase in low birth weight infants

- But...
  - Many women unaware of gestational weight gain guidelines
  - 40 % of normal weight women exceed the IOM recommendations
  - > 60% of overweight/obese women exceed the IOM recommendations


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


What actually works?

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Case History

- 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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<tr>
<td>Implementing policy into practice</td>
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<tr>
<td>Educating the community</td>
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<tr>
<td>Preventing chronic disease</td>
</tr>
<tr>
<td>Improving preconception service delivery</td>
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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)

QUESTIONS?

Our future ... for unborn generations

Aim
To develop a flagship study to investigate novel scientific questions focused on gaining a greater understanding of the mechanisms occurring before and during pregnancy and beyond that dispose to the future progression of obesity, diabetes and cardiovascular disease and related disorders

Why is this study different?
- Preconception recruitment of both men and women
- Will assess stimuli within appropriate critical windows
- Will nest interventional studies into the cohort
- Will translate evidence into practice