Maternal gestational weight gain; relationship with obesity risk in the offspring?

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1. Some aspects of the policy background to the field
   - Foresight
   - UN High Level meeting on NCDs
   - IOM recommendations
   - UK NICE guidance

2. Physiological & metabolic considerations

3. Evidence linking gestational weight gain with offspring obesity risk
Foresight “Tackling Obesities: Future Choices”

Considered 17 different potential governmental policy responses across built, health, fiscal, research, educational, regulatory, social structure & family domains.

The only one with a significant impact on obesity in all three scenario contexts explored was ...

“... to promote/implement a programme of early interventions at birth or in infancy”.

Since 2007, new evidence suggests that inventions before/during pregnancy may have even greater impact, but Foresight still concluded:

“Intervention in early life generated the highest average impact across all scenarios.”

“Greatest success was achieved in scenarios where a long-term approach prevailed, .... & where society was prepared to measure success over longer timeframes.”
14. In 2008, an estimate 36 million of the 57 million global deaths were due to NCDs, ... & that nearly 80% of those deaths occurred in developing countries.

26. Note also with concern that maternal & child health is inextricably linked with NCDs & their risk factors, specifically as prenatal malnutrition & low birth weight create a predisposition to obesity, high blood pressure, heart disease & diabetes later in life; & that pregnancy conditions, such as maternal obesity & gestational diabetes, are associated with similar risks in both the mother & her offspring.

37. Acknowledge the contribution & important role played by all relevant stakeholders, including individuals, families, & communities, intergovernmental organizations & religious institutions, civil society, academia, media, voluntary associations, & where & as appropriate, the private sector & industry, in support of national efforts for NCD prevention & control.
We therefore commit to

43i. Promote, protect & support breastfeeding, ........

45b. Pursue, as appropriate, ... a life course approach given the often chronic nature of NCDs

45b. Promote multisectoral & multi-stakeholder engagement in order to reverse, stop & decrease the rising trends of obesity in child, youth & adult populations respectively

45o. Promote the inclusion of NCD prevention & control within sexual & reproductive health & maternal & child-health programmes, especially at the primary health-care level, as well as other programmes

54. Engage non-health actors & key stakeholders, where appropriate, including the private sector & civil society, in collaborative partnerships to promote health & to reduce NCD risk factors, including through building community capacity in promoting healthy diets & lifestyles
IOM-recommended levels of gestational weight gain according to prepregnancy BMI categories

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>Range of Recommended Absolute Weight Gain, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5 kg/m²)</td>
<td>12.5–18</td>
</tr>
<tr>
<td>Normal weight (18.5–24.9 kg/m²)</td>
<td>11.5–16</td>
</tr>
<tr>
<td>Overweight (25–29.9 kg/m²)</td>
<td>7–11.5</td>
</tr>
<tr>
<td>Obese (≥30 kg/m²)</td>
<td>5–9</td>
</tr>
</tbody>
</table>

In deriving recommendations little account taken of offspring adiposity outcomes (sparse data available)
Weight management before, during and after pregnancy

Pregnant women

- Measure weight & height at the first contact
- Do not rely on self reported measures of weight & height
- Do not routinely weigh women repeatedly during pregnancy unless important to the clinical management of their care
- Discuss eating habits & physical activity
Pregnant women with a BMI of 30 or more

- Explain how their weight poses a risk to their health and that of their unborn child
- Explain that they should not try to diet while pregnant as this may harm the unborn child
- Offer a referral for specialist advice on healthy eating and physical activity
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2. Physiological & metabolic considerations
   - Linkage with parity & prepregnancy body composition
   - Gestational weight gain as a marker of several physiological processes
   - Interwoven with diet & physical activity

3. Evidence linking gestational weight gain with offspring obesity risk
Mother’s own fetal growth, diet, parity, body composition, weight gain & endocrine status
Maternal & offspring genetic diversity & epigenetic effects

Developmental plastic responses
- fetal/placental epigenetic changes
- regional blood flow & body composition

Early fetal growth trajectory
- determines fetal nutrient demand

Maintenance of the growth trajectory
- determined by materno-placental nutrient supply

Modification in infancy
- weight gain & catch-up growth
- nutrition & infection
- parent-child interactions

Amplification in childhood
- growth & body composition
- environmental challenges & lifestyle

Vulnerability to coronary heart disease, type 2 diabetes, osteoporosis, mental ill-health, atopy & obstructive airways disease
Dutch Hunger Winter: maternal famine in pregnancy

Maternal weight (post-partum)

Prevalence of obesity among adult male offspring

NEJM 1976;295:349–353
Maternal diet & body composition may influence offspring health without necessarily affecting size at birth

- **High weight / adiposity / pregnancy weight gain:**
  obesity, insulin deficiency/type-2 diabetes, CHD *(UK, US, Finland, India)*

- **Low weight / body mass index / pregnancy weight gain:**
  obesity, insulin resistance, ↑ lipids *(UK, Holland, Finland, China, Philippines)*

- **Low energy intake:**
  obesity, ↑ lipids, insulin resistance, CHD, ↑ IMT *(Holland, UK)*

- **Dietary quality, e.g. folate or vitamin D inadequacy:**
  neurocognitive development, bone density *(UK, Holland, India, US)*

- **Dietary balance, low or high protein density:**
  ↑ BP, IGT/insulin deficiency, stress responses *(UK, Holland, Philippines)*

CHD – coronary heart disease; IMT – intima-media thickness; BP – blood pressure; IGT – impaired glucose tolerance
The EarlyNutrition Project
Long-term effects of early nutrition on later health (FP7)

Genes and Environment

Fetal Overnutrition
  e.g. maternal obesity, high pregnancy weight gain, diet in pregnancy, gestational diabetes

Postnatal Nutrition and Growth
  e.g. short duration of breastfeeding, overfeeding, excessive protein intake

Obesity/visceral adiposity
  Metabolic syndrome
  Diabetes
  Hypertension
  Cardiovascular disease
  Asthma

Fuel mediated in utero hypothesis

Mismatch hypothesis

Fetal Undernutrition and Postnatal Overnutrition
  e.g. maternal nutritional imbalances, placental dysfunction
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3. Evidence linking gestational weight gain with offspring obesity risk
   - Childhood adiposity, rather than simply BMI
   - Trimester specificity
   - Maternal body composition dependency
SWS: Shorter duration of breast feeding associated with greater adiposity (DXA) age 4 years, but no association with child’s BMI

Adjusted for maternal age, BMI, height, education, social class, smoking in late pregnancy, infant birth weight, and age of introduction of solid foods.

Values are mean & 95% CI; JCEM 2009
The relation between adult body mass index & diabetes varies in different populations - partly reflecting differences in body composition for a given BMI.
Childhood obesity is associated with doubling of adult mortality before age 55 years

5000 Native Americans followed up for 24 years:

Compared to those with a BMI in the lowest quartile, children with a BMI in the top quartile age 11 years more than twice as likely to die before age 55 years

NEJM 2010
Waist circumference aged 28-31 years is greater in firstborn offspring, higher maternal pregnancy BMI (& higher maternal weight gain or lower fish intake in pregnancy)

Accounting for mother’s BMI, firstborn adults averaged a 3.5 cm larger waist

Adjusted for age, sex & current smoking; n=276

Reynolds & Godfrey et al. JCEM 2010
Risk of adult BMI >25 kg/m² greater if mother:

- had a higher antenatal BMI
- ↑ pregnancy weight gain
- primiparous

<table>
<thead>
<tr>
<th>Motherwell men &amp; women aged 28-31 yrs (n=203)</th>
<th>Odds ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject’s gender (1=male, 2=female)</td>
<td>0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“ smoking (0=no, 1=yes)</td>
<td>0.51</td>
<td>0.028</td>
</tr>
<tr>
<td>Maternal 1st antenatal BMI (z)</td>
<td>1.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“ antenatal weight gain (z)</td>
<td>1.40</td>
<td>0.018</td>
</tr>
<tr>
<td>Primiparous mother (0=multip, 1=primip)</td>
<td>1.75</td>
<td>0.043</td>
</tr>
</tbody>
</table>

Reynolds & Godfrey et al. JCEM 2010
**SWS Pregnancy weight gain** *(US Institute of Medicine categories)*

**UK women:** Inadequate 21%, Adequate 30%, Excessive 49%

Excessive pregnancy weight gain associated with ↑ fat mass at birth, 4 years & at 6 years *(n=948)*

**Neonatal fat mass**

*P*=0.0004 (linear relation)

**4-year fat mass**

*P*=0.08 (U-shaped relation)

**6-year fat mass**

*P*=0.01 (U-shaped relation)

Fat mass measured by DXA scanning

*a* adjusted for sex, gestation, age at measurement, length, & maternal smoking, age, height, parity & educational attainment

*b* adjusted for sex, age at measurement, childhood height, & maternal smoking, age, height, parity, educational attainment & breastfeeding duration

Means & 95% CI; AJCN 2010
Maternal weight by gestational age for mothers of boys (----) & girls (---) in ALSPAC (n=5,154)

First trimester: any wt gain incrementally associated with ↑ child adiposity age 9–14 weeks; only weight gain >500 g/wk associated with ↑ offspring adiposity.
Estimated weight in early, mid & late pregnancy generally had U-shaped associations with offspring adiposity
• with null or inverse associations in women gaining low levels of weight
• null associations in the middle range of estimated weight gain
• positive associations at high levels of weight gain

Adjustment for prepregnancy weight, smoking & parity attenuated the inverse associations in women with low weight gain

No evidence that associations of estimated gestational weight gain with any outcomes were modified by prepregnancy BMI
1st trimester weight gain interacts with maternal BMI in relation to offspring BMI age 5 yrs

(Child Health and Development Studies, US; n=3015)
Maternal weight gain 10 wks gestation - 12 hrs post delivery in relation to offspring BMI in early adulthood (146,894 Swedish conscripts; <10% of sample non-sibs)

**Associations differed by mothers’ early pregnancy BMI**

(Interaction $P < 0.0001$):

- In offspring of normal-weight women, maternal weight gain positively associated with BMI age 18 y, but only between unrelated men (no within-sibling association)

- In overweight & obese women in contrast, associations were found both within-siblings & between unrelated men

“In normal-weight mothers, most of the association between maternal weight gain & later offspring BMI is explained by shared familial (genetic & early environmental) characteristics, whereas evidence indicates a contribution of intrauterine mechanisms in overweight & obese women”

*Lawlor et al, AJCN 2011*
Changing diet & physical activity to reduce gestational weight gain: a meta-analysis

“overall, diet and physical activity change was effective in reducing gestational weight gain, but there was considerable heterogeneity in outcomes”

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference IV, Fixed, 95% CI [kg]</th>
<th>Mean Difference IV, Fixed, 95% CI [kg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbee (21)</td>
<td>13.02 5.67</td>
<td>16.15 7.03</td>
<td>4.5%</td>
<td>-3.13 [-5.70, -0.56]</td>
</tr>
<tr>
<td>Claesson, Sydsjö (15)</td>
<td>8.7 5.51</td>
<td>11.3 5.8</td>
<td>18.4%</td>
<td>-2.60 [-3.87, -1.33]</td>
</tr>
<tr>
<td>Gray-Donald (18)</td>
<td>12 6.4</td>
<td>13.2 8.3</td>
<td>7.7%</td>
<td>-1.20 [-3.17, 0.77]</td>
</tr>
<tr>
<td>Guelinckx (active) (31a)</td>
<td>9.8 7.6</td>
<td>10.6 6.9</td>
<td>2.1%</td>
<td>-0.80 [-4.54, 2.94]</td>
</tr>
<tr>
<td>Guelinckx (passive) (31b)</td>
<td>10.9 5.6</td>
<td>10.6 6.9</td>
<td>2.5%</td>
<td>0.30 [-3.16, 3.76]</td>
</tr>
<tr>
<td>Hui (16)</td>
<td>14.2 5.3</td>
<td>14.2 6.3</td>
<td>2.5%</td>
<td>0.00 [-3.43, 3.43]</td>
</tr>
<tr>
<td>Kinnunen (19)</td>
<td>14.6 5.4</td>
<td>14.3 4.1</td>
<td>8.6%</td>
<td>0.30 [-1.55, 2.15]</td>
</tr>
<tr>
<td>Olson (39)</td>
<td>14.1 4.51</td>
<td>14.8 4.68</td>
<td>45.2%</td>
<td>-0.70 [-1.51, 0.11]</td>
</tr>
<tr>
<td>Polley (normal) (17a)</td>
<td>15.4 7.1</td>
<td>16.4 4.8</td>
<td>3.2%</td>
<td>-1.00 [-4.05, 2.05]</td>
</tr>
<tr>
<td>Polley (overweight) (17b)</td>
<td>13.6 7.2</td>
<td>10.1 6.2</td>
<td>2.1%</td>
<td>3.50 [-0.25, 7.25]</td>
</tr>
<tr>
<td>Shirazian (22)</td>
<td>8.06 7.4</td>
<td>15.42 7.52</td>
<td>1.4%</td>
<td>-7.36 [-11.93, -2.79]</td>
</tr>
<tr>
<td>Wolff (20)</td>
<td>6.6 7.2</td>
<td>13.3 7.5</td>
<td>1.8%</td>
<td>-6.70 [-10.78, -2.62]</td>
</tr>
</tbody>
</table>

| Total (95% CI)               | 744          | 911     | 100.0%                               | -1.19 [-1.74, -0.65]                  |

Heterogeneity: $\chi^2 = 32.03$, df = 11 ($P = 0.0008$); $R^2 = 66$
Test for overall effect: $Z = 4.29$ ($P < 0.0001$)

Maternal gestational weight gain; relationship with obesity risk in the offspring?

1. Current policies do not acknowledge the potential for an influence of gestational weight gain on obesity risk in the offspring.

2. Gestational weight gain is linked with the mother’s prepregnancy body composition, parity, diet & physical activity, & should not be considered in isolation from these.

3. Increasing evidence suggests that gestational weight gain, perhaps both inadequate & excessive, is linked with the obesity risk of the offspring.

4. Perceptions of the importance of pregnancy weight gain vary enormously around the world, & the pragmatic value of a focus on weight gain is likely to be context dependent.