Obesity and Lifestyle Modifications for the Reduction of Maternal Morbidity

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Disclosure:
Member, Clinicians Advisory Board
Novo Nordisk, Obesity Team
PREGNANCY: Major contributor to the obesity epidemic

- Physical inactivity, and excessive caloric intake are recognized as independent risk factors for:
  - Obesity
  - Insulin resistance
  - Type 2 diabetes
  - Preeclampsia

- The physiological and hormonal changes of pregnancy magnify these risks.
- There are close similarities in the pathophysiology of GDM and type 2 GDM
Obesity Treatment Pyramid

Surgery

Pharmacotherapy

Lifestyle Modification

Diet

Physical Activity
(1983) Emerging Lifestyle Intervention in Obese Pregnant Women with GDM

Weight Restriction and Diet
Physiological Rationale

• Insulin resistance develops at the level of skeletal muscles
• Exercise increases insulin sensitivity
  Glucose uptake into large skeletal muscles increases 20 to 50 fold (by GLUT 4 translocation)
  Affects proteins involved in insulin transduction (AMPK and AKT substrate ASI60)

• Exercise increases the amount of aerobic enzymes in skeletal muscles by as much as 20 fold (up-regulating lipid oxidation and mitochondrial biogenesis)
Relative Risk of GDM

**Pregravid Pregnancy Physical Activity**

(n = 21,765)

Conversion from MET/hr/wk to Kcal/wk is estimated on body weight of 100 kg

Exercise for pregnant women to prevent GDM (Cochrane database)

- 5 trials – 1,115 subjects
  - Moderate risk of bias
  - No significant difference in GDM incidence
  - No significant difference in BMI
  - No significant difference in insulin sensitivity

Han S, Middleton P, Crowther CA, Cochrane Database of Systematic Reviews 2012
Published studies comparison and inconsistent results

- Sample size – underpowered
- Adherence to protocols varied (as low as 16%)
- Subjects at low risk for GDM, normal BMI with few exceptions
- Only 3 studies restricted participation to overweight or obese subjects
- Type of exercise (endurance, resistance)
- Timing of exercise
- Diet control
- No information on molecular/metabolic (muscle structure effects)
- Loss to follow-up was as high as 33%

Estimating treatment outcomes of meta-analysis depends on the analysis strategy (sensitivity analysis)
Systematic review and meta-analysis suggest a 28% lower risk for GDM among exercising subjects.

Demographic and maternal characteristics  
\((n = 12,290)\)

<table>
<thead>
<tr>
<th>Pre-Pregnancy BMI</th>
<th>Number</th>
<th>(%) GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.8 - 26.0</td>
<td>6,615</td>
<td>1.8</td>
</tr>
<tr>
<td>26.1 - 29.0</td>
<td>1,660</td>
<td>4.0</td>
</tr>
<tr>
<td>29.1 -33.0</td>
<td>1,261</td>
<td>4.4</td>
</tr>
<tr>
<td>&gt;33.0</td>
<td>1,243</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Prevalence of GDM by BMI and physical activity
(Central New York – 1995/6)

Physical Activity and the Risk of Preeclampsia

15 studies: 11 cohort, 4 case-control

**Results and Conclusions:**

<table>
<thead>
<tr>
<th>Activity Type</th>
<th>RR reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest pre-pregnancy PA</td>
<td>20 -30%</td>
</tr>
<tr>
<td>Prior and early pregnancy PA</td>
<td>36%</td>
</tr>
<tr>
<td>High intensity PA in early pregnancy</td>
<td>50%</td>
</tr>
<tr>
<td>BMI adjustments</td>
<td>23%</td>
</tr>
</tbody>
</table>

Limitations: Dose response and analyses of type of hypertension and effects of weight not addressed.

Aune D. et al, Epidemiology 2014;25:331
GWG Recommendations – NO CHANGE for Over 25 Years

I.O.M 1990

<table>
<thead>
<tr>
<th>Pre -Pregnancy BMI</th>
<th>Adults * (BMI)</th>
<th>Weight Gain Goal Singleton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>28-40 lb</td>
</tr>
<tr>
<td>Average Weight</td>
<td>18.5 – 24.9</td>
<td>25-35 lb</td>
</tr>
<tr>
<td>Overweight &gt; 120% IBW</td>
<td>25-29</td>
<td>15-25 lb</td>
</tr>
<tr>
<td>Obese</td>
<td>&gt;29</td>
<td>&gt;15 lb</td>
</tr>
</tbody>
</table>

I.O.M. 2009

<table>
<thead>
<tr>
<th></th>
<th>Range in lbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5 kg/m2)</td>
<td>28 – 40</td>
</tr>
<tr>
<td>Normal Weight (18.5 – 24.9 kg/m2)</td>
<td>25 – 35</td>
</tr>
<tr>
<td>Overweight (25.0 – 29.9 kg/m2)</td>
<td>15 – 25</td>
</tr>
<tr>
<td>Obese (&gt; = 30.0 kg/m2)</td>
<td>11 – 20</td>
</tr>
</tbody>
</table>

No distinction between BMI Obesity Classes
## PREGNANCY OUTCOMES BY WEIGHT CHANGE STATUS

<table>
<thead>
<tr>
<th>Weight</th>
<th>Subjects who lost weight or no weight change (n=30)</th>
<th>Subjects who gained (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>Mean + SD n %</td>
<td>Mean + SD n %</td>
</tr>
<tr>
<td>Infant birth weight (g)</td>
<td>3286.3 +399.0</td>
<td>3339.5±612.0</td>
</tr>
<tr>
<td>Infant weight category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>23 95.8</td>
<td>43 76.8</td>
</tr>
<tr>
<td>Large for gestational age (&gt;4000g)</td>
<td>1 4.2</td>
<td>10 17.9</td>
</tr>
<tr>
<td>Small for gestational age (&lt;2500g)</td>
<td>0 0.0</td>
<td>3 5.4</td>
</tr>
<tr>
<td>Gestational age at delivery (week)</td>
<td>38.6+1.4</td>
<td>38.1±1.5</td>
</tr>
<tr>
<td>Delivery method</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-Section</td>
<td>10 41.7</td>
<td>28 49.1</td>
</tr>
<tr>
<td>Vaginal</td>
<td>14 58.3</td>
<td>29 50.9</td>
</tr>
</tbody>
</table>
Reuters News Organization – July 2015 News Release:

• In USA 53% of prepregnancy women are overweight or obese
• In Germany 28% of prepregnancy women are overweight or obese
• In Germany 39% of women gain less weight than recommended
• In USA 20% of women gain less weight than recommended
• 1 in 3 women stayed with the recommended GWG
Current Commentary:

Weight Gain Recommendations in Pregnancy and The Obesity Epidemic

Raul Artal, MD, Charles J. Lockwood, MD, and Haywood L. Brown, MD
Funnel plots for effect of Weight Loss with SGA (<10th percentile multivariable), in a systematic review of gestational weight loss in obese women and adverse pregnancy outcomes.


http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0132650
Funnel plots for effect of weight loss with LGA (>$90$th percentile multivariable), in a systematic review of gestational weight loss in obese women and adverse pregnancy outcomes.


http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0132650
Weight Loss vs. Weight Gain in Obese Women

Compared to Gestational Weight Gain within IOM Guidelines

GWL – had higher odds of SGA < 10th (AOR 1.76; 95.6 CI 1.45-2.14) and lower odds of LGA < 90th

Graded relationship between SGA and obesity class:

<table>
<thead>
<tr>
<th>Class</th>
<th>AOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>1.73</td>
</tr>
<tr>
<td>Class II</td>
<td>1.63</td>
</tr>
<tr>
<td>Class III</td>
<td>1.39</td>
</tr>
</tbody>
</table>

Kapadia MZ et al PLOS One 2015;10(7)

LGA and Macrosomia significantly less in obese women with GWL
Other primary outcomes were not assessed. Focus on LGA and SGA only
Published Studies on GWG
Strengths and Weaknesses

• Numerous potential biases and methodological issues:
  – Selection bias
  – Recall bias
  – No controlling for potential confounders
  – No assessment and verification of GA at delivery for SGA or premature delivery
  – And other

The Arguments Against Weight Loss in Pregnancy

The Contrarian View

• Do not advise weight loss until additional studies demonstrate benefits and no adverse consequences to the mother and/or fetus. 
  
  *Contrarian view: Studies are available, additional GWG detrimental*

• **Obligatory Physiological changes** that should result in a “net maternal gain” to reflect the products of conception and other. 
  
  *Contrarian view: The concept implies risks, not supported by data.*

  Ketonuria/Ketonemia causes delayed neurodevelopment . 
  
  *Contrarian view: No credible data to support this myth.*

• Weight loss will result in SGA newborns. 
  
  *Contrarian view: In 2013 we have better tools for early diagnosis of SGA than in 1980...and intervene: ULTRASOUND*

  No distinction between symmetric, asymmetric SGA/IUGR
Maternal Weight Gain and Infant Birth Weight

-100
-50
0
50
100
150
200
250
300
350
400
450

New York Suppl. (1980)
New York Comp. (1980)
Montreal (1963-1974)
Dutch Famine (1944-1946)

Maternal weight gain
Birth weight differences
Conclusions: Lower infant weight gain was not associated with poorer neurodevelopmental outcomes in healthy, term-born 3-year-old children. These results should aid in determining optimal growth patterns in infants to balance risks and benefits of health outcomes through the life course.
Weight Gain During Pregnancy

For an obese pregnant woman who is gaining less weight than recommended but has an appropriately growing fetus, no evidence exists that encouraging increased weight gain to conform with the update IOM guidelines will improve maternal or fetal outcomes.
The optimal gestational weight gain for Class III obese women (n=19,025)

Modified from:
D.W. Kiel, E.A. Dodson, R. Artal, et.al
Obstet Gynecol 110: 752-8, 2007
Physiological Rationale for weight control

• Caloric restriction also plays an important role in improving insulin sensitivity

• Increased fat deposition leads to increased adiponectin and leptin

• Adiponectin regulates insulin sensitivity and glucose homeostasis

• Further increase in adiponectin increases the oxidative stress that contributes to insulin resistance
The Finish GDM Prevention Study (RADIEL)

- N = 269, BMI > 30
- Randomized control study
- No weight gain I and II trimester
- Physical Activity (Exercise) > 150 min/week

<table>
<thead>
<tr>
<th>Intervention Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>GWG – 7.6kg (16.7lb)</td>
<td>7.7kg (16.9lb)</td>
</tr>
<tr>
<td>B.W. – 3,626gm</td>
<td>3,680gm</td>
</tr>
<tr>
<td>Macrosomia – 4.2%</td>
<td>4.0%</td>
</tr>
<tr>
<td>GDM – 13.9%</td>
<td>21.6%</td>
</tr>
</tbody>
</table>

INTERVENTIONS TO REDUCE OR PREVENT OBESITY IN PREGNANT WOMEN

26 studies – 468,858 subjects

Results and Conclusions:
Dietary and physical activity interventions are effective at reducing:
• maternal weight gain
• preeclampsia
• gestational hypertension
• GDM

NO EVIDENCE OF HARM ASSOCIATED WITH THE INTERVENTIONS TO MANAGE WEIGHT IN PREGNANCY

S. Thangaratinam et al. Health Technology Assessment 2012;16(31):1366
The effects of physical activity alone and physical activity + diet interventions in pregnancy

- 7 trials with pregnant women
- 4 trials postpartum

Pregnant women in the intervention groups gained approx. 2 lbs. less.
Postpartum women in the intervention groups lost approx. 2.7 lbs.

Conclusion:
PA + diet interventions require more than advice.
- Supervision
- Personalized prescription goals
PREGNANCY IS AN IDEAL TIME FOR LIFE STYLE MODIFICATION

- Subjects more prone to comply
- Access to medical care
- Close medical supervision

Short and long-term benefits for mother, fetus, and beyond
Optimizing Breastfeeding
Approx. 500 cal/day

<table>
<thead>
<tr>
<th>CURRENT</th>
<th>2020 GOAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% Initiate in Hospital</td>
<td>82%</td>
</tr>
<tr>
<td>50% at 6 Months</td>
<td>60%</td>
</tr>
<tr>
<td>27% at 1 Year</td>
<td>34%</td>
</tr>
</tbody>
</table>

The influence of grandmothers on breastfeeding rates: a systematic review: Joel Negin, BMC 2016;16
Interpregnancy Weight Loss and Birth Weight

1. For Class I and II obese women loss of >2 BMI reduces LGA risk by 40-50% and no increase in SGA

2. For Class III weight loss of >6BMI is necessary to reduce LGA risk

Jain, A et al AJOG, March 2013
5As of Obesity Management for Adults

This tool kit providers health practitioners with five steps to better manage patients’ weight and related health issues:

• **ASK** for permission to discuss weight and explore readiness
• **ASSESS** obesity related risks and “root causes” of obesity
• **ADVISE** on health risks and treatment options
• **AGREE** on health outcomes and behavioral goals
• **ASSIST** in accessing appropriate resources and providers
To Achieve a 300 kcal Negative Energy Balance:

Reduce intake by:

- Eliminating 2 oz potato chips

- Substituting 2 diet sodas for 2 regular sodas

Or increase activity by:

- Running 3 miles in 30 min
  - Or
  - Walking 2.5 miles in 60 minutes

- Bicycling 8 miles in 30 min
Energy Expenditure of Physical Activity

- All-out competitive sports
- Running 10 mph
- Running 6 mph
- Climbing stairs
- Sexual intercourse
- Gardening
- Walking 4 mph
- Bicycling
- Walking 2 mph
- Chewing gum (11 kcal/h)

SUMMARY AND CONCLUSIONS

• Pregnancy is an ideal time for lifestyle modifications
• Lifestyle modification, diet and exercise, significantly reduces co-morbidities: GDM, Preeclampsia, Macrosomia
• Physical activity prior and during pregnancy can prevent GDM and LGA.
• Exercise programs should expend approximately 1400 kcal/week or more to attain euglycemia
• Weight restriction is a safe intervention in obese patients in all phases of life, including pregnancy
• Providers reluctance to prescribe exercise and patients acceptance/compliance remain major barriers