The Continuing Controversy Over Screening for Gestational Diabetes

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Obstetrics, Gynecology & Reproductive Sciences
Maternal-Fetal Medicine

I have nothing to disclose.

GDM & Controversy

- The nature of screening tests
- Why screening for GDM matters
- The major controversies
- Possible sources of those controversies
- What I think you should do
The Nature of Screening Tests

• Screening is the identification of an asymptomatic disease, harmful condition or risk factor.
• When deciding how to screen, the following must be considered:
  - Burden of suffering caused by the condition
  - Therapeutic interventions available
  - Performance of available screening tests

How great is the burden of suffering caused by GDM?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Overall %</th>
<th>RR/OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrosomia</td>
<td>20</td>
<td>~1.4</td>
</tr>
<tr>
<td>Pre-Eclampsia</td>
<td>15</td>
<td>~1.7</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>Varies</td>
<td>~1.2</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>3-5</td>
<td>~1.2</td>
</tr>
<tr>
<td>IUFD</td>
<td>~0.05</td>
<td>~2</td>
</tr>
</tbody>
</table>

Blinded study of ~25,000 women at 15 centers, 9 countries
Primary predictor: Levels of hyperglycemia
Primary outcomes: Birth weight > 90%ile, primary CD, neonatal hypoglycemia, cord-blood C-peptide level

Why should we be concerned with GDM at all?

Fletcher et al. Clinical Epidemiology: The Essentials, 5th Ed, Lippincott Williams & Wilkins 2013

### HAPO Results

Increasing maternal glycemia is associated with increased risk of maternal and fetal complications.


### How good is the therapeutic intervention for GDM?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention Group N = 485 (%)</th>
<th>Control Group N = 473 (%)</th>
<th>Relative Risk</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICU Admission</td>
<td>9</td>
<td>11.6</td>
<td>0.77 (0.51 – 1.18)</td>
<td>0.19</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>5.9</td>
<td>14.3</td>
<td>0.41 (0.26 – 0.66)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neonatal Hypoglycemia</td>
<td>5.3</td>
<td>6.8</td>
<td>0.77 (0.44 – 1.36)</td>
<td>0.32</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>1.5</td>
<td>4.0</td>
<td>0.37 (0.14 – 0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cesarean Delivery</td>
<td>26.9</td>
<td>33.8</td>
<td>0.79 (0.64 – 0.99)</td>
<td>0.02</td>
</tr>
<tr>
<td>Preeclampsia or GHTN</td>
<td>8.6</td>
<td>13.6</td>
<td>0.63 (0.42 – 0.96)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Landon – Trial of Treatment for GDM


Crowther – Trial of Treatment for GDM


- *Any serious perinatal complication
- Admission to NICU
- Macrosomia
- Neonatal hypoglycemia
- Preeclampsia
- Cesarean Delivery

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention Group N= 490 (%)</th>
<th>Routine Care N= 510 (%)</th>
<th>Adjusted RR or Treatment Effect</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Any serious perinatal complication</td>
<td>1</td>
<td>4</td>
<td>0.33 (0.14 – 0.75)</td>
<td>0.01</td>
</tr>
<tr>
<td>Admission to NICU</td>
<td>71</td>
<td>61</td>
<td>1.13 (1.03 – 1.23)</td>
<td>0.04</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>10</td>
<td>21</td>
<td>0.47 (0.34 – 0.64)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neonatal hypoglycemia</td>
<td>7</td>
<td>5</td>
<td>1.42 (0.87 – 2.32)</td>
<td>0.16</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>12</td>
<td>18</td>
<td>0.7 (0.51 – 0.95)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cesarean Delivery</td>
<td>31</td>
<td>32</td>
<td>0.97 (0.81 – 1.16)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

* One or more of: death, shoulder dystocia, bone fracture, nerve palsy
Increasing maternal glycemia is associated with worse perinatal outcomes.

Treatment improves outcomes.

What's the controversy?!

How good are the screening tests for GDM?

(How good is too good?)

GDM Controversies

One-Step Testing v. Two-Step Testing
Carpenter Coustan v. National Diabetes Data Group
Universal Screening v. Risk-Based Screening
Early Screening v. 24-28 Week Screening
Hemoglobin A1c v. No Hemoglobin A1c
Blood sugar testing for 1 abnormal value v. No testing

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One-Step vs. Two-Step Testing

Two-Step

Step 1: Non-Fasting, 50 g, 1 hr serum glucose measurement
≥ 130/140 mg/dL → Step 2

Step 2: Fasting, 100 g, 3 hr glucose test
2+ abnormal values → GDM

GDM prevalence ~ 5-10%

One-Step

Fasting, 75 g, 1 & 2 hr serum glucose measurement
1+ abnormal value → GDM

GDM prevalence ~ 20%

Controversies

One-Step Testing v. Two-Step Testing

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Carpenter-Coustan v. NDDG

<table>
<thead>
<tr>
<th></th>
<th>Fasting (mg/dL)</th>
<th>1 hr (mg/dL)</th>
<th>2 hr (mg/dL)</th>
<th>3 hr (mg/dL)</th>
<th>GDM Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Diabetes Data Group</td>
<td>105</td>
<td>190</td>
<td>165</td>
<td>145</td>
<td>3.4%</td>
</tr>
<tr>
<td>Carpenter-Coustan Criteria</td>
<td>95</td>
<td>180</td>
<td>155</td>
<td>140</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

GDM Controversies

One-Step Testing v. Two-Step Testing

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Blood sugar testing for 1 abnormal value v. No testing
Universal vs. Risk-Based Screening


4th & 5th International Workshop on GDM: (1997 & 2005): Risk-Based Screening

<table>
<thead>
<tr>
<th>Table 1 — Screening strategy for detecting GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>GDM risk assessment: Should be ascertained at the first prenatal visit</td>
</tr>
<tr>
<td>- Low risk: Blood glucose testing not routinely required if all of the following characteristics are present:</td>
</tr>
<tr>
<td>- Member of an ethnic group with a low prevalence of GDM</td>
</tr>
<tr>
<td>- No known diabetes in first-degree relatives</td>
</tr>
<tr>
<td>- Age &lt;$25 years</td>
</tr>
<tr>
<td>- Weight normal before pregnancy</td>
</tr>
<tr>
<td>- Weight normal at birth</td>
</tr>
<tr>
<td>- National Cooperative</td>
</tr>
<tr>
<td>- Carbohydrate metabolism</td>
</tr>
<tr>
<td>- History of poor obstetric outcome</td>
</tr>
</tbody>
</table>


“All pregnant patients should be screened for GDM, whether by the patient’s medical history, clinical risk factors, or laboratory screening test results to determine blood glucose levels.”

Universal vs. Risk-Based Screening

U.S. Preventive Services Task Force

January 2014

“[There is] adequate evidence that screening for and treatment of GDM can significantly reduce the risk for preeclampsia, fetal macrosomia, and shoulder dystocia... as a result of the evidence...

The USPSTF recommends screening for gestational diabetes mellitus in asymptomatic pregnant women after 24 weeks of gestation (B recommendation).”

http://www.uptodate.com/contents/gestational-diabetes-mellitus}

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Early Screening

- Detecting women with pre-existing diabetes or glucose intolerance (pre-diabetes)
- ACOG: History of GDM, known impaired glucose metabolism, obesity
- ADA: Severe obesity, strong family history, personal history of GDM, impaired glucose metabolism, glucosuria

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Hemoglobin A1c

Diagnosing Type 2 DM:
- A1c ≥ 6.5 → DM2
- A1c 5.7 – 6.5 → Glucose Intolerance
- A1c < 5.7 → Normal

Average HbA1c Values Non-Diabetic Women

<table>
<thead>
<tr>
<th>HbA1c %</th>
<th>Non-Pregnant</th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.8 – 5.5</td>
<td>4.3 – 5.4</td>
<td>4.4 – 5.4</td>
<td>4.7 – 5.7</td>
</tr>
<tr>
<td></td>
<td>(5.2)</td>
<td>(5.0)</td>
<td>(4.9)</td>
<td>(5.1)</td>
</tr>
</tbody>
</table>

http://www.uspreventiveservicestaskforce.org/uspstf13/gdm/gdmfinalrs.htm

“The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for GDM in asymptomatic pregnant women before 24 weeks of gestation.”

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Pregnancy Outcomes for Women with 1 Abnormal Value on 3 hour

Table II. Adverse perinatal outcomes in pregnant women with normal screening GFT values, compared with pregnant women with 1 abnormal GFT value

<table>
<thead>
<tr>
<th>GFT value</th>
<th>Normal GFT value (%)</th>
<th>One abnormal GFT value (%)</th>
<th>P value</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean delivery</td>
<td>15.6</td>
<td>26.9</td>
<td>&lt;.001</td>
<td>1.40</td>
<td>1.12-2.28</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>9.5</td>
<td>12.6</td>
<td>.05</td>
<td>1.49</td>
<td>1.09-2.03</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>4.4</td>
<td>8.4</td>
<td>.05</td>
<td>1.49</td>
<td>1.03-2.14</td>
</tr>
<tr>
<td>Birth weight &lt; 4000 g</td>
<td>10.7</td>
<td>18.0</td>
<td>&lt;.001</td>
<td>1.46</td>
<td>1.26-1.88</td>
</tr>
<tr>
<td>Birth weight &gt; 4000 g</td>
<td>1.3</td>
<td>3.1</td>
<td>.066</td>
<td>2.23</td>
<td>1.30-3.87</td>
</tr>
<tr>
<td>Intensive care nursery admittance</td>
<td>6.9</td>
<td>8.3</td>
<td>.036</td>
<td>1.82</td>
<td>1.04-3.22</td>
</tr>
</tbody>
</table>

* N = 12,456.
† N = 4,400.
‡ Multivariate logistic regression adjusted for potential confounding factors included maternal age, parity, race/ethnicity, gestational age at delivery, epidural anesthesia (for cesarean delivery), and length of labor (for chorioamnionitis); the baseline comparison group was white women with normal GFT results.
§ Nulliparas women only.

Treatment for Patients With 1 Abnormal Value

Table 2. Birth and neonatal characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Untreated (n = 53)</th>
<th>Treated (n = 60)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GGT at delivery (wk)**</td>
<td>38.8 ± 1.7</td>
<td>38.9 ± 1.7</td>
<td>.85</td>
</tr>
<tr>
<td>Route of delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal†</td>
<td>57 (59%)</td>
<td>46 (67%)</td>
<td>.96</td>
</tr>
<tr>
<td>Operation vaginal†</td>
<td>1 (2%)</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>VBAC†</td>
<td>0</td>
<td>2 (3%)</td>
<td>—</td>
</tr>
<tr>
<td>Cesarean‡</td>
<td>19 (33%)</td>
<td>21 (35%)</td>
<td>.89</td>
</tr>
<tr>
<td>Unplanned cesarean‡</td>
<td>8 (14%)</td>
<td>8 (12%)</td>
<td>.88</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>3389.4 ± 649.8</td>
<td>3478.7 ± 554.7</td>
<td>.41</td>
</tr>
<tr>
<td>Birthweight &gt;4000 g</td>
<td>8 (14%)</td>
<td>10 (14%)</td>
<td>.64</td>
</tr>
<tr>
<td>Apgar 1†</td>
<td>9 (1-9)</td>
<td>8 (0-9)</td>
<td>.15</td>
</tr>
<tr>
<td>Apgar 5†</td>
<td>9 (6-10)</td>
<td>9 (7-10)</td>
<td>.88</td>
</tr>
<tr>
<td>Shoulder dystocia‡</td>
<td>2 (4%)</td>
<td>2 (3%)</td>
<td>.86</td>
</tr>
<tr>
<td>NICU admission‡</td>
<td>5 (9%)</td>
<td>4 (8%)</td>
<td>.51</td>
</tr>
<tr>
<td>Neonatal metabolic complication‡</td>
<td>3 (5%)</td>
<td>3 (6%)</td>
<td>.86</td>
</tr>
</tbody>
</table>

* GGT = gestational age at delivery.
† Vaginal delivery considered normal.
‡ Cesarean delivery considered normal.
**Sensitivity v Specificity**

<table>
<thead>
<tr>
<th>One-Step</th>
<th>Two-Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpenter Coustan</td>
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</tr>
<tr>
<td>Hemoglobin A1c</td>
<td>No Hemoglobin A1c</td>
</tr>
<tr>
<td>Testing for 1 abnormal value</td>
<td>No f/u for 1 abnormal value</td>
</tr>
</tbody>
</table>

**More Sensitive, Less Specific**
- More women with disease test positive
- More women WITHOUT disease test positive
- Diagnosing women who might not actually have clinically important disease

**Less Sensitive, More Specific**
- Fewer women with disease test positive
- Fewer women WITHOUT disease test positive
- Missing a clinically important diagnosis

**What constitutes disease?**

Dichotomization of a continuous process is bound to result in disagreement.
Lack of unambiguous evidence that aggressive diagnosis improves clinically important pregnancy outcomes

- The Landon study included women with 2 abnormal values on a 3-hour
- Studies of treatment are within the confines of strict clinical trials
- No study has compared outcomes between women who rule-in by 1-step approach but rule out by 2-step approach

“Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials.”

Worry about the over-medicalization of pregnancy and increased anxiety about diagnosis

Differences in Perceived Goals of Testing
(Probably) the Ultimate Source of Controversy

Costs v Benefits

1-step screening strategy would:
- Increase frequency of GDM 2-3 fold → 15-20%
- Annually Add:
  - 450,000 patient education visits
  - 1 million prenatal testing appointments
  - 1 million clinic visits
- Increase cost of care for GDM by > $1 billion

What I Think You Should Do
What I Think You Should Do

- Pre-conception planning
- Easy access to laboratory services
- Universal access to nutritional counseling
- Ample time and access to exercise facilities
- Appropriate emotional support
- Long-term follow up

CUT THE CONTROVERSY!

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Blood sugar testing for 1 abnormal value v. No testing

What Is NOT Controversial

Health risks go up with increasing blood sugar.
There is no risk of harm from encouraging women to follow a healthy diet and get regular physical activity.
SOME portion of women will change their behavior after being made aware of an increased risk of disease.

Determine what testing strategy generally fits your circumstances best

Be flexible!
Thank You