Induction of labor: Not as bad as you think!
ARRIVE

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When is the best time for delivery?

- ≥ 42 wks
- < 39 wks

39 - 41 wks?
Increasing maternal and perinatal risks after 39 weeks
Maternal Complications

• Pregnancies that continue beyond 39 weeks are associated with increased risks of:
  – Cesarean delivery
  – Operative vaginal delivery
  – 3\textsuperscript{rd} and 4\textsuperscript{th} degree lacerations
  – Febrile morbidity
  – Hemorrhage
Perinatal Complications

• Pregnancies that continue beyond 39 weeks are associated with increased risks of:
  – Stillbirth
  – Meconium aspiration syndrome
  – Mechanical ventilation
  – Birth trauma
  – Neonatal seizures/ICH/ encephalopathy
  – Neonatal sepsis
  – UA pH ≤7/BE < -12
Perinatal Death

- Perinatal death nadirs between 37-38 weeks and increases steadily thereafter

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Loss Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>0.7/1000</td>
</tr>
<tr>
<td>38</td>
<td>1.3/1000</td>
</tr>
<tr>
<td>39</td>
<td>1.4/1000</td>
</tr>
<tr>
<td>40</td>
<td>2.4/1000</td>
</tr>
<tr>
<td>41</td>
<td>2.8/1000</td>
</tr>
</tbody>
</table>
When is the best time for delivery?

39 - 41 weeks
Induction and cesarean delivery: Common wisdom

• Retrospective cohort studies
  – Induction of labor prior to 41 weeks of gestation is associated with an approximately 2-fold higher risk of cesarean delivery in nulliparous women

Yeast et al, AJOG 1999
Elective inductions only
When is the best time for delivery?

Delivery

Expectant management

39 - 41 weeks
Patients undergoing induction of labor should be counseled about a 2–fold increased risk of cesarean.
The problem

• Spontaneously laboring women are not the right comparison group
  – Cannot choose between EIOL (strategy) and spontaneous labor (event)
  – Choice is between EIOL and expectant management
    • The latter may lead to spontaneous labor
    • Also conveys downstream possibilities that may increase the CS rate
39 weeks
N= 100

Spontaneous labor
CS rate=20%
N=20

IOL
CS rate=35%
N=35
39 weeks
N=100
30% Spontaneous labor

N=6
70

50% labor at 40 weeks

CS rate=20%
N=6

CS rate=30%
N=11

Medical or Post dates IOL

N=14
35

CS rate=40%

CS rate=31%

IOL

CS rate=35%
N=35
## Induction vs. Expectant Management (CS%)

<table>
<thead>
<tr>
<th>Week of Induction</th>
<th>IOL</th>
<th>Spontaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>38 weeks</td>
<td>11.9%</td>
<td>7.0%</td>
</tr>
<tr>
<td>39 weeks</td>
<td>14.3%</td>
<td>9.1%</td>
</tr>
<tr>
<td>40 weeks</td>
<td>20.4%</td>
<td>10.9%</td>
</tr>
<tr>
<td>41 weeks</td>
<td>24.3%</td>
<td>14.9%</td>
</tr>
</tbody>
</table>

Caughey et al, AJOG 2006;195:700-5
# Induction vs. Expectant Management (CS%)

<table>
<thead>
<tr>
<th>Week of Induction</th>
<th>IOL</th>
<th>Spontaneous</th>
<th>Expectant</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>38 weeks</td>
<td>11.9%</td>
<td>7.0%</td>
<td>13.3%</td>
<td>1.80 (1.29-2.53)</td>
</tr>
<tr>
<td>39 weeks</td>
<td>14.3%</td>
<td>9.1%</td>
<td>15.0%</td>
<td>1.39 (1.08-1.80)</td>
</tr>
<tr>
<td>40 weeks</td>
<td>20.4%</td>
<td>10.9%</td>
<td>19.0%</td>
<td>1.24 (1.27-1.62)</td>
</tr>
<tr>
<td>41 weeks</td>
<td>24.3%</td>
<td>14.9%</td>
<td>26.0%</td>
<td>1.26 (0.99-1.61)</td>
</tr>
</tbody>
</table>

Caughey et al, AJOG 2006;195:700-5
Conclusions

• We know that at 41-42 weeks, IOL better than EM
• We know that before 39 weeks, EM better than IOL
• Between 39 and 41 weeks:
  – Common wisdom that EM is better than IOL
    • Maternal and neonatal outcomes worsen with delivery after 39 weeks
    • The concern that IOL increases CD is founded on methodologically flawed study design
  – Common practice is moving away from EM
  – We actually don’t know whether EM or IOL is better
Conclusions

An adequately powered study of elective induction of nulliparous women is needed
Induction in Nulliparous Women at 39 Weeks to Prevent Adverse Outcomes: A Randomized Controlled Trial

A Randomized Trial of Induction Versus Expectant Management (ARRIVE)
Objective

To test the hypothesis that elective induction of labor at 39 weeks compared with expectant management among low-risk nulliparous women reduces the risk of a composite of perinatal mortality and severe neonatal morbidity.
Methods

• Randomized, controlled, parallel group, unmasked trial
• Inclusion criteria
  – Nulliparous women
  – Singleton gestations
  – Reliably dated
  – No contraindication to vaginal delivery
  – Low risk
Methods

- Randomized between 38 0/7 and 38 6/7 weeks of gestation
  - IOL vs. EM
  - Cervical examination at randomization
  - Post-delivery interviews
    - Labor pain
    - Labor Agentry Scale
Methods: Primary outcome

- Composite describing perinatal mortality or severe morbidity
  - Fetal or neonatal death
  - Respiratory support within the first 72 hours of life
  - Apgar score ≤ 3 at 5 minutes
  - Hypoxic ischemic encephalopathy
  - Seizure
  - Infection
  - Meconium aspiration syndrome
  - Birth trauma
  - Intracranial or subgaleal hemorrhage
  - Hypotension requiring pressor support
Methods: Maternal outcomes

- Cesarean delivery
- Hypertensive disorder of pregnancy
- Postpartum hemorrhage
- Chorioamnionitis
- Endometritis
- Post-partum length of stay
- Labor pain
- Labor Agentry Scale
Methods: Subgroup analysis

- Race/ethnicity
- Maternal age
- BMI
- Modified Bishop score
Methods: Sample Size

- Expected rate of the primary outcome: 3.5%
- Compliance with group assignment: 92.5%
- Power: 85%
- Alpha: 5%
- RR decrease: 38%
- N = 6000
Results
Results: CONSORT diagram

50,581 eligibility screening

6,106 randomized

3062 IOL
- 1 lost F/U
- 2 withdrew
  - 3059 analyzed

3044 EM
- 2 lost F/U
  - 3037 analyzed

27,600 ineligible
16,875 declined
### Results: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>IOL</th>
<th>EM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age – yr.</td>
<td>24 (21-28)</td>
<td>23 (20-28)</td>
</tr>
<tr>
<td>Race and ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1329 (43.4)</td>
<td>1359 (44.7)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>707 (23.1)</td>
<td>699 (23.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>87 (2.8)</td>
<td>106 (3.5)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>866 (28.3)</td>
<td>808 (26.5)</td>
</tr>
<tr>
<td>Other or unknown</td>
<td>73 (2.4)</td>
<td>72 (2.4)</td>
</tr>
<tr>
<td>Private insurance for prenatal care</td>
<td>1404 (45.9)</td>
<td>1335 (43.9)</td>
</tr>
<tr>
<td>Previous pregnancy loss</td>
<td>698 (22.8)</td>
<td>778 (25.6)</td>
</tr>
<tr>
<td>BMI ≥30 kg/m² at randomization</td>
<td>1633 (53.6)</td>
<td>1575 (52.0)</td>
</tr>
<tr>
<td>Modified Bishop score at randomization &lt;5</td>
<td>1919 (62.7)</td>
<td>1954 (64.2)</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) or N (%).
Results

• IOL vs. EM:
  – 39.3 weeks vs. 40.0 weeks, P < .001
  – 3300g vs. 3380g, P < .001
## Results: Perinatal

<table>
<thead>
<tr>
<th>Condition</th>
<th>IOL N (%)</th>
<th>EM N (%)</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal composite</td>
<td>133 (4.3)</td>
<td>164 (5.4)</td>
<td>0.80</td>
<td>0.64 - 1.00</td>
</tr>
<tr>
<td>Respiratory support</td>
<td>91 (3.0)</td>
<td>127 (4.2)</td>
<td>0.71</td>
<td>0.55 - 0.93</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>2 (0.1)</td>
<td>2 (0.1)</td>
<td>0.66</td>
<td>0.12 - 3.33</td>
</tr>
<tr>
<td>Apgar ≤ 3 at 5 minutes</td>
<td>12 (0.4)</td>
<td>18 (0.6)</td>
<td>0.66</td>
<td>0.32 - 1.37</td>
</tr>
<tr>
<td>HIE</td>
<td>13 (0.4)</td>
<td>19 (0.6)</td>
<td>0.68</td>
<td>0.34 – 1.37</td>
</tr>
<tr>
<td>Seizure</td>
<td>11 (0.4)</td>
<td>4 (0.1)</td>
<td>2.73</td>
<td>0.91 – 8.12</td>
</tr>
<tr>
<td>Infection</td>
<td>10 (0.3)</td>
<td>12 (0.4)</td>
<td>0.83</td>
<td>0.36 - 1.91</td>
</tr>
<tr>
<td>MAS</td>
<td>17 (0.6)</td>
<td>26 (0.9)</td>
<td>0.65</td>
<td>0.35 - 1.19</td>
</tr>
<tr>
<td>Birth trauma</td>
<td>14 (0.5)</td>
<td>18 (0.6)</td>
<td>0.77</td>
<td>0.38 - 1.55</td>
</tr>
<tr>
<td>ICH or subgaleal hemorrhage</td>
<td>9 (0.3)</td>
<td>7 (0.2)</td>
<td>1.28</td>
<td>0.48 - 3.42</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3 (0.1)</td>
<td>5 (0.2)</td>
<td>0.60</td>
<td>0.13 - 2.27</td>
</tr>
</tbody>
</table>
## Results: Maternal

<table>
<thead>
<tr>
<th>Condition</th>
<th>IOL N (%)</th>
<th>EM N (%)</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean delivery</td>
<td>569 (18.6)</td>
<td>674 (22.2)</td>
<td>0.84</td>
<td>0.76 - 0.93</td>
</tr>
<tr>
<td>Hypertensive disorder of pregnancy</td>
<td>277 (9.1)</td>
<td>427 (14.1)</td>
<td>0.64</td>
<td>0.56 - 0.74</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>407 (13.3)</td>
<td>429 (14.1)</td>
<td>0.94</td>
<td>0.83 - 1.07</td>
</tr>
<tr>
<td>Third or fourth degree perineal laceration</td>
<td>103 (3.4)</td>
<td>89 (2.9)</td>
<td>1.15</td>
<td>0.87 - 1.52</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>142 (4.6)</td>
<td>137 (4.5)</td>
<td>1.03</td>
<td>0.82 - 1.29</td>
</tr>
<tr>
<td>Postpartum infection</td>
<td>50 (1.6)</td>
<td>65 (2.1)</td>
<td>0.76</td>
<td>0.53 - 1.10</td>
</tr>
<tr>
<td>Admission to intensive care unit</td>
<td>4 (0.1)</td>
<td>8 (0.3)</td>
<td>0.50</td>
<td>0.13 – 1.55</td>
</tr>
</tbody>
</table>
## Results: Maternal

<table>
<thead>
<tr>
<th></th>
<th>IOL</th>
<th>EM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PP length of stay - day</td>
<td>2 (2-2)</td>
<td>2 (2-2)</td>
<td>.01</td>
</tr>
<tr>
<td>Labor Agentry Score after delivery</td>
<td>168 (148-183)</td>
<td>164 (143-181)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Labor Agentry Score 6 wk after delivery</td>
<td>176 (157-189)</td>
<td>174 (154-188)</td>
<td>.01</td>
</tr>
<tr>
<td>Worst labor pain</td>
<td>8 (7-10)</td>
<td>9 (8-10)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median overall labor pain</td>
<td>7 (5-8)</td>
<td>7 (5-9)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

All data are presented as medians (interquartile range)
Subgroup analyses

**Primary**

- All patients
- White
- Black
- Asian
- Hispanic
- Other, unknown, or more than one race
- Modified Bishop score < 5
- Modified Bishop score ≥ 5
- Body mass index < 30 kg/m²
- Body mass index ≥ 30 mg/m²
- Age < 35 years
- Age ≥ 35 years

**Cesarean**

- All patients
- White
- Black
- Asian
- Hispanic
- Other, unknown, or more than one race
- Modified Bishop score < 5
- Modified Bishop score ≥ 5
- Body mass index < 30 kg/m²
- Body mass index ≥ 30 mg/m²
- Age < 35 years
- Age ≥ 35 years
Conclusion

• Labor induction:
  – No change in perinatal composite outcome
  – Lower frequency of
    • Neonatal respiratory support
    • Cesarean delivery
    • Hypertensive disorder of pregnancy
  – Shorter postpartum hospital stay
  – Lower perceived pain in labor
  – Greater perceived control during childbirth
Conclusion

• Strengths
  – Size
  – Strict criteria for dating
  – Generalizability
Conclusion

• Limitations
  – Not masked
  – Low power to detect differences in infrequent outcomes
  – Generalizability
Induce Everyone?

- Of course not!
- Reasonable option for some
- Avoiding induction is unlikely to reduce cesarean rates overall
- Cost analyses
- Many other secondary analyses
- Caution: Hold bias and passion and focus on quality data
What do you see?
By shifting perspective you might see an old woman or a young woman.