Clinical Research: What are the Important Questions?

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Clinical Questions

- What is a “Good” clinical question?
  - Anything that has not been asked, may have been asked but asked over 15 years ago, asked but you have a different twist on the question.
  - Proper literature search (this may in itself be a paper)
Clinical Question

- I am going to do an MFM fellowship
  - I have done no research to date (none in my residency)
  - I need to do a research project, write a paper, have that paper accepted in a peer review journal, and then defend that paper at the time of my MFM ORAL examination
- Suggestion of a project by Tom Nolan MD while jogging at Naval Training Center in Orlando Florida in 1990
- The AFI, even though it is only an estimate of amniotic fluid volume, we know it represents the ACTUAL amniotic fluid volume
Clinical Question

- Naval Hospital Camp LeJeune: Do we have less blood loss with manual removal of the placenta or spontaneous removal of the placenta at the time of cesarean delivery?
  - Rapid placental removal allows the uterine incision to be closed more rapidly stopping the incisional blood loss
  - Spontaneous removal allows the uterus to contract decreasing blood loss by the contraction of uterine muscle around spiral arteries.
The Clinical Research Journey
Average Blood Loss at Delivery

- Classic study by Pritchard in 1962
  - Vaginal delivery: 500 ml
  - Cesarean delivery: 1000 ml
  - Repeat cesarean + hysterectomy: 1500 ml

- Postpartum hemorrhage
  - Change in the HCT of 10 between admission and postpartum period
  - Need for RBC transfusion
  - Blood loss in excess of 1000 ml
Calculation of Blood Loss at Cesarean

- Weigh lap pads and sponges wet and dry
- 2 suction machines
- Steri-drapes with side pockets
- HCT pre-op and post op
  - Identification of additional agents used to control blood loss
  - IV fluids administered
Camp LeJeune Study

- Prospective randomised trial
- Manual vs. spontaneous removal
- Manual blood loss: 967 ml
- Spontaneous blood loss: 666 ml
- HCT drop: manual > spontaneous (p < 0.001)
- (AJOG 1992;167:1363-7)
Camp LeJeune Study

- Risk of endometritis:
  - Manual (23%)
  - Spontaneous (3%)
  - (p < 0.001)
Mississippi Study

- In situ vs. exteriorization for repair
  - 1967 study by Hershey > with in situ
- Blood loss
  - Spontaneous in situ
  - Spontaneous exteriorized
  - Manual in situ
  - Manual exteriorized

(Surg Gynec Obstet 1993;177:389-92)
Mississippi Study

- Spontaneous exteriorized and spontaneous in situ (600 – 630 ml)
- Manual exteriorized and spontaneous in situ (1100 – 1300 ml)
- Confirmed by drop in HCT
Mississippi Study on Endometritis

- Prospective randomized trial
- 4 groups
  - Spon in situ
  - Spon ext
  - Manual in situ
  - Manual ext
- Exclusion criteria: chorioamnionitis, no labor or refusal

(Infect Dis Obstet Gynecol 1993;1:65-70)
Endometritis

- Manual ext (61%)
- Spon in situ, spon ext, manual in situ (35 – 40%)
PRE-OP Skin Preparation and Intraoperative Pelvic Irrigation

- Does skin preparation of pelvic irrigation influence post op endometritis
- 4 groups
  - Standard skin prep + saline
  - Standard skin prep + antibiotic irrigation
  - Short prep + saline
  - Short prep + antibiotic irrigation

(Obstet Gynecol 1993;81:922-5)
Pre Op Skin and Antibiotic Irrigation

- Endometritis occurred more frequently in the groups irrigated with saline alone
- No difference in skin preps
Infectious Morbidity, Operative Blood Loss, and Length of Procedure by Placental Method

- Prospective randomized trial
- 4 groups
  - Spon in situ
  - Spon ext
  - Manual in situ
  - Manual ext
- Exclusion criteria: chorioamnionitis, labor, and refusal

Infectious Morbidity, Operative Blood Loss, and Length of Procedure by Placental Method

- Endometritis: manual ext (45%) vs 18-30% in the other 3 groups.
- Blood loss in manual group was 1000 – 1300 ml vs. 600 – 650 in the spontaneous group.
- Operative time was 6 minutes longer in the ext group.
Factors Affecting C/S Operative Time and Effect of Operative Time on Pregnancy Outcomes.

- Prospective observational study of women undergoing CS with multiple antepartum, intrapartum and neonatal outcomes evaluated
- 386 (23%) ≤ 30 min, 1070 (65%) 31-60 min, 200 (12%) > 60 min
  - Women < 18 (p = 0.004), C/S for distress (P < 0.001) shortest operations
  - Women > 35, BMI ≥ 30, pre-exist hypertension, prior C/S, uterine incision other than transverse, 1st year as primary surgeon, accompanying sterilization procedure. (P < 0.001) had longest operations.

(Aust NZ J Obstet Gynecol 2008;48:286-91)
Factors Affecting C/S Operative Time and Effect of Operative Time on Pregnancy Outcomes

- Operative time was significantly linked with:
  - Blood loss (P< 0.001)
  - Umbilical cord pH < 7.1 ( P<0.001)
  - Apgar score at 5 minutes < 7 (P < 0.001)
Accuracy of Blood Loss Estimation

- Blood loss estimation by operating surgeon and anesthesia
- Blood loss calculated
- Blood loss ranged from 400 – 2200 ml
- Most common estimate was 800 ml

(J Mater Fetal Med 1994;3:171-4)
Accuracy of Blood Loss Estimation

- If loss < 800 ml it was overestimated
- If loss > 800 ml it was underestimated
- Blood loss calculations were almost identical to those calculated in 1960 by Pritchard
- Operating surgeon was correct < 50% of time
- Blood loss can be calculated with minimal additional time
Extrafascial Wound Dehiscence

- Secondary closure vs. healing by secondary intention
- Time to complete healing
  - Secondary closure: 17.6 days
  - Secondary intention: 61 days

(Obstet Gynecol 1992;80:321-4)
Extrafascial Wound Dehiscence

- Deep en bloc closure vs. superficial skin closure
  Polypropylene through the entire thickness of the wound or vertical mattress suture

(Obstet Gynecol 1994;83:142-5)
Extrafascial Wound Dehiscence

- **Time**
  - En bloc 27 minutes
  - Superficial 18 minutes

- **Pain score**
  - En bloc: 43
  - Superficial: 16

- Time to wound healing was similar
Extrafascial Wound Dehiscence

- Suture closure vs. Noninvasive adhesive bandage
- Time, pain, and cost > in suture closure
- Time to heal was similar

(J Pelvic Surg 1995;1:88-91)
Stitch Vs. Subcutaneous Drain to Prevent Wound Disruption

- Prospective randomized trial of 964 women who after randomization 590 were randomized: 205 no closure, 191 stitch closure, 194 with drain
- Wound disruptions defined:
- No closure: 9.7%, stitch 10.4%, and drain 10.3%
  (AJOG 2002;186:1119-23)
Uterine Wiping and the Rate of Post Cesarean Endometritis

- Removal with dry lap pad vs removal with tissue forceps
- 614 vs. 616
- Rate of endometritis was 10.5% in wipe group and 10.7% in the no wipe group
- Both methods are comparable

(J Matern Fetal Med 2001;10:318-22)
Method of Expanding the Primary Uterine Incision

- Rodriguez study: blunt vs. sharp, no difference in blood loss
- Prospective randomized trial with 470 in blunt group and 475 in sharp group
- Does the method of expanding the uterine incision affect intraoperative blood loss?

(BJOG 2002;109:448-52)
Method of Expanding the Primary Uterine Incision

- Estimated blood loss: sharp (886 ml) vs Blunt (843 ml) \( (p < 0.001) \)
- Change in HCT: sharp 6.1 vs. 5.5 in blunt group \( (p = 0.003) \)
- Need for transfusion: sharp (9) vs. blunt (2) \( (RR 1.65, 95\% CI 1.25, 2.21) \)
Obesity and Pregnancy (752 Pounds)
Obstetric Challenges of Obesity Complicating Pregnancy

- Retrospective case control study
- Women weight > 300 pounds compared with lean women (160 pounds)
- Obese women:
  - Greater chronic hypertension and diabetes
  - Primary CS was more frequent (CPD)
  - Greater risk of PP endometritis
  - Longer hospital stay

J Perinatol 1994;1:10-14
Mode of Delivery in Morbidly Obese with Prior CS

- Pregnant women weighing > 300 pounds on 1st prenatal visit and with 1 prior CS (Prospective observational trial)
- 69 patients met criteria in 24 months
- Options repeat CS (39 or 57%) vs. VBAC (30 or 43%)
- VBAC success rate 13%; labor arrest 46%, distress 38%, failed induction 15%
- VBAC endometritis rate 30%, wound breakdown 23% vs. 20% and 8% in R-CS group (OR 1.78)

(Am J Obstet Gynecol 2001;185:349-54)
VBAC vs. RCS: Weight based Controls

- Pre-pregnancy Weight:
  - Group 1 (<200 pounds) #70
  - Group 2: 200-300 pounds #70
  - Group 3: > 300 pounds # 69

- VBAC success rate
  - Group 1: 81.8%
  - Group 2: 57.1%
  - Group 3: 13.3%

- Infectious morbidity
  - Group 1: 5.7%
  - Group 2: 11.4%
  - Group 3: 39%

(Am J Obstet Gynecol 2003;188:1516-20)
Pre-Pregnancy BMI and Pregnancy Outcomes

- **BMI at 16 – 18 weeks**
  - 331 underweight (BMI < 18.5)
  - 1982 normal (BMI 18.5 – 25)
  - 326 overweight (BMI 25-30)
  - 188 obese (BMI > 30)

- **Obese women were more likely:**
  - Gestational diabetes (p<0.001)
  - Underlying CHTN (p < 0.001)
  - Develop preeclampsia (p < 0.001)
  - Need labor induction (p < 0.001)
  - CS for fetal distress (p< 0.001)
  - PPH (p = 0.003)
  - Need neonatal resuscitation (p = 0.001)
  - Hypoglycemic neonate (p = 0.007)

(Int J Gynaecol Obstet 2006;95:242-7)
# Effects of an Increasing Gradient of Maternal Obesity of Pregnancy Outcomes


<table>
<thead>
<tr>
<th>BMI</th>
<th>&lt;18.5 (n=276)</th>
<th>18.5-24.9 (n=1965)</th>
<th>25-29.9 (n=1072)</th>
<th>30-34.9 (n=551)</th>
<th>35-39.9 (n=317)</th>
<th>40-44.9 (n=167)</th>
<th>≥45 (n=142)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>19 (6.9)</td>
<td>116 (5.9)</td>
<td>65 (6.1)</td>
<td>66 (12.0)</td>
<td>45 (14.2)</td>
<td>39 (23.4)</td>
<td>42 (29.6)</td>
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<tr>
<td>UTI</td>
<td>15 (5.4)</td>
<td>130 (6.6)</td>
<td>81 (7.6)</td>
<td>34 (6.2)</td>
<td>45 (14.2)</td>
<td>17 (10.2)</td>
<td>26 (18.3)</td>
</tr>
<tr>
<td>Gestational Diabetes†</td>
<td>6 (2.2)</td>
<td>56 (2.9)</td>
<td>64 (6.0)</td>
<td>48 (9.0)</td>
<td>34 (11.4)</td>
<td>23 (15.0)</td>
<td>15 (11.9)</td>
</tr>
<tr>
<td>Preterm Delivery</td>
<td>72 (26.1)</td>
<td>278 (14.2)</td>
<td>122 (11.4)</td>
<td>76 (13.9)</td>
<td>54 (17.2)</td>
<td>47 (28.1)</td>
<td>41 (28.9)</td>
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<tr>
<td>Induction of labor</td>
<td>49 (17.8)</td>
<td>278 (14.1)</td>
<td>186 (17.4)</td>
<td>111 (20.1)</td>
<td>79 (24.9)</td>
<td>53 (31.7)</td>
<td>59 (41.5)</td>
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<tr>
<td>CS Delivery</td>
<td>59 (21.4)</td>
<td>462 (23.5)</td>
<td>329 (30.7)</td>
<td>187 (33.9)</td>
<td>124 (39.1)</td>
<td>71 (42.5)</td>
<td>79 (55.6)</td>
</tr>
<tr>
<td>PPH</td>
<td>5 (1.8)</td>
<td>52 (2.6)</td>
<td>46 (4.3)</td>
<td>17 (3.1)</td>
<td>17 (5.4)</td>
<td>11 (6.6)</td>
<td>18 (12.7)</td>
</tr>
<tr>
<td>Endometritis</td>
<td>6 (2.2)</td>
<td>131 (6.7)</td>
<td>56 (5.2)</td>
<td>32 (5.8)</td>
<td>29 (9.1)</td>
<td>17 (10.2)</td>
<td>38 (26.8)</td>
</tr>
<tr>
<td>Wound Infection‡</td>
<td>-</td>
<td>5 (1.1)</td>
<td>4 (1.2)</td>
<td>12 (6.4)</td>
<td>6 (4.8)</td>
<td>16 (22.5)</td>
<td>20 (25.3)</td>
</tr>
<tr>
<td>Shoulder Dystocia††</td>
<td>3 (1.4)</td>
<td>22 (1.5)</td>
<td>13 (1.8)</td>
<td>20 (5.5)</td>
<td>10 (5.2)</td>
<td>7 (7.3)</td>
<td>2 (3.2)</td>
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<tr>
<td>Meconium</td>
<td>1 (0.4)</td>
<td>8 (0.4)</td>
<td>8 (0.7)</td>
<td>8 (1.5)</td>
<td>2 (0.6)</td>
<td>2 (1.2)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>SGA</td>
<td>33 (12.0)</td>
<td>127 (6.5)</td>
<td>45 (4.2)</td>
<td>27 (4.9)</td>
<td>17 (5.4)</td>
<td>13 (7.8)</td>
<td>10 (7.0)</td>
</tr>
<tr>
<td>LGA</td>
<td>5 (1.8)</td>
<td>91 (4.6)</td>
<td>101 (9.4)</td>
<td>62 (11.3)</td>
<td>45 (14.2)</td>
<td>15 (9.0)</td>
<td>16 (11.3)</td>
</tr>
</tbody>
</table>
The Use of Telemedicine in Obstetrics

- Literature search revealed 268 article of which 60 were the basis of the review
- Telemedicine use: read US, interpret NST, counsel patients, manage diabetes, manage PP depression
- Reduction in time lost from work, transportation costs, more efficiency of the health care provider
- Technology has not been shown to have adverse effects but neither has it demonstrated unequivocal benefits.

(Obstet Surv 2011;66:170-8)
Telemedicine and MFM Referrals

- 16 Clinical guidelines and 23 clinical conditions were MFM co-management or consultation is recommended
- 108,703 pregnancies with 110,890 neonates.
  - MFM contact unchanged at 22%
  - Face to face contact decreased 14.6% to 8.7%, telemed consults increased 7.6% to 13.3%
  - Health Dept most likely and family practice least likely to refer to MFM
- Referrals: cardiac disease, renal disease, systemic disorders, PPROM, fetal anomalies and CI.
- Increased contract between MFM and local providers increased referrals.

(Arch Gynecol Obstet 2012;86:1383-92)
Role of telephone triage in obstetrics.

- Telephone; Primary method for patient to communicate with physician’s office
- Telephone triage
  - Physicians office
  - Telephone answering service
  - Labor and delivery nurses
  - Dedicated telephone triage system using algorithms.
- Currently insufficient information to recommend one method over another method

(Obstet Gynecol Surv 2012;67:810-816)
Telemedicine in Obstetrics

- Trends and obstetric applications of telemedicine
- Literature review from March 2010 to September of 2012
- Telemedicine plays an important role as an adjunct to delivery of health
  - Remote patients with inadequate medical access
  - Limited resources with emphasis on efficient use of those resources

(Clin Obstet Gyneco 2013;56:422-33)
Maternal Response to High-Risk Pregnancies when Prognosis is Poor

- Qualitative Descriptive Study
- Evaluated maternal response when she learned her fetus/neonate had a poor prognosis via telemedicine vs. face to face contact
- Overall the experience was positive, however several simple changes could improve that process

(Aust NZ J Obstet Gynecol 2013 May 2)
Other Clinical Questions

- Singleton pregnancy, amniotic fluid volume and pregnancy outcomes
- Twin pregnancy, amniotic fluid volume, and pregnancy outcomes
- Work and exercise and pregnancy outcomes.
- Blood loss and the third stage of labor
  - Prolonged third stage of labor, > 30 minutes?
    - Third stage of labor 20 vs. 30 minutes
    - At 15 minutes the blood loss is increased 6 Fold
- Hydramnios and adverse pregnancy outcome
- SARA studies [fetal brain activity and Mg, Progesterone, Steroids]
- Pet Therapy
Clinical Questions 1991-2013
The Journey to Find the Answers

- Abstracts presented at local, national, and international meetings: 279
- Peer review publications: 288
- Book Chapters: 33