**The Gerard W. Ostheimer Lecture**

**What’s New in Obstetric Anesthesia?
2013**

**Lisa Leffert, MD**

**Objective:** The primary objective is to appraise and synthesize key concepts and novel research presented in the published literature from January to December 2013, on topics related to obstetric anesthesia, obstetric practice and maternal and perinatal health. Further, the goal is to identify strategies to impact future practice and research, highlight obstetric anesthesiologists’ role as perioperative physicians and improve multidisciplinary coordination of care.

**Summary:** This endeavor features the relevant literature through an annotated syllabus and oral presentation of the most impactful articles published in 2013 for obstetric anesthesiologists and other related professionals. These articles are discussed in the framework of themes and trajectories for future medical practice and scientific exploration.

**Methods:** Article selection was derived primarily from a monthly, manual review of the tables of contents from a broad selection of relevant journals from January-December 2013, supplemented using key word searches performed via multiple search engines (e.g. Google Scholar, PubMed, Ovid Search, Lexis/Nexis), and electronic and print media including medical newsletters (e.g. MDlink, OB Div News (Joanne Douglas)), Obstetric Anesthesia Digest, general news outlets (e.g. Wall Street Journal), Faculty of 1000 and electronic RSS feeds. Accompanying editorials, replies and letters were included in the syllabus to supplement the primary article of focus.

Several types of research designs were included, with a focus on randomized controlled trials, observational studies, systematic reviews and investigations of diagnostic devices. Because of the need to be selective, case reports, articles not published in English, and most animal studies were excluded.

Over 1200 articles were then categorized in a citation manager (i.e., EndNote) using a pre-defined library of major topics and subtopics, and after vetting, were assigned variables and ranking. This method assisted in defining themes that were useful in determining which topics had ample research dedicated to it. A systematic approach highlighting each article’s relevance, importance, clinical and research implications, novelty or uniqueness, validity, definitiveness and educational value was applied using criteria defined in the Systems to Rate the Strength of Scientific Evidence report (*West et al.*, The Research Triangle Institute–University of North Carolina Evidence-based Practice Center, commissioned by the Agency for Healthcare Research and Quality (AHRQ Publication No. 02-E016, Rockville, MD 2002; URL: <http://www.thecre.com/pdf/ahrq-system-strength.pdf>). Level of evidence was interpreted using the protocol from the Oxford Centre for Evidence-Based Medicine when appropriate (*Howick, et al*. Oxford Centre for Evidence Based Medicine, Oxford, UK: http://www.cebm.net/index.aspx?o=5653)

The speaker wishes to acknowledge that there were an abundance of excellent contributions that were not able to be included because of the scope of the project, and to express her admiration for the investigators and authors thereof.

# Anesthesia Journals

Acta Anaesthesiologica Scandinavica

Anaesthesia

Anaesthesia and Intensive Care

Anesthesia & Analgesia

Anesthesiology

Anesthesiology Clinics of North America

ASA Newsletters

British Journal of Anaesthesia

Canadian Journal of Anaesthesia

Current Opinion in Anesthesiology

European Journal of Anesthesiology

European Journal of Pain

International Anesthesiology Clinics

International Journal of Obstetric Anesthesia

Journal of Clinical Anesthesia

Journal of Pain

Obstetric Anesthesia Digest

Pain

Regional Anesthesia and Pain Medicine

Trends in Anesthesia and Critical Care

# General Medical/Science Journals

American Journal of Emergency Medicine

American Journal of Epidemiology

Annals of Internal Medicine

British Medical Journal

British Journal of Haemotology

Circulation

Cochrane Database of Systematic Reviews

Critical Care Medicine

Epidemiology

Heart

Journal of the American Medical Association

Journal of Clinical Epidemiology

Journal of Graduate Medical Science

Lancet

Nature

New England Journal of Medicine

Physiology

PloS One

Proceedings of the National Academy of Sciences

Resuscitation

Science

## Obstetric and Gynecology Journals

Acta Obstetrica et Gynecologica Scandinavica

American Journal of Maternal/Child Nursing

American Journal of Obstetrics & Gynecology

Archives of Gynecology and Obstetrics

Best Practices and Research in Clinical Obstetrics

BMC Pregnancy and Childbirth

British Journal of Obstetrics and Gynaecology

Clinical Obstetrics and Gynecology

Current Opinion in Obstetrics and Gynecology

European Journal of Obstetrics & Gynecology and Human Reproduction

Hypertension in Pregnancy

International Journal of Gynecology & Obstetrics

Journal of Maternal-Fetal & Neonatal Medicine

Journal of Perinatology

Obstetric Medicine: The Medicine of Pregnancy

Obstetrical & Gynecological Survey

Obstetrics & Gynecology

Obstetrics & Gynecology Clinics of North America

Placenta

Pregnancy Hypertension

Reproductive Biology

The Australian and New Zealand Journal of

# Pediatrics Journals

Archives of Disease in Childhood

BMC Pediatrics

Journal of Paediatrics and Child Health

Journal of Pediatrics

Journal of Perinatal Medicine

Pediatrics

# Simulation Journals

Simulation Healthcare

# Women’s Health

Archives in Women’s Mental Health

# Other Specialties

Hypertension

Lancet- Neurology

Lancet- Obstetrics

Transfusion

# Patient Safety/Health Policy

Academic Medicine

Applied Health, Economics and Health Policy

Health Affairs

Journal of Patient Safety

Morbidity and Mortality Weekly Report

Quality and Safety in Health Care

# Glossary:

BMI: Body Mass Index (kg/m2)

BP: Blood Pressure (mmHg)

CD: Cesarean Delivery

CI: Confidence Interval(s)

CSE: Combined Spinal-Epidural

HDP: Hypertensive Disorders of Pregnancy

HELLP: Hemolysis, Elevated Liver Enzymes and Low Platelets

HIV: Human Immunodeficiency Virus

HR: Hazard Ratio

HTN: Hypertension

ICU: Intensive Care Unit

IQR: Interquartile Range

LOS: Length of Stay

NICU: Neonatal Intensive Care Unit

OB/GYN: Obstetrics and Gynecology

OBs: Obstetricians

OR: Odds Ratio(s)

PDPH: Post Dural Puncture Headache

PPH: Postpartum Hemorrhage

PTD: Preterm Delivery
RCT: Randomized Controlled Trial

RF: Risk Factor(s)

RR: Relative Risk(s)

TAP: Transversus Abdominis Plane (Block)

TOLAC: Trial of Labor after Cesarean

VD: Vaginal Delivery

I2 : A statistic that indicates the percentage of variance in a meta-analysis that is attributable to study heterogeneity

# Citations featured in the Ostheimer Lecture are highlighted in bold

# -TABLE OF CONTENTS-

# QUALITY AND SAFETY

**Background** [1-2]

**Metrics:/Severity of Illness**

* Patient Level [3-5]
* Hospital Level [6-8]

**Quality Improvement**

* Communication [9-10]
* Training [11]

 **Cost** [12-13] **PREGNANCY: ANTEPARTUM**
 **Maternal Comorbid Disease
(Indirect Causes)**

* Obesity [14-15]
* Respiratory/Pulmonary
* Asthma [16-17]
* Infectious Diseases
* Influenza [18]
* HIV [19-20]
* Diabetes [21]
* Cardiovascular Disease
(Non-Hypertensive
Disorders of Pregnancy) [22-23]

**PREGNANCY: INTRAPARTUM**

 **Labor**

* Preterm Labor
* Risks [35-36]
* Related Therapy[37-40]
* Induction of Labor
* Methods [41]
* Maternal and Fetal Effects [42-44]
* Other [45]
* PO Status During Labor [46]
* Delivery Setting [47]

 **Cesarean Delivery**

* Malplacentation [61-62]
* Cesarean vs. Vaginal Delivery
* General [63]
* Maternal Request [64-65]
* Infection [66-67]
* Other [68]

**Maternal Comorbid Disease
(Direct Causes)**

* Hypertensive Disorders of Pregnancy
* General [24]
* Risk Factors [25-26]
* Eclampsia [27-28]
* Therapy [29-31]
* Fetal Outcomes [32]
* Future Disease [33-34]

 **Labor Analgesia**

* Neuraxial Anesthesia
* Spinal vs. CSE [48]
* Predictors [49]
* Dosing [50-56]
* Evaluation [57]
* Other Labor Analgesia
* Hypnosis [58-59]
* Remifentanil [60]

 **Cesarean Delivery Anesthesia**

* Neuraxial Anesthesia [69-73]
* General Anesthesia
	+ Airway [74-77]
	+ Postpartum Hemorrhage [78]
	+ Intraoperative Awareness [79]
* TAP Blocks [80-82]

**PREGNANCY: POSTPARTUM**

**Maternal Morbidity/Mortality**

* Postpartum Hemorrhage and Hemostasis
	+ Epidemiology/Risk Stratification of PPH [83-85]
	+ Prevention and Management of PPH [86-92]
* Identifying Who’s Sick [93-98]
* Anesthetic Complications/Side Effects
	+ Respiratory Depression [99]
	+ Local Anesthetic Toxicity [100]
	+ Epidural Hematoma [101-102]
	+ Post Dural Puncture Headache [103-105]
	+ Nausea/Vomiting [106-107]

 **Post Operative Pain**

* Predictive Tools [108-109]
* Biological Profiles [110]
* Chronic Pain [111-113]
* Other [114-115]

**FETAL COMPLICATIONS/OUTCOMES**

 **TOOLS OF OUR TRADE**

# Timing of Delivery

* Guidelines [116-117]
* Fetal outcomes [118-120]

# Perinatal Exposures

# Anesthetics [121-123]

# Other Maternal Medications [124-127]

#

# Effect of Delivery Mode [128-130]

**Technology**

* Ultrasound [134-136]
* Videotaping [137]

**Publications** [138]

**Fetal Heart Rate Monitoring** [131-133]

# QUALITY AND SAFETY

 **Background**

 ([1](#_ENREF_1)) Gee RE, Winkler R: Quality Measurement: What it means for obstetricians and gynecologists. *Obstet Gynecol* 2013, 121(3):507-510.

This discussion summarizes how the relevant national organizations (e.g. the National Quality Forum, the US Department of Health and Human Services) and the field of OB/GYN have embraced the Institute of Medicine’s challenge to raise the bar for quality of medical care as articulated in their 2001 report entitled “Crossing the Quality Chasm”. Key themes include minimizing elective deliveries < 39 weeks and CD without medical indication, treating both mothers and babies preemptively to reduce the morbidity associated with infection and premature delivery, identifying who is sick, and optimizing communication.

([2](#_ENREF_2)) Maxfield DG, Lyndon A, Kennedy HP, O'Keeffe DF, Zlatnik MG: Confronting safety gaps across labor and delivery teams. *Am J Obstet Gynecol* 2013, 209(5):402-408.e403.

This survey (N=3,282) addressed 4 safety concerns within labor and delivery teams: dangerous shortcuts, missing competencies, disrespect, and performance problems. Among participants, 92% of physicians, 93% of midwives, and 98% of nurses reported at least 1 concern within the preceding year. Most stated that these concerns undermined patient safety, harmed patients, or caused them to seriously consider transferring/leaving their positions. Only 9% of physicians, 13% of midwives, and 13% of nurses disclosed their concerns with the individuals involved, which suggests that organizational silence is prevalent among labor and delivery teams and requires substantial improvement. However, potential limitations of the study include convenience sampling and non-response bias among professionals.

**Metrics/Severity of Illness**

***Patient Level***

**(**[**3**](#_ENREF_3)**) Bateman BT, Mhyre JM, Hernandez-Diaz S, Huybrechts KF, Fischer MA, Creanga AA, Callaghan WM, Gagne JJ: Development of a comorbidity index for use in obstetric patients. *Obstet Gynecol* 2013, 122(5):957-965.**

This study developed and validated a comorbidity index to predict severe maternal morbidity (i.e. the occurrence of acute maternal end-organ injury or mortality) using the Medicaid Analytic eXtract data set (N=854,823 pregnancies, 1.2% complicated by the primary study outcome; 2000-2007). Using the development cohort (2/3 sample), a logistic regression model predicting the primary outcome was created that ultimately included 20 -candidate comorbid conditions and maternal age. Each condition was then assigned a weight used to calculate a maternal comorbidity index. For predicting the primary outcome, the OR per point increase in the score was 1.37 (95% CI: 1.35 -1.39). The derived score performed significantly better than available comorbidity indices in predicting maternal morbidity and mortality, and may provide a simple measure for summarizing the burden of maternal illness.

*Associated content: Editorial*

Macones GA: Understanding and reducing serious maternal morbidity: a step in the right direction. *Obstet Gynecol* 2013, 122(5):945-946.

([4](#_ENREF_4)) Carle C, Alexander P, Columb M, Johal J: Design and internal validation of an obstetric early warning score: secondary analysis of the Intensive Care National Audit and Research Centre Case Mix Programme database. *Anaesthesia* 2013, 68(4):354-367.

This study developed and validated an aggregate obstetric weighted early warning scoring system (EWS) analyzing physiological variables collected in the first 24 hr on admission to the ICU. The area under the ROC was 0.995 and 0.957 for the statistical and clinical score, respectively. By developing the model around the highest acuity patients (i.e. those who required admission to the ICU), there may be a missed opportunity to identify earlier, more subtle pathology.

**(**[**5**](#_ENREF_5)**) Hocking G, Weightman WM, Smith C, Gibbs NM, Sherrard K: Measuring the quality of anaesthesia from a patient's perspective: development, validation, and implementation of a short questionnaire. *Br J Anaesth* 2013, 111(6):979-989.**

In part I of this study, a short psychometric instrument for assessing patient’s perception of the quality of anesthesia (PQA) was developed and validated. Principle component analysis highlighted 5 key factors: attention/gentleness, pain management, information/confidence, postoperative nausea/vomiting, and concerns addressed, the last three of which were rated as being the most important by patients. Part II of this study demonstrated that when the anesthesia provider received feedback from this tool, there was a decrease in the number of patients reporting at least one unsatisfactory PQA factor (45.2% [95% CI: 43.1-47.4%] to 35% [32.6-37.6]) during the post-feedback period.

***Hospital Level***

([6](#_ENREF_6)) Snowden JM, Darney BG, Cheng YW, McConnell KJ, Caughey AB: Systems factors in obstetric care: the role of daily obstetric volume. *Obstet Gynecol* 2013, 122(4):851-857.

This population-based retrospective study (N = 462,322) linked birth certificate data to hospital discharge records to compare quality of obstetric care (i.e. birth asphyxia and CD rates in nulliparous, term, singleton, vertex parturients) on high volume dates to low- or average-volume days (weekend vs. weekdays). In lower volume hospitals only, high-volume weekend days were associated with an elevated risk of asphyxia (P = 0.013), and significantly lower CD rates (P = 0.009) vs. low- or average-volume days. The authors postulate that the lower weekend CD rate occurs in the context of a higher weekend staffing ratio and a higher threshold for intervention.

([7](#_ENREF_7)) Smithson DS, Twohey R, Rice T, Watts N, Fernandes CM, Gratton RJ: Implementing an obstetric triage acuity scale: interrater reliability and patient flow analysis. *Am J Obstet Gynecol* 2013, 209(4):287-293.

This study developed a 5-Category Obstetric Triage Acuity Scale (OTAS) and tested for subsequent inter-rater reliability and impact on patient flow. Using patient vignettes (N = 110), the consistency of 8 triage nurses was measured and OTAS was found to perform with substantial (Kappa = 0.61-0.77, OTAS 1-4) and strong correlation (0.87, OTAS 5). Two-thirds of triage visits were found to be low acuity and LOS decreased (median [IQR]) from OTAS 1 (120 [156] min) to OTAS 3 (75 [120.8] min). Using OTAS, the % of patients admitted to the antenatal or birthing unit decreased from 80% (OTAS 1) to 12% (OTAS 5). Although the sample size is small, OTAS may provide reliable assessment of acuity and an opportunity to improve patient flow and to compare performance across organizations.

([8](#_ENREF_8)) Bailit JL, Grobman WA, Rice MM, Spong CY, Wapner RJ, Varner MW, Thorp JM, Leveno KJ, Caritis SN, Shubert PJ *et al*: Risk-adjusted models for adverse obstetric outcomes and variation in risk-adjusted outcomes across hospitals. *Am J Obstet Gynecol* 2013, 209(5):446.e1-446.e30.

This cohort study (N= 115,502 women and neonates) established risk-adjusted models for 5 obstetric outcomes (venous thromboembolism, PPH, peripartum infection, severe perineal laceration, and a composite of neonatal adverse outcome) and assessed 25 hospitals’ performance. None of the comparisons of hospital risk-adjusted frequencies between outcomes were significantly correlated. The conclusion was that evaluations based on a single risk-adjusted outcome cannot be generalized to overall hospital obstetric performance, and thus multiple markers of quality of care are required.

**Quality Improvement**

***Communication***

**(**[**9**](#_ENREF_9)**) Arriaga AF, Bader AM, Wong JM, Lipsitz SR, Berry WR, Ziewacz JE, Hepner DL, Boorman DJ, Pozner CN, Smink DS *et al*: Simulation-Based Trial of Surgical-Crisis Checklists. *N Engl* *J Med* 2013, 368(3):246-253.**

This randomized study compared the impact of an intervention (the use of a surgical crisis checklist) vs. no checklist on

adherence to critical processes of care (primary outcome) and perceived benefit (secondary outcome). Seventeen operating

room teams, 3 institutions and 106 surgical-crisis simulations were used. Failure to adhere to lifesaving processes of care

occurred significantly less frequently with the tool than without (6% vs 23% missed steps, respectively, p <0.001), and these

findings were sustained in multivariate model accounting for clustering, institution, scenerio and learning/fatigue effects.

Almost all (97%) physicians reported that they’d desire the checklist in real-life events.

*Associated Content: Letters to Editor*
Watkins SC, Maruthappu M, Shalhoub J: A Simulation-Based Trial of Surgical-Crisis Checklists. *N Engl J Med* 2013, 368(15):1459-1460.

([10](#_ENREF_10)) Mohammed A, Wu J, Biggs T, Ofili-Yebovi D, Cox M, Pacquette S, Duffy S: Does use of a World Health Organization obstetric safe surgery checklist improve communication between obstetricians and anaesthetists? A retrospective study of 389 caesarean sections. *Br J Obstet Gynecol* 2013, 120(5):644-648.

This retrospective study (N= 389; 2009-2011) assessed the impact of the WHO Checklist on perioperative (written) communication between anesthetists and OBs in a UK-based teaching hospital. Specifically, concurrence of CD “grade” (i.e. urgency) in patient records was compared before and after checklist introduction: “communication failure”= disagreement of CD grades and “good communication”= agreement of CD grades. Grading differences were observed in 24.1% CD pre-checklist vs. 10.3% CD post-checklist (P <0.001), with smaller, statistically insignificant findings in emergency CD. These results suggest that the WHO checklist enhances the communication of CD urgency within the team.

*Related Content*Cullati S, Le Du S, Raë AC, et al: Is the Surgical Safety Checklist successfully conducted? An observational study of social interactions in the operating rooms of a tertiary hospital. *Br Med J Qual Saf* 2013, 8: 639-46.

***Training***

([11](#_ENREF_11)) Crofts JF, Fox R, Draycott TJ, Winter C, Hunt LP, Akande VA: Retention of factual knowledge after practical training for intrapartum emergencies. *Int J Gynaecol Obstet* 2013, 123(1):81-85.

This study tested knowledge retention 1 year post training. Participants (22 junior and 23 senior physicians, 47 junior and 48 senior midwives) from 6 UK hospitals were randomly recruited to undergo practical training on site or at a simulation center, with or without additional teamwork training. Changes in factual knowledge were determined using a 185-item questionnaire before/after training. Mean scores at 6 (97.6 + 23, N = 107) and 12 (98.2 + 21.6, N = 98) months remained higher than those before training (79.6 + 21.9, N = 133, both P < 0.001), but were lower than those immediately after training (101 + 21.3, N = 133, P < 0.001 and P < 0.007 respectively). Training type, location or inclusion of teamwork training had no effect on knowledge retention.

**Cost**

([12](#_ENREF_12)) Huynh L, McCoy M, Law A, Tran KN, Knuth S, Lefebvre P, Sullivan S, Duh MS: Systematic Literature Review of the Costs of Pregnancy in the US. *Pharmacoeconomics* 2013, 31(11):1005-1030.

This systematic review analyzed pregnancy cost drivers using information from low-moderate bias pregnancy publications (N=40; 2000-2012) pertaining to costs (overall, unintended, planned, complications, facilities). Top cost drivers were inpatient care, pregnancy delivery, multiple births and complicated CD. Overall mean cost/ hospital stay has increased from $3,306 (2008) to $9,234 (2012). The mean cost of pregnancy-related complications related to PTD was $326,953. Over 50% of live births were estimated to be unintended, with a difference in cost estimated at $536 million. A limitation of this review was the exclusion of model-based cost-studies due to high degree of variation.

**(**[**13**](#_ENREF_13)**) Carvalho B, Tan J, Macario A, El-Sayed Y, Sultan P: A cost analysis of neuroaxial anesthesia to facilitate external cephalic version for breech fetal presentation. *Anesth Analg* 2013, 117(1):155-159.**

In this study using computer (cost) modeling and published data, the authors estimated the total expected delivery costs for breech presentation with external cephalic version (ECV) with/without neuraxial anesthesia. With a 60% average probability of successful ECV with neuraxial anesthesia vs. 38% without, the total cost of delivery may be decreased (~ $720) or increased (~$112) depending on its success. Overall, the increased ECV success with neuraxial anesthesia, coupled with the reduction in breech CD, rate may offset the costs of providing anesthesia to facilitate ECV.

*Associated Content*

Preston R, and Jee, R: Anesthesia-facilitated external cephalic version: pennywise or pound-foolish? *Obstet Anesth Digest*, 2013, 33(4), 191.

# PREGNANCY: ANTEPARTUM

**Maternal Comorbid Disease (Indirect Causes)**

***Obesity***

([14](#_ENREF_14)) Morken N-H, Klungsoyr K, Magnus P, Skjaerven R: Pre-pregnant body mass index, gestational weight gain and the risk of operative delivery. *Acta Obstet Gynecol Scand* 2013, 92:809-815.

This is a prospective, population-based cohort (Norwegian Mother and Child Cohort Study; N = 50,416) that investigated the RR of operative VD vs. CD. Women with pre-pregnancy BMI > 40 had an increased risk for CD (RR = 3.4 [95% CI: 2.8-4.1]) and vacuum extraction (RR = 1.5 [1.04-2.2]). Women with gestational weight gain > 16 kg had increased risk across all operative interventions.

([15](#_ENREF_15)) Blomberg M: Maternal obesity, mode of delivery, and neonatal outcome. *Obstet Gynecol* 2013, 122(1):50-55.

A follow-up cohort study (Swedish Medical Birth Registry: N = 1,024,471; 1998-2008) to Dr. Blomberg’s 2011 study investigating the association between birth injuries or newborn illness, maternal BMI and delivery mode. Women with BMI > 40 were at an increased risk of birth injury to the peripheral nervous system (PNS), skeletal birth injury, respiratory distress syndrome (RDS), bacterial sepsis, convulsions and hypoglycemia (OR = 2.1 [95% CI: 1.9-2.3] for RDS to 3.8 [2.8-5.1] for PNS). For morbidly obese women, elective CD and VD were associated with twice the increased risk of adverse neonatal outcomes. However, preterm labor/delivery was not adjusted for as a confounder and several of the associated outcomes are related to preterm labor/delivery.

***Respiratory/Pulmonary***

Asthma

([16](#_ENREF_16)) Mendola P, Laughon SK, Mannisto TI, Leishear K, Reddy UM, Chen Z, Zhang J: Obstetric complications among US women with asthma. *Am J Obstet Gynecol* 2013, 208(2):127 e121-128.

A multicenter retrospective cohort study (N = 223,512) that characterized pregnancy and delivery complications associated with maternal asthma. Asthmatic women had higher odds of preeclampsia (OR = 1.1 [95% CI: 1.1-1.2]), superimposed preeclampsia (OR = 1.3 [1.2-1.6]), gestational diabetes (OR = 1.1 [1.0-1.2]), placental abruption (OR = 1.2 [1.1-1.4]), and previa (OR = 1.3 [1.1-1.6]). Asthmatic women had higher risk for PTD overall (OR = 1.2 [1.1-1.2]), medically indicated PTD (OR = 1.1 [1.0-1.3]), breech (OR = 1.1 [1.1-1.2]), hemorrhage (OR = 1.1 [1.0-1.2]), pulmonary embolism (OR = 1.7 [1.1-2.8]), and maternal ICU admission (OR = 1.3 1[1.0-1.7]), and were less likely to have spontaneous labor (OR = 0.9 [0.8-0.9]) and VD (OR = 0.8 [0.8-0.9]), even after adjusting for potential confounders.

([17](#_ENREF_17)) Murphy V, Wang G, Namazy J, Powell H, Gibson P, Chambers C, Schatz M: The risk of congenital malformations, perinatal mortality and neonatal hospitalisation among pregnant women with asthma: a systematic review and meta- analysis. *Br J Obstet Gynecol* 2013, 120(7): 812-822.

A meta-analysis of cohort studies (N=21 trials; 1975-2012) to illustrate the effect of maternal asthma on congenital malformations, neonatal complications or perinatal mortality. Maternal asthma was associated with a significant risk of congenital malformations (RR = 1.1 [95% CI: 1.0-1.2]), cleft lip (RR = 1.3 [1.0-1.7]), neonatal death (RR = 1.5 [1.1-2.0]), and neonatal hospitalization (RR = 1.5 [1.0-2.2]). There were no significant effects on major malformations or stillbirth, and neither exacerbations nor use of bronchodilators/inhaled corticosteroids were associated with congenital malformation risk. Heterogeneity (I2) across subgroups ranged from very low (neonatal death, neonatal sepsis) to high (newborn transient tachypnea).

***Infectious Disease***

Influenza

([18](#_ENREF_18)) Martin A, Cox S, Jamieson D, Whiteman M, Kulkarni A, Tepper N: Respiratory Illness Hospitalizations Among Pregnant Women During Influenza Season, 1998–2008. *Matern Child Health J* 2013, 17(7):1325-1331.

This retrospective, population based study (NIS database; N= 17,548,022) examined the health care burden and pregnancy outcomes of respiratory vs. non-respiratory illnesses with hospitalization during influenza season. Among respiratory illness hospitalizations, there was an increased odds of intrauterine fetal demise (OR = 2.5 [95 % CI: 2.0–3.2]), PTD (OR = 3.8 [3.5–4.1]), CD (OR = 3.5 [3.2–3.7]), and fetal distress (OR = 2.3 [2.2–2.5]). The presence of comorbid high risk medical conditions that confer higher risk for influenza complications did not significantly impact pregnancy outcomes. This study supports universal vaccination and early antiviral (flu) therapy in pregnant women.

HIV

([19](#_ENREF_19)) Briand N, Jasseron C, Sibiude J, Azria E, Pollet J, Hammou Y, Warszawski J, Mandelbrot L: Cesarean section for HIV- infected women in the combination antiretroviral therapies era, 2000-2010. *Am J Obstet Gynecol* 2013, 209(4):335.e331-e312.

This French Perinatal Cohort Study (N=8977; 2000-2010) investigated mother-to-child transmission (MTCT) of HIV in women with anti-retroviral therapy and low viral load (<400 copies/mL) in VD vs. CD. The mode of delivery in term deliveries did not effect the MCTC rate and rates of VD increased from 25-53% over the time period. The MCTC rates were higher with VD in PTD. Unfortunately, this analysis of transmission rates could not be compared between the French and U.S. standard acceptable viral load for VD (<400 copies/ml and <1000 copies/ml , respectively) because the subgroup sample size was too small.

([20](#_ENREF_20)) Calvert C, Ronsmans C: HIV and the Risk of Direct Obstetric Complications: A Systematic Review and Meta-Analysis. *PloS One* 2013, 8(10):e74848.

Using 44 trials, this systematic review and meta-analysis summarized the frequency of obstetric hemorrhage, HDP, dystocia, and intrauterine infections between HIV infected and uninfected women, unrestricted to language, international-region and study type. The risk of puerperal sepsis in HIV positive women was >3 (OR = 3.4 [95% CI: 2.0 to 5.9], low heterogeneity) for all modes of delivery to almost 6 times (OR = 5.8 [2.4 to 14.0], high heterogeneity) for CD compared with HIV negative women, supporting the use of antibiotic prophalaxis. Investigation of other potential associations was limited by a high risk of bias and high heterogeneity.

***Diabetes***

([21](#_ENREF_21)) Feig DS, Shah BR, Lipscombe LL, Wu CF, Ray JG, Lowe J, Hwee J, Booth GL: Preeclampsia as a Risk Factor for Diabetes: A Population-Based Cohort Study. *PLoS Med* 2013, 10(4):e1001425.

A retrospective, population-based, cohort study (N = 1,010,068; 1994-2008) examined whether preeclampsia and gestational HTN were RF for postpartum diabetes. Preeclampsia, alone, (HR = 2.1 [95% CI: 2.0–2.2]) and gestational HTN, alone, (HR=2.0 [1.8–2.1]) were RF for developing diabetes in women followed for more than 15 years postpartum. Gestational diabetes mellitus (GDM), alone, conferred an elevated risk of postpartum diabetes (HR=12.8 [12.4–13.1]) and the additional presence of preeclampsia or gestational HTN further elevated this risk (HR=15.8, [14.5–17.1] and HR=18.5 [17.1-20.0], respectively). Longitudinal data on obesity, a potential confounder, were absent. A history of preeclampsia or GDM should alert clinicians to the need for preventative counseling and vigilant screening for future diabetes.

***Cardiovascular Disease (Non-Hypertensive Disorders of Pregnancy)***

([22](#_ENREF_22)) Kampman MAM, Balci A, van Veldhuisen DJ, van Dijk APJ, Roos-Hesselink JW, Sollie-Szarynska KM, Ludwig-Ruitenberg M, van Melle JP, Mulder BJM, Pieper PG *et al*: N-terminal pro-B-type natriuretic peptide predicts cardiovascular complications in pregnant women with congenital heart disease. *Eur Heart J* 2013. doi: 10.1093/eurheartj/eht526

This national, multicenter prospective cohort trial (N= 213, congenital heart disease patients) examined the role of N-terminal pro-B type natriuretic peptide (NT-proBNP) levels as a predictor of adverse cardiovascular outcomes in parturients with congenital heart disease. In the 10% of pregnancies with adverse outcomes, NT-proBNP >128 pg/mL at 20-weeks gestation, the presence of a mechanical valve, and subpulmonary ventricular dysfunction before conception were each independently associated with adverse events (OR = 10.6 [P <0.039], OR = 12.0 [P < 0.016], and OR = 4.2 [P <0.041]), respectively. NT-proBNP >128 pg/mL at 20 weeks had additional benefit in predicting cardiovascular events in addition to other identified RF (P= 0.035). The negative predictive value of NT-proBNP < 128 pg/mL was 96.9%. It may be useful to pre-screen NT-proBNP levels in these parturients for risk stratification.

([23](#_ENREF_23)) Kao DP, Hsich E, Lindenfeld J: Characteristics, Adverse Events, and Racial Differences Among Delivering Mothers With Peripartum Cardiomyopathy. *JACC: Heart Failure* 2013, 1(5):409--416.

This multi-state retrospective study of peripartum cardiomyopathy (PPCM) compared maternal and fetal outcomes for “delivering mothers” with (N = 535) and without (N = 4,003,379) PPCM. Classical RF for PPCM (i.e. >30 years old, African American race, HTN, preeclampsia/eclampsia) and novel RF (i.e. anemia and asthma) were found to be significantly associated in the multivariate analysis. The rate of PPCM increased exponentially with each additional associated RF. The authors propose a “multi-hit” hypothesis for the observed associations between PPCM and autoimmune disease and PPCM and substance abuse. A composite of major adverse maternal events (i.e. death, cardiac arrest, heart transplantation, or mechanical circulatory support) were also significantly associated with PPCM (OR = 436 [95% CI: 303.1-607.7]).

**Maternal Comorbid Disease (Direct Causes)**

***Hypertensive Disorders of Pregnancy***

General

**(**[**24**](#_ENREF_24)**) American College of Obstetrics and Gynecology: Task force on hypertension in pregnancy. *Obstet Gynecol* 2013; 122: 1122-1131.**

This publication provides evidence-based recommendations for clinical practice related to HDP according to the Grading of Recommendations Assessment, Development & Evaluation (GRADE) Working Group (<http://www.gradeworkinggroup.org/index.htm>). Overall, the diagnostic criteria from 2002 were continued with the following modifications: 1) If HTN and signs or symptoms of systemic disease are present after 20 weeks, proteinuria is not required for diagnosis of preeclampsia, 2) fetal growth restriction is no longer a signature finding indicative of severe preeclampsia, and 3) “mild” preeclampsia is removed from the nomenclature. Strategies for treating patients with HDP and insights into the available evidence on screening appropriateness, preventive strategies, and management of current and future disease in women with a history of HDP are also discussed.

Risk Factors

([25](#_ENREF_25)) Boyd HA, Tahir H, Wohlfahrt J, Melbye M: Associations of personal and family preeclampsia history with the risk of early-, intermediate- and late-onset preeclampsia. *Am J Epidem* 2013, 178(11):1611-1619.

This observational study (N = 1,377,479; 1978-2008) examined the recurrence and familial aggregation of preeclampsia by onset timing as a marker of severity, using personal and family histories of women delivering live singletons in Denmark. Primary results demonstrate that early onset preeclampsia (EO-PE) appears to have the biggest genetic component (strongest associations among female relatives, ranges from 24-163%), while late onset preeclampsia (LO-PE) is more susceptible to environmental factors. Previous EO-, intermediate-, or LO-PE increased the risk of recurrent preeclampsia with the same timing of onset 25.2 times (95% CI: 21.8-29.1), 19.7 times (17.0-22.8), and 10.3 times (9.9-10.9), respectively, vs. no such history. The role of paternal genes in the etiology of preeclampsia appears to be limited.

([26](#_ENREF_26)) Lisonkova S, Joseph KS: Incidence of preeclampsia: Risk factors and outcomes associated with early- versus late-onset disease. *Am J Obstet Gynecol* 2013, 209(6): 544e1-12.

In this state population-based study (N = 456,668; 2003-2008), the timing of preeclampsia onset was found to be correlated with the degree of maternal and fetal morbidity. Early onset disease (<34 0/7 weeks’ gestational age) was associated with a substantially higher risk of perinatal death or severe neonatal morbidity (aOR = 16.4 [95% CI: 14.5-18.6]) and was more strongly associated with risk factors such as chronic hypertension and African race compared with later onset disease (aOR = 2.0 [1.8-2.3]). Late-onset disease was more strongly associated with younger maternal age, nulliparity, and diabetes. The findings suggest that preeclampsia is heterogeneous, and that the timing of disease may be an indicator of both disease severity and possibly distinct etiologies.

Eclampsia

([27](#_ENREF_27)) Fong A, Chau CT, Pan D, Ogunyemi DA: Clinical morbidities, trends, and demographics of eclampsia: a population- based study. *Am J Obstet Gynecol* 2013, 209(3):229.e221-227.

This state-based study describes the trends, demographics and morbidities of eclamptic (N = 1,888) compared to normotensive women (N = 2,768,983; 2001- 2007). The incidence of eclampsia has declined, from 8 to 5.6 cases per 10,000 deliveries. Antepartum morbidities positively associated with eclampsia include preexisting cardiac disease (OR = 6.8 [95% CI: 5.4-8.7]), lupus (OR = 3.7 [1.5-8.9]), and twin gestation (OR = 3.3 [2.7-4.09]). Peripartum complications associated with eclampsia include cerebrovascular hemorrhage/disorders (OR = 112.2 [77.5-162.4]), cardiomyopathy (OR = 12.9 [6.1-27.3]), amniotic fluid embolism (OR = 11.9 [3.6-39.2]), and venous thromboembolism (OR = 10.7 [5.1-22.3]). While eclampsia is in temporal decline, it remains associated with severe morbidity.

([28](#_ENREF_28)) van Veen TR, Panerai RB, Haeri S, Griffioen AC, Zeeman GG, Belfort MA: Cerebral autoregulation in normal pregnancy and preeclampsia. *Obstet Gynecol* 2013, 122(5):1064-1069.

This prospective cohort study (N = 40) queried whether preeclampsia is associated with dynamic cerebral autoregulation, by comparing measures of cerebral blood flow velocity of the middle cerebral artery (via transcranial Doppler), BP (via noninvasive arterial volume clamping), and end-tidal CO2 during a resting period in women with preeclampsia and normotensive women. From these metrics, an autoregulation index was calculated between 0 (absent) to 9 (perfect). The autoregulation index was significantly reduced in women with preeclampsia (5.5+1.7 vs. 6.7+0.6, P = 0.004), as well as the resistance index, pulsatility index, resistance-area product and cerebral perfusion pressure. There was no correlation between the autoregulation index and BP. This suggests that women with preeclampsia have impaired dynamic cerebral autoregulation, and may explain why cerebral complications (i.e. eclampsia) can occur without sudden or excessive BP spikes.

Therapy

**(**[**29**](#_ENREF_29)**) Churchill D, Duley L, JG T, Jones L: Interventionist versus expectant care for severe pre eclampsia before term. *Cochrane Db Syst Rev* 2013(7):CD003106.**
This Cochrane meta-analysis (4 trials, N = 425 women) included all adequately RCTs comparing interventionist (“aggressive”) with expectant care (“delayed delivery”) for women with severe early onset preeclampsia (24 to <34 weeks). There was insufficient data to compare maternal outcomes or effects on stillbirth or neonatal death after delivery. Neonatal outcomes for mothers with interventionist treatment included more intraventricular hemorrhage (RR = 1.8 [95% CI: 1.1- 3.1]), hyaline membrane disease (RR = 2.3 [1.4-3.8]) more ventilation requirement (RR = 1.5 [1.1- 2.0]), lower gestation at birth in days (average mean difference (AMD) = -9.9 [-16.4 to -3.5]), more NICU admissions (RR = 1.4 [1.2-1.6]) and longer NICU stays (AMD = 11.1 days [1.6-20.7]). The interventionalist group were more likely to have a CD (RR = 1.1 [1.0-1.2]). The expectant approach may be associated with decreased fetal morbidity but follow-up studies are needed.

**(**[**30**](#_ENREF_30)**) Duley L, Meher S, Jones L: Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Db Syst Rev* 2013, 7:CD001449.**

A Cochrane meta-analysis (35 RCTs, N=3,573 women) weighed the efficacy of 15 antihypertensive medications in women with severe HTN in pregnancy. The authors concluded that until better evidence is available, the choice of antihypertensive medication should depend on practitioner choice, adverse effects and patient preferences. They recommend avoiding nimodipine, diazoxide, ketanserin, and MgSO4 (although indicated as an anticonvulsant for prevention/treatment of eclampsia).

**(**[**31**](#_ENREF_31)**) Shekhar S, Sharma C, Thakur S, Verma S: Oral nifedipine or intravenous labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. *Obstet Gynecol* 2013, 122(5):1057- 1063.**

This RCT (N = 60) in women with severe preeclampsia and HTN examined the time to achieve target BP <150 mmHg/100 mmHg using nifedipine oral (10 mg x 5 doses) and saline injections, or IV labetalol injections and placebo tablets. Median endpoint time to reach target BP was 40 min (IQR = 20-60 min) and 60 min (IQR = 40-85 min) for nifedipine and labetalol, respectively (P = 0.008). Median dose was a third less for nifedipine than labetalol (P = 0.008). Neither groups experienced drug-related adverse maternal or perinatal side effects. The labetalol group was marked with a higher failure rate requiring cross-over into the other group. These findings indicate that oral nifedipine lowers BP during a hypertensive emergency, and addresses concerns regarding overshoot hypotension in this population.

Fetal Outcomes

([32](#_ENREF_32)) Strand KM, Heimstad R, Iversen AC, Austgulen R, Lydersen S, Andersen GL, Irgens LM, Vik T: Mediators of the association between pre-eclampsia and cerebral palsy: population based cohort study. *Br Med J* 2013, 347:f4089.

This population-based cohort study (Norwegian Cerebral Palsy Registry and Medical Birth Registry; N = 849 with CP and N = 616,658 without CP) assessed the risk of developing cerebral palsy (CP) in relation to exposure to preeclampsia. The effect of preeclampsia on CP was found to vary with duration of pregnancy. At term, preeclampsia, alone, was not associated with increased CP but small for gestational age babies were three times more likely to have CP. Very preterm but appropriately grown and preeclampsia-exposed babies had half the risk of CP compared to unexposed babies. Overall, there was no evidence for a direct effect of preeclampsia on the risk of CP.

*Related Content*Gibbins KJ, Browning KR, Lopes VV, Anderson BL, Rouse DJ: Evaluation of the clinical use of magnesium sulfate for cerebral palsy prevention. *Obstet Gynecol* 2013, 121(2, PART 1):235-240.

Future Disease

**(**[**33**](#_ENREF_33)**) Mannisto T, Mendola P, Vaarasmaki M, Jarvelin MR, Hartikainen AL, Pouta A, Suvanto E: Elevated blood pressure in pregnancy and subsequent chronic disease risk. *Circulation* 2013, 127(6):681-690.**

This long-term, prospective study (Northern Finland Birth Cohort, N = 12,055; 1966 data) explored lifetime cardiovascular disease (CVD) risk after pregnancy-related HTN. Average follow up time was 39.4 years. HTN during pregnancy was associated with an increased risk of future CVD and hypertension. Gestational HTN was associated with death from myocardial infarct, kidney disease, heart failure, myocardial infarcts, ischemic stroke, diabetes, and ischemic heart disease (HR ranging from 3.0 to 1.4). Isolated systolic HTN was associated with an increased risk of myocardial infarct death, heart failure, and diabetes (HR ranging from 2.2 to 1.4). Isolated diastolic HTN was only associated with an increased risk of ischemic heart disease (HR 1.3). These associations remained even in women without known classical RF. Isolated systolic/diastolic HTN was also associated with subsequent risk.

([34](#_ENREF_34)) Ranthe MF, Andersen EA, Wohlfahrt J, Bundgaard H, Melbye M, Boyd HA: Pregnancy loss and later risk of atherosclerotic disease. *Circulation* 2013, 127(17):1775-1782.

This retrospective cohort study (N= 1,031,279; 1977-2008) analyzed the relationship between pregnancy loss (stillbirth and miscarriage) and atherosclerotic disease (myocardial infarctions, cerebral infarctions, renovascular HTN). Compared to women without pregnany loss, the incidence rate ratio of women with stillbirth was 2.7 (95% CI; 2.1-3.5), 1.7 (1.3-2.3), and 2.4 (1.6-3.7) for myocardial infarction, cerebral infarction, and renovascular HTN respectively. Women with miscarriages had 1.1 (1.0-1.2), 1.2 (1.1-1.3), and 1.2 (1.1-1.4) times the rates of these same ordered outcomes. Each additional miscarriage increased the rates of the outcomes by 9-19%. The findings support a shared etiology of inflammatory pathology. Women with a history of pregnancy loss should be carefully monitored for risk of atherosclerotic disease.

# PREGNANCY: INTRAPARTUM

 **Labor**

***Preterm Labor***

Risks

**(**[**35**](#_ENREF_35)**) Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, Lackritz EM, Lee SK, Mason E, Serazin AC *et al*: Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet* 2013, 381(9862):223-234.**

This analysis of PTD in 39 countries was undertaken to identify a rate reduction target to accomplish previously identified WHO/multi-national organizational goals. The estimated 2010 PTD rate in high income countries varies from 5.3 per 100 (Latvia) to 14.7 per 100 live births (Cyprus). In the US, where the PTD rate is paradoxically increasing, half of the change is unexplained, although non-medically indicated labor induction and CD and assisted reproductive techniques are important drivers. A conservative target of a relative reduction in PTD rates of 5% by 2015 was put forth which projects to roughly 58,000 PTDs averted and total annual economic cost savings of about US $3 billion.

*Associated Content: Comment on*Norman, J. E. and A. H. Shennan: Prevention of preterm birth--why can't we do any better? *Lancet* 2013, 381(9862): 184-185.

**(**[**36**](#_ENREF_36)**) Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, Granath F: Maternal obesity and risk of preterm delivery. *JAMA* 2013, 309(22):2362-2370.**

This population-based cohort study (Swedish Medical Birth Register; N = 1.5 million; 1992-2010) analyzed the association of maternal obesity and risk of PTD. Risk of extremely, very, and moderately PTD increased with BMI, and the overweight and obesity related risks were greatest among extremely PTD (22-27 weeks). Risk of spontaneous extremely PTD increased with BMI >30, as did risks of medically indicated PTD. The authors posit that inflammatory mediators might be the cause.

Related Therapy

([37](#_ENREF_37)) Brownfoot FC, Gagliardi DI, Bain E, Middleton P, Crowther DA. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2013, 8: CD006764.

This meta-analysis (12 trials; N = 1557 women, N=1661 infants) assessed the efficacy and timing of antenatal corticosteroids to prevent respiratory distress syndrome (RDS) in preterm infants. Dexamethasone was associated with a reduced risk of intraventricular hemorrhage (RR = 0.44; [95% CI: 0.21 to 0.92]), and a modestly shorter NICU length of stay (mean difference = -0.91 days [-1.77 to -0.05]) vs. β-methasone. No statistically significant differences were seen for RDS or perinatal death, or other biophysical parameters. Oral vs. intramuscular dexamethasone may increase the risk of neonatal sepsis (RR = 8.48 [1.11 to 64.93]). Results suggest that 12-hr dosing may be as effective as 24-hr dosing. There is a paucity of long-term data on which to base recommendations.

([38](#_ENREF_38)) American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 139: Premature rupture of membranes. *Obstet Gynecol* 2013, 122: 918-930.

This practice bulletin provided an updated expert-opinion and evidence-based management recommendations for premature rupture of membrane (PROM). Key components were 1) for PROM patients < 34 0/7 weeks, expectant management (without maternal or fetal contraindications) and a 7-day course of antibiotic therapy to reduce risk of infection and 2) For patients between 24 0/7 – 34 0/7 weeks with threatened preterm delivery, a single course of corticosteroids. In the setting of PROM with active labor, therapeutic tocolysis is not recommended as it has not been proven to prolong latency or benefit neonatal outcomes.

**(**[**39**](#_ENREF_39)**) Roos C, Spaanderman ME, Schuit E, Bloemenkamp KW, Bolte AC, Cornette J, Duvekot JJ, van Eyck J, Franssen MT, de Groot CJ *et al*: Effect of maintenance tocolysis with nifedipine in threatened preterm labor on perinatal outcomes: a randomized controlled trial. *JAMA* 2013, 309(1):41-47.**

This double blind RCT (N = 406) found that maintenance tocolysis with nifedipine does not reduce adverse perinatal outcomes related to PTD. However, more work is needed to draw definitive conclusions since the control arm had fewer adverse outcomes than anticipated. This research, combined with previous findings, suggests that the problem with nifedipine is not that it is ineffective as a uterine relaxant, but rather that treatment of uterine contractions to prevent PTD is an ineffective strategy.

**(**[**40**](#_ENREF_40)**) Crowther CA, McKinlay CJ, Middleton P, Harding JE: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. *Cochrane Db Syst Rev* 2013, (6):CD003935.**

This Cochrane meta-analysis (10 RCT: N = 4,730 women, N = 5,650 babies, low-moderate risk of bias) demonstrated that women who had already received a single course of corticosteroids >7 days previously and still had risk of PTD (23-34 weeks) benefited from an additional course in terms of reduced risk of the primary outcomes: respiratory distress syndrome (RR = 0.8, [95% CI: 0.8 -0.9], 8 trials, 3,206 infants, *numbers needed to treat (NNT*) 17) and serious infant outcome (RR = 0.8 [0.8 -0.9], 7 trials, 5,094 infants, *NNT* 30). Treatment with repeat dose(s) of corticosteroid was associated with a reduction in mean birth weight (mean difference = -75.8 g [-117.6 to -34.0], 9 trials, 5,626 infants). However, outcomes that adjusted birth weight for gestational age did not differ between treatment groups. Also, at early childhood follow-up, no significant differences were seen for exposed or unexposed infants for the primary or secondary outcome growth assessments. The authors conclude that the short-term benefits for babies of less respiratory distress and fewer serious health problems in the first few weeks after birth support the use of repeat dose(s) of prenatal corticosteroids for women still at risk of preterm birth 7 days or more after an initial course.

***Induction of Labor***

Methods

([41](#_ENREF_41)) Jozwiak M, Ten Eikelder M, Rengerink KO, de Groot C, Feitsma H, Spaanderman M, van Pampus M, de Leeuw JW, Mol BW, Bloemenkamp K *et al*: Foley Catheter versus Vaginal Misoprostol: Randomized Controlled Trial (PROBAAT-M Study) and Systematic Review and Meta-Analysis of Literature. *Am J Perinatol* 2013. Advance publish online, doi: DOI: 10.1055/s-0033-1341573

This RCT (N = 120 women) assessed differences in CD rate (primary outcome), maternal and neonatal morbidity and time to birth (secondary outcomes) in women with singleton term pregnancies randomized to 30-mL Foley catheter (N = 56) or 25-mcg vaginal misoprostol tablets (N = 64) for induction. CD rates did not differ significantly between groups. In the Foley catheter group, more CD due to failure to progress occurred (14% vs. 3%; RR = 4.6, 95% CI 1.0 to 20.6) and time from induction to birth was longer (36 hrs vs. 25 hrs; p < 0.001). Meta-analysis showed no difference in CD rate (moderate heterogeneity)and reduced instrumented VD (no heterogeneity)and hyperstimulation with FHR changes (low heterogeneity) in the Foley catheter group. All other outcomes were comparable. Overall, the authors support the use of the Foley catheter as an alternative cervical ripening agent to misoprostol.

Maternal and Fetal Effects

([42](#_ENREF_42)) Chen HY, Chauhan SP, Grobman WA, Ananth CV, Vintzileos AM, Abuhamad AZ: Association of labor induction or stimulation with infant mortality in women with failed versus successful trial of labor after prior cesarean. *J Matern Fetal Neonatal Med* 2013, 26(12):1162-1165.

This cohort study (N = 164,113; 2000-2004) used linked birth and infant death data to investigate whether TOLAC at 34-41 weeks was associated with increased infant mortality. These women had “induction” or “stimulation” of labor. After adjustment for potential confounding factors, a failed TOLAC (which occurred 41% of the time) was found to be associated with a 1.4 fold (95% CI: 1.1-1.7) increased risk of infant mortality and this effect was true at virtually every gestational week assessed. Noted limitations included an inability to determine the events leading to fetal demise or the indications for CD and a lack of comparison data between women undergoing TOLAC vs. planned repeat CD. Although women who had a failed TOLAC had a statistically higher chance of infant mortality, the attributable risk was small (0.7 per 1000). What we cannot tell from this study is the optimal plan for a woman with a prior CD who requires delivery for fetal or maternal indications.

([43](#_ENREF_43)) Darney BG, Snowden JM, Cheng YW, et al: Elective induction of labor at term compared with expectant management: Maternal and neonatal outcomes. *Obstet Gynecol* 2013, 122(4): 761-769.

This retrospective state-based study (N = 362,154) investigated CD rate, perinatal mortality and NICU admission rate for elective term induction vs. expectant management. The odds of CD were lower among women with elective induction vs. expectant management across all gestational age and parity: at 37 weeks OR = 0.4 (95% CI: 0.3-0.6); 38 weeks OR = 0.4 (0.4 -0.5), 39 weeks OR = 0.5 (0.4-0.5), 40 weeks OR = 0.6 (0.5-0.6). Elective induction was not associated with increased odds of severe lacerations, operative VD, perinatal death, NICU admission, respiratory distress, or macrosomia but was associated with increased odds of hyperbilirubinemia at 37 and 38 weeks and shoulder dystocia at 39 weeks.

**(**[**44**](#_ENREF_44)**) Gregory SG, Anthopolos R, Osgood CE, Grotegut CA, Miranda M: Association of autism with induced or**

**augmented childbirth in north carolina birth record (1990-1998) and education research (1997-2007) databases. *JAMA Pediatrics* 2013, 167(10):959-966.**

This retrospective review (North Carolina Detailed Birth Records; N = 625,042) examined whether induced and/or augmented births were associated with a higher odds of autism by using school records with 5,500 documented autism cases. Roughly 1.3% of male and 0.4% of female children were diagnosed with autism. In successive statistical models, researchers found that children had an increased odds for autism if born to mothers who were induced only (1.1 [95% CI: 1.0-1.2]), or augmented only (1.2 [1.1 -1.2]) or induced and augmented (1.3 [1.0-1.5]). There are several limitations to this study, including the lack of control for important residual confounders (e.g. indications for induction, obesity), some of which have also increased over the time period, and the unexplained overall decrease in autism over the time in the dataset.

*Associated Content: Editorial*Vintzileos AM, Ananth CV: Does augmentation or induction of labor with oxytocin increase the risk for autism? *Am J Obstet Gynecol* 2013; 209:502-4.

Other

([45](#_ENREF_45)) Balki M, Erik-Soussi M, Kingdom J, Carvalho JC: Oxytocin pretreatment attenuates oxytocin-induced contractions in human myometrium in vitro. *Anesthesiology* 2013, 119(3):552-561.

This *in vitro* interventional study measured the contractile response of human pregnant myometrium to oxytocin pretreatment (N = 62). Pretreatment with oxytocin 10-5 and 10-8 M significantly reduced motility index (P = 0.005 and P = 0.02, respectively) and area under the curve (AUC, P = 0.04 and P = 0.05, respectively), whereas pretreatment with oxytocin 10-10 M did not. Increase in duration of oxytocin pretreatment also significantly decreased amplitude (P = 0.003), motility index (P = 0.03), and AUC (P = 0.02), but not the frequency of contractions. These findings are clinically applicable to adverse obstetrical outcomes (e.g., PPH from uterine atony, uterine hyperstimulation) found in other studies of high-dose oxytocin induction methods.

***PO Status During Labor***

([46](#_ENREF_46)) Vallejo MC, Cobb BT, Steen TL, Singh S, Phelps AL: Maternal outcomes in women supplemented with a high-protein drink in labour. *Aust N Z J Obstet Gynaecol* 2013, 53(4):369-374.

This randomized interventional study (N = 150) assessed whether a high protein drink supplementation (Group P; 325 ml) in labor affected nausea, emesis, patient satisfaction, and rate of gastric emptying. There were no differences in the overall incidence of nausea and emesis between groups. Median patient satisfaction scores were higher in Group P than in Group C (water/ice chips) (P = 0.007). To evaluate gastric emptying, 18 additional patients were added and ultrasound gastric emptying t½ rates were analyzed (PG = 25.5 ± 15.9 min [95% CI: 15.2 – 35.9] vs. CG = 20.0 ± 8.7 min [14.3 – 25.7], P = 0.2)]. Patient satisfaction in labor was improved with high-protein drink supplementation vs. ice chips/water with similar rates of side effects and gastric emptying.

***Delivery Setting***

([47](#_ENREF_47)) de Jonge A, Mesman JA, Mannien J, Zwart JJ, van Dillen J, van Roosmalen J: Severe adverse maternal outcomes among low risk women with planned home versus hospital births in the Netherlands: nationwide cohort study. *Br Med J* 2013, 346:f3263.

This Netherlands cohort study (N = 92,333) investigated the morbidity associated with home births in low risk women. The rate of severe acute maternal morbidity (ICU admission, eclampsia, blood transfusion of four or more packed cells, and other serious events) among planned primary care births was 2.0 per 1,000 births. Low risk women in primary care at the onset of labor with planned home birth had lower rates of severe acute maternal morbidity, PPH, and manual removal of placenta than those with planned hospital birth. For parous women, these differences were statistically significant. Absolute risks were small in both groups. Ultimately, there was little evidence that planned home birth among low risk women leads to an increased risk of severe adverse maternal outcomes in a quality maternity care system.

**Labor Analgesia**

***Neuraxial Anesthesia***Spinal vs. CSE

**(**[**48**](#_ENREF_48)**) Gambling D, Berkowitz J, Farrell TR, Pue A, Shay D: A randomized controlled comparison of epidural analgesia and combined spinal-epidural analgesia in a private practice setting: pain scores during first and second stages of labor and at delivery. *Anesth Analg* 2013, 116(3):636-643.**

In this prospective, single-center RCT (N=800) investigators assessed verbal pain scores during the 1st and 2nd stages of labor and at delivery (primary outcome) in women receiving combined spinal epidural (CSE) or traditional epidural analgesia. The average “typical” verbal rating pain score during the 1st stage was lower in the CSE group (1.4 vs. 1.9; P < 0.001). Pain scores during the 2nd stage of labor and at delivery were the same between groups. Fewer patients received epidural top-up doses in the CSE group (16.4% vs. 25.6%; P = 0.002). Side effects (itching, fetal bradycardia) were more common in CSE group. There were no emergency CD in either group. Comparatively, CSE analgesia provided better 1st stage analgesia (although pain scores were low in both) and fewer epidural top-up injections by an anesthesiologist.

*Associated Content: Editorial*Booth JL, Pan PH: Combined spinal epidural or traditional epidural technique: who wins? *Anesth Analg* 2013, 116(3):515-516.

Predictors

([49](#_ENREF_49)) Guglielminotti J, Mentre F, Bedairia E, Montravers P, Longrois D: Development and evaluation of a score to predict difficult epidural placement during labor. *Reg Anesth Pain Med* 2013, 38(3):233-238.

This study was designed to prospectively develop and validate a 3 risk group score to predict difficult epidural placement (DEP) during labor. Three independent RF for DEP were identified: difficult interspinous space palpation (OR= 6.1 [95% CI: 2.8-13.9]), spinal deformity (OR=2.4 [1.1-5.3]), and inability to flex the back (OR= 3.0 [1.2-7.8]). The C-index of the model was 0.81 (0.74-0.88) in the training set and 0.78 (0.70-0.86) in the validation set. A 5-point score was then created to define groups with low risk (score 0), intermediate risk (score 1-2), and high risk (score 3-4), with predicted rates of DEP of 9.7%, 30.3%, and 68.9%, respectively. The C-index of the score was 0.79 [0.72-0.86] in the training set and 0.76 [0.69-0.84] in the validation set. DEP frequency was 30%. Dural puncture was more frequent in DEP patients (4% vs. 0%, P = 0.007). This score may be useful in counseling patients about risk of inadvertent dural puncture and in planning which patients might particularly benefit from ultrasound guided placement.

Dosing

([50](#_ENREF_50)) Mhyre J, Hong R, Greenfield MH, Pace N, Polley L: The median local analgesic dose of intrathecal bupivacaine with hydromorphone for labour: a double-blind randomized controlled trial. *Can J Anesth* 2013, 60(11):1061-1069.

This double-blind RCT (N= 88 laboring parturients) tested the hypothesis that intrathecal hydromorphone (100 mcg) reduces the dose requirement for intrathecal bupivacaine to induce rapid analgesia for women in the 1st stage of labor. A decrease was observed in the median local analgesic doses (effective dose [ED50]) estimated according to the formulas of Dixon and Massey, with a between-group difference of −0.45 mg). However, since the estimate had a wide range (95% CI: −1.2 to 0.3), no definitive conclusion can be drawn.

([51](#_ENREF_51)) Morrison AP, Hunter JM, Halpern SH, Banerjee A: Effect of intrathecal magnesium in the presence or absence of local anaesthetic with and without lipophilic opioids: a systematic review and meta-analysis. *Br J Anaesth* 2013, 110(5):702-712.

This systematic review and meta-analysis (N=15 trials; N = 980 patients) included RCTs in patients undergoing all types of surgery and in women in labor that compared the effect of intrathecal Mg+/- local anesthetic (LA) +/- lipophilic opioid (experimental group) with the use of either intrathecal lipophilic opioids +/- LA or LA only (control group) on duration of spinal anesthesia (primary outcome), onset and time to maximal sensory blockade, onset of motor block, and duration of sensory and motor blockade (secondary outcomes). Increased duration of spinal anesthesia was seen in the experimental group in the non-obstetric studies (standard mean difference (SMD) = -1.4 [P = 0.0002]), but not in obstetric studies (SMD -0.6 [P = 0.41]). Onset of motor and sensory blockade and incidence of hypotension and pruritus was similar between groups. Unfortunately, heterogeneity was high in all outcome measures (I2 = 88-94%).

([52](#_ENREF_52)) George RB, Allen TK, Habib AS: Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: a systematic review and meta-analysis. *Anesth Analg* 2013, 116(1):133-144.

This systematic review and meta-analysis of RCTs (N=9 trials; N = 694; all with low risk of bias) compared the performance of continuous epidural infusion (CEI) with intermittent epidural bolus (IEB) for labor analgesia. There was no statistical difference detected between IEB and CEI in the rate of CD or the need for anesthetic intervention. IEB did result in a weakly significant reduction in local anesthetic usage (MD, -1.2 mg bupivacaine equivalent per hr; [95% CI, -2.2 to -0.3]). Maternal satisfaction score (100-mm visual analog scale) was higher with IEB (MD, 7.0 mm; [6.2-7.8]). Heterogeneity was very low.

([53](#_ENREF_53)) Abdallah FW, Abrishami A, Brull R: The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. *Anesth Analg* 2013, 117(1):271-278 .

This systematic review and meta-analysis included RCTs (7 trials, intermediate to high quality; N=364 patients) that investigated the effects of IV administration of dexmedetomidine on single-injection local anesthetic-based spinal anesthesia. Sensory block duration was prolonged by IV dexmedetomidine by 38% (P < 0.00001), motor block duration was prolonged by 21% (P < 0.00001), and time to first analgesic request was increased by 60% (P < 0.00001). The use of dexmedetomidine was associated with a 3.7-fold increase (P = 0.004) in transient reversible bradycardia and there was no difference in the incidence of hypotension or postoperative sedation, and none of the patients experienced respiratory depression.

**(**[**54**](#_ENREF_54)**) Sia AT, Leo S, Ocampo CE: A randomised comparison of variable-frequency automated mandatory boluses with a basal infusion for patient-controlled epidural analgesia during labour and delivery. *Anaesthesia* 2013, 68(3):267-275.**

This RCT (N=102) compared the analgesic efficacy of administering variable-frequency automated boluses (5 ml 0.1% ropivacaine + fentanyl 2 mic/ml) at a rate proportional to the patient's needs with fixed continuous basal infusion in patient-controlled epidural analgesia during labor and delivery. The incidence of breakthrough pain requiring supplementation was significantly lower in the automated bolus group compared with the infusion group (5.9% vs. 23.5%, P = 0.023). The time-weighted mean (SD) hourly consumption of ropivacaine was similar in both groups. Parturients from the automated bolus group reported higher satisfaction scores compared with those in the infusion group (96.5 vs. 89.2/100, respectively [p < 0.001]). There was no difference in the incidence of maternal side effects or in obstetric and neonatal outcomes.

([55](#_ENREF_55)) **Sultan P, Murphy C, Halpern S, Carvalho B: The effect of low concentrations versus high concentrations of local anesthetics for labour analgesia on obstetric and anesthetic outcomes: a meta-analysis. *Can J Anaesth* 2013, 60(9):840-854.**

This meta-analysis of RCTs (11 trials; N= 1,997 women) examined whether low concentration (LC) local anesthetics (N= 1,145 patients) vs. high concentration (HC) local anesthetics (N = 852 patients) were associated with a decreased incidence of assisted vaginal delivery. LC was defined as < 0.1% bupivacaine or <0.17% ropivacaine. A reduction in the incidence of assisted VD was found for HC vs. LC (OR = 0.7, P < 0.001). Heterogenity was low for this outcome. There was no difference in the incidence of CD (OR 1.1, P = 0.7). The LC group also had significantly less motor block, greater ambulation, less urinary retention, and a shorter 2nd stage of labor compared with the HC group. There were no differences between groups in pain scores, maternal nausea and vomiting, hypotension, fetal heart rate abnormalities, 5-minApgar scores, and need for neonatal resuscitation. There was more pruritus in the LC group and greater odds of 1-min Apgar scores < 7 in the LC group, perhaps due to the higher concentrations of neuraxial fentanyl. Overall, LC local anesthetics are recommended for labor epidural analgesia to optimize obstetric outcome.

([56](#_ENREF_56)) Pratt S, Hess P, Vasudevan A: A prospective randomized trial of lidocaine 30 mg versus 45 mg for epidural test dose for intrathecal injection in the obstetric population. *Anesth Analg* 2013, 116(1):125-132.

This prospective, double-blinded RCT (N=100) evaluated whether lidocaine 30 mg epidural test dose was as effective as 45 mg epidural test dose in creating subjective or objective evidence of sensory or motor block within 3 mins. When administered intrathecally, both 30mg and 45mg produced rapid evidence of spinal sensory blockade at 3 mins (100% patients). Motor blockade was found in 83% of 30mg and 100% 45mg at 3 mins. When administered epidurally, at 3 mins, no patient in the 30mg and 2 patients in 45mg group had motor blocks; however several patients had subjective heavy or warm feelings in both groups. Side effects were not decreased with 30mg. On basis of a intrathecal catheter rate of 1:380, the negative predictive value of no sensory change at 3 mins was 100% for epidural 30mg (95% CI, 99.9-100.5) and 100% for 45mg (99.9-100.5) but the positive predictive value was low (specificity was 74% [55-88%] with epidural 30mg and 59% [41-74%] with epidural 45 mg). Ultimately, the authors were unable to confirm whether the 30mg test dose was a better discriminator because of the small sample size.

*Associated Content: Editorial*Mhyre JM: Why do pharmacologic test doses fail to identify the unintended intrathecal catheter in obstetrics? *Anesth Analg* 2013, 116(1):4-5.

Evaluation

**(**[**57**](#_ENREF_57)**) Thangamuthu A, Russell IF, Purva M: Epidural failure rate using a standardised definition. *Int J Obstet Anesth* 2013, 22(4):310-315.**

This study proposes a standardized definition of epidural failure using a modified Delphi approach. Using experts from the Obstetric Anaesthetists’ Association (OAA) Executive Committee, anonymized and detailed data from 1,521 epidurals insertions were included. Epidural failure was defined as having one or more of the following characteristics: lack of adequate pain relief by 45 min, dural puncture, re-siting the epidural or abandoning the procedure, or maternal dissatisfaction at the follow-up visit. The overall failure rate was 23% (most commonly due to inadequate pain relief), but generally improved with training time (Year 2, 3, 4 vs.5). The re-site rate was significantly higher for Year 2 and Year 4 trainees vs. Year 5 and above. The accidental dural puncture rate was highest among Year 3 trainees (2.2%). Cervical dilatation, time of day, and position for insertion were not significantly associated with the failure rate. A standardized definition of epidural failure can be useful both in quality assessment and for consistency across research investigations.

***Other Labor Analgesia***

Hypnosis

([58](#_ENREF_58)) Werner A, Uldbjerg N, Zachariae R, Rosen G, Nohr E: Self-hypnosis for coping with labour pain: a randomised controlled trial. *Br J Obstet Gynecol* 2013, 120(3):346-353.

In this RCT (N=1,222), an intervention group of nulliparous women was provided a brief course in self-hypnosis (three 1-hr courses and audio-recordings) to ease childbirth pain. No differences in use of epidural analgesia (primary outcome) or self-reported pain experience (secondary outcome) were found across study groups. The authors comment that there may be particular patient subgroups or different training regimens that are more effective.

([59](#_ENREF_59)) Cyna AM, Crowther CA, Robinson JS, Andrew MI, Antoniou G, Baghurst P: Hypnosis Antenatal Training for Childbirth: a randomised controlled trial. *Br J Obstet Gynecol:* 2013, 120(10):1248-1259.

This RCT (N=448 women) tested whether antenatal hypnosis with or without accompanying compact discs (CD) vs. a control group without either reduced the need for pharmacological analgesia. No difference was found comparing hypnosis + CD with control, or comparing CD only with control. The Hypnosis Antenatal Training for Childbirth (HATCh) intervention with CD did not reduce the use of pharmacological analgesia during childbirth.

Remifentanil

([60](#_ENREF_60)) Tveit TO, Halvorsen A, Seiler S, Rosland JH: Efficacy and side effects of intravenous remifentanil patient- controlled analgesia used in a stepwise approach for labour: an observational study. *Int J Obstet Anesth* 2013, 22(1):19-25.

In this prospective, observational study (N=41), pain scores were examined during the 1st and 2nd stages of labor using IV patient-controlled analgesia with remifentanil using stepwise bolus doses without background infusion. Pain scores were significantly reduced in the first 3 hr of patient-controlled analgesia compared to baseline, and at the end of the 1st and 2nd stages of labor (P<0.05). Maximal pain reduction was 60% (P<0.01). The mean highest dose of remifentanil was 0.7mcg/kg [range 0.3-1.0]. Ninety-three percent (93%) of patients were satisfied with their analgesia. The lowest O2 saturation was 91%, the lowest respiratory rate was 9 breaths/min and 27% parturients received supplemental O2 due to O2 saturations <92%. Monitoring (maternal O2 sat and heart rate) was considered to be mandatory as maternal sedation was moderate. Neonatal data was reassuring.

*Associated content*
Kranke P, Girard T, Lavand'homme P, Melber A, Jokinen J, Muellenbach RM, Wirbelauer J, Honig A: Must we press on until a young mother dies? Remifentanil patient controlled analgesia in labour may not be suited as a "poor man's epidural". *BMC pregnancy and childbirth* 2013, 13:139.

**Cesarean Delivery**

***Malplacentation***

([61](#_ENREF_61)) Weiniger CF, Einav S, Deutsch L, Ginosar Y, Ezra Y, Eid L: Outcomes of prospectively-collected consecutive cases of antenatal-suspected placenta accreta. *Int J Obstet Anesth* 2013, 22(4):273-279.

This prospective study developed a predictive score for antenatal diagnosis of placenta accreta via mathematical modeling using 3 clinical variables (placenta previa, number of previous CD and/or ultrasound suspicion of placenta accreta) followed by surgically confirmed diagnosis. 52/92 (56%) cases were confirmed surgically. From the ROC curve, a cut-point with 94.2% (95% CI: 84.1-98.8%) and 52.5% specificity (36.1-68.5%) was achieved, compared with 86.6% sensitivity (74.2%–94.4%) and 60.0% specificity (43.3%–75.1%) using ultrasound alone. As this was a proof-of-concept study, findings require further validation before clinical application.

([62](#_ENREF_62)) Kamara M, Henderson J, Doherty D, Dickinson J, Pennell C: The risk of placenta accreta following primary elective caesarean delivery: a case-control study. *Br J Obstet Gynecol* 2013, 120(7):879-886.

This retrospective case-control study (N=177) compared the risk of placenta accreta in subsequent pregnancies with placenta previa following a primary CD without labor vs. a primary emergency CD. Compared with primary emergency CD, primary elective CD significantly increased the risk of placenta accreta in a subsequent pregnancy in the presence of placenta previa (OR = 3.0; 95% CI 1.5-6.1; P = 0.025). This suggests that the active and inactive human uterus may represent two phenotypically distinct entities.

***Cesarean vs. Vaginal Delivery***

General

([63](#_ENREF_63)) Boyle A, Reddy UM, Landy HJ, Huang CC, Driggers RW, Laughon SK: Primary cesarean delivery in the United States. *Obstet Gynecol* 2013, 122(1): 33-40.

This retrospective cohort study (N=38,484 CD/228,562 total deliveries; 2002-2008) at participating sites in the Consortium on Safe Labor sought to identify strategies to promote VD. The most common indications for primary CD were failure to progress (35.4%), non-reassuring fetal heart rate tracing (27.3%), and fetal malpresentation (18.5%); frequencies for each indication varied by parity. In “failure to progress”, 42.6% of primiparous women and 33.5% of multiparous women never progressed beyond 5 cm dilation before delivery. In women who reached the 2nd stage of labor, 17.3% underwent CD for arrest of descent before 2 hrs, and only 1.1% was given a trial of operative VD. 45.6% of primary CD was performed on primiparous women at term with a singleton fetus in cephalic position. The authors recommend using 6 cm as the active labor cut off, allowing sufficient time for the 2nd stage of labor, when appropriate, and encouraging operative VD to reduce the primary CD rate, particularly in the primiparous woman at term with a singleton fetus in cephalic presentation.

Maternal Request

**(**[**64**](#_ENREF_64)**) American College of Obstetrics and Gynecology: ACOG committee opinion no. 559: Cesarean delivery on maternal request. *Obstet Gynecol* 2013, 121(4):904-907.**

The ACOG Committee on Obstetric Practice defines *CD on maternal request* as a primary prelabor CD (on maternal request) in the absence of maternal or fetal implications. The potential risks are said to include an increase risk of infant respiratory difficulties and greater complications in subsequent pregnancies. Potential short-term benefits of planned CD vs. planned VD (which could lead to unplanned CD) include decreased risk of hemorrhage, transfusion and urinary incontinence in the 1st year postpartum and fewer surgical complications. Overall, the committee concluded that VD is safe and appropriate in the absence of maternal or fetal indications for CD. When CD on maternal request is planned, delivery should not be performed before 39 weeks gestation or be motivated by the unavailability of effective pain management, or be undertaken in women desiring several children.

([65](#_ENREF_65)) Karlstrom A, Lindgren H, Hildingsson I: Maternal and infant outcome after caesarean section without recorded medical indication: findings from a Swedish case-control study. *Br J Obstet Gynecol* 2013, 120(4):479-486.

This retrospective case-control study (Swedish Medical Birth Registry; N=19,651) assessed women undergoing CD without medical indication (N= 5,877) and a control group (N=13,774) with spontaneous onset of labor (some of whom had VD and others who had unplanned CD) for maternal and fetal outcomes. Maternal complications were more common in women undergoing CD, specifically, bleeding complications, OR = 2.5 (95% CI: 2.1-3.0) for elective CD and 2.0 (95% CI: 1.5-2.6) for emergency CD group with OR = 2.6 in both groups for infection. Breastfeeding complications were most common in women having an elective CD, OR = 6.8 (95% CI: 3.2-14.5). Infants had higher incidence of respiratory distress (OR = 2.7 (95% CI: 1.8-3.9)) in the elective CD group vs. emergency CD group. Overall, CD was associated with higher incidence of maternal and fetal morbidity.

*Associated Content: Comment On*Bhide, A: Commentary on Maternal and infant outcome after caesarean section without recorded medical indication: findings from a Swedish case-control study. *Br J Obstet Gynecol*2013, 120(4): 486.

***Infection***

([66](#_ENREF_66)) Baaqeel H, Baaqeel R: Timing of administration of prophylactic antibiotics for caesarean section: a systematic review and meta-analysis. *Br J Obstet Gynecol*2013, 120(6):661-669.

This systematic review and meta-analysis (6 RCTs; N= 2,313 women and N= 2,345 newborns) compared maternal and neonatal outcomes with preoperative vs. intraoperative administration of antibiotics. Preoperative antibiotic administration was associated with a significantly lower rate of endometritis compared with intraoperative administration (RR = 0.6 [95% CI: 0.4 -0.9]). In the preoperative group, there were nonsignificant reductions in the rates of wound infection (RR = 0.7 [0.4-1.1]) maternal febrile morbidity (RR = 0.9 [0.5 -2.0]), neonatal sepsis (RR = 0.8 [0.5 -1.4]), neonatal septic work-up (RR = 0.9 [0.7-1.2]) and NICU admission (RR = 0.9 [0.7 -1.3]). There were nonsignificant increases in the rates of maternal pyelonephritis (RR = 1.1 [0.5 -2.4]) and neonatal pneumonia (RR = 3.4 [0.6 -20.5]). The analyses had minimal heterogeneity. However, the lack of neonatal adverse effects should be cautiously interpreted given the limited power of the trials to detect such effects.

*Associated Content: Letter to the Author(s) and Reply*Jørgensen J, Hyldig N, Weber T and Lamont R: Timing of antibiotic prophylaxis for caesarean section. *Br J Obstet Gynecol* 2013, 120: 778.

Baaqeel H, and Baaqeel R: Timing of antibiotic prophylaxis for caesarean section. *Br J Obstet Gynecol* 2013, 120: 778–779.

([67](#_ENREF_67)) Duggal N, Poddatorri V, Noroozkhani S, Siddik-Ahmad RI, Caughey AB: Perioperative oxygen supplementation and surgical site infection after cesarean delivery: a randomized trial. *Obstet Gynecol* 2013, 122(1):79-84.

In this double-blinded, prospective RCT (N = 831), investigators evaluated whether supplemental perioperative O2 decreases surgical site wound infections or endometritis up to 6 weeks postpartum. The allocation was to either 30% FI02 or 80% FI02 O2 during the CD and for 1 hr post-op. An intention-to-treat analysis found no significant difference in surgical site infection or in endometritis. Overall, administration of 80% vs. 30% supplemental O2 did not confer a lower rate of a surgical site infection.

*Related Content*Klingel ML, Patel SV: A meta-analysis of the effect of inspired oxygen concentration on the incidence of surgical site infection following cesarean section. *Int J Obstet Anesth* 2013, 22(2):104-112.

***Other***

([68](#_ENREF_68)) Rosseland LA, Hauge TH, Grindheim G, Stubhaug A, Langesæter E: Changes in blood pressure and cardiac output during cesarean delivery: The effects of oxytocin and carbetocin compared with placebo. *Anesthesiology* 2013, 119:541-551

This is a double-blinded RCT (N = 77) comparing the effects of 100 mcg carbetocin (N = 26), 5 U IV oxytocin (N = 25), and placebo (N = 26) on hemodynamics, uterine tone, adverse events and blood loss after elective CD under spinal anesthesia. Heart rate and cardiac output increased in all groups, and stroke volume increased after oxytocin and carbetocin but remained unchanged for placebo. The hemodynamic side effects of the two intervention drugs were comparable, with modestly different time courses. The absence of stroke volume increase in the placebo group challenges the theory that uterine contraction causes autotransfusion of uterine blood, which, in turn, increases preload.

**Cesarean Delivery Anesthesia**

 ***Neuraxial Anesthesia***

**(**[**69**](#_ENREF_69)**) Jain K, Bhardwaj N, Sharma A, Kaur J, Kumar P: A randomised comparison of the effects of low-dose spinal or general anaesthesia on umbilical cord blood gases during caesarean delivery of growth-restricted foetuses with impaired Doppler flow. *Eur J Anaesthesiol* 2013, 30(1):9-15.**

This prospective, RCT (N=40) explored the effects of low-dose spinal (LDSA) (8mg hyperbaric bupivacaine 0.5% with fentanyl 20 mcg) vs. standard general anesthesia (GA) on the umbilical cord gases of growth restricted fetuses for elective CD. Systolic BP was maintained between 80-100% of baseline. There was no difference in the primary outcome variables of mean umbilical cord arterial and venous base deficit. The mean umbilical artery pH was significantly lower in the LDSA group than in the GA group (7.2 +/- 0.1 vs. 7.3 +/- 0.04, P = 0.01). Higher partial pressures of O2 occurred in the GA group (20.9 +/- 6.5 kPa) than in the LDSA group (13.6 +/- 6.1 kPa, P = 0.001). LDSA was associated with hypotension of short duration (0.7+/-1.1 min) and adequate surgical block. No difference was observed between groups in 1 and 5-min Apgar scores. Limitations of this study include small sample size, very low intrathecal dose, and mixed etiologies of growth restricted fetuses. Studies with larger sample sizes and more homogeneous patients are needed to confirm whether there are clinically important differences in neonatal acidosis in patients with vulnerable fetuses who receive LDSA vs. GA.

*Associated Content: Comment On*Habib AS: Anaesthesia for caesarean delivery of growth-restricted foetuses: a bird in the hand is worth two in the bush. *Eur J Anaesthesiol* 2013, 30(1):5-6.

([70](#_ENREF_70)) Kathirgamanathan A, Douglas MJ, Tyler J, Saran S, Gunka V, Preston R, Kliffer P: Speed of spinal vs general anaesthesia for category-1 caesarean section: a simulation and clinical observation-based study. *Anaesthesia* 2013, 68(7): 753-759.

This simulation study addressed the question of whether effective spinal anesthesia can occur as quickly as general anesthesia (GA) for a category-1 CD (non-elective, emergency). To test this, 16 consultants and 3 fellows were timed performing spinal and GA for simulated category-1 CD. Time to spinal block attainment was estimated from 100 actual cases. The median (IQR [range]) times for spinal procedure, onset of spinal block and GA were 2:56 min (2:32 - 3:32 [1:22 - 3:50]), 5:56 (4:23 - 7:39 [2:9 - 13:32]) and 1:56 min (1:39 - 2:9 [1:13 - 3:12]), respectively. The limiting factor in urgent spinal anesthesia was found to be the unpredictable time needed for adequate surgical block to develop.

([71](#_ENREF_71)) Beatty NC, Arendt KW, Niesen AD, Wittwer ED, Jacob AK: Analgesia after Cesarean delivery: a retrospective comparison of intrathecal hydromorphone and morphine. *J Clin Anesth* 2013, 25(5):379- 383.

This retrospective, comparative study (N=114) investigated analgesia and side effects of intrathecal morphine and intrathecal hydromorphone in patien0ts after elective CD. The authors found that among 38 patients who received intrathecal hydromorphone 0.04 mg, compared with 76 patients given 0.1 mg of intrathecal morphine, there were no significant differences in overall frequency of opioid-related complications (primary outcome), or 24-hr opioid consumption, or pain scores at any time point up to 24 hours (secondary outcomes). This study is timely given the relative lack of availability of intrathecal morphine.

([72](#_ENREF_72)) Subedi A, Biswas BK, Tripathi M, Bhattarai BK, Pokharel K: Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: a randomised, double-blind study. *Int J Obstet Anesth*2013, 22(4):316-321.

This double-blind, RCT (N=80) evaluated the effect of adding intrathecal tramadol (10 mg) to intrathecal hyperbaric bupivacaine (10 mg) vs. intrathecal fentanyl (10mug) to the same local anesthetic dose for elective CD on the resulting block characteristics and neonatal outcome. Median [IQR] duration of postoperative analgesia in the tramadol and the fentanyl groups was 300 [240-360] min and 260 [233-300] min, respectively (P=0.02). The incidence of shivering was lower in patients who received tramadol than those who received fentanyl (5% vs. 32%, P=0.003). Apgar scores, umbilical cord acid-base measurement and neurologic and adaptive capacity scores were equivalent between the two groups. Adding intrathecal tramadol (10mg) instead of fentanyl (10 mcg) to spinal anesthesia for CD may increase duration and decrease maternal shivering.

**(**[**73**](#_ENREF_73)**)** **Singh SI, Rehou S, Marmai KL, Jones, M. P: The efficacy of 2 doses of epidural morphine for postcesarean delivery analgesia: A randomized noninferiority trial. *Anesth Analg* 2013, 117(3):677-685.**

This double-blinded, noninferiority RCT (N= 90) investigated whether half the traditional dose of epidural morphine (EM, 1.5mg) was associated with noninferior analgesia and fewer side effects as part of multimodal therapy for pain relief after CD . Noninferiority was demonstrated as the difference in median 24-hr opioid consumption between groups less than the pre-specified 3.33 mg. No significant differences were found between the 3.0mg and 1.5mg EM groups in the median 24- to 48-hr additional opioid consumption or total opioid consumption within 48 hr. Pain scores, overall pain relief, and satisfaction at 24, 48-hr, and 12 weeks were also not significantly different. The 1.5 mg EM group had less moderate and severe pruritus at 6 and 12 hr (RR 0.4 [95% CI, 0.2–0.9] and RR 0.4 [0.2–0.8], respectively) and had less nausea and vomiting at 6 hrs (RR 0.2 [0.1–0.9]). When used as part of a multimodal analgesia regimen, the 1.5 mg of epidural morphine provided noninferior post-CD analgesia and caused fewer side effects.

***General Anesthesia***

Airway

**(**[**74**](#_ENREF_74)**) Quinn AC, Milne D, Columb M, Gorton H, Knight M: Failed tracheal intubation in obstetric anaesthesia: 2 year national case-control study in the UK. *Br J Anaesth* 2013, 110(1):74-80.**

This case-control study (N = 57 completed reports [100% response]; 2008-2010) estimated the rate RF of failed intubation in OB anesthesia using the UK Obstetric Surveillance System. The incidence of failed intubation (defined as “failure to achieve tracheal intubation during a rapid sequence induction, thereby initiating a failed intubation drill”) was estimated to be 1 per 224 (95% CI: 179-281). Controls were GA’s administered to parturients without failed intubation. Multivariate analyses showed that age, BMI, and a recorded Mallampati score were significant independent predictors of failed tracheal intubation. The risk for failed intubation was greater for a junior trainee than when a consultant was present (2.4 [1.1-5.5], p=0.4). The classical LMA was the most commonly used rescue airway. There was one emergency surgical airway but no deaths or hypoxic brain injuries. Gastric aspiration occurred in 8% of index cases. Index cases were more likely to have maternal morbidities.

**(**[**75**](#_ENREF_75)**) Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, Hagberg CA, Caplan RA, Benumof JL, Berry FA *et al*: Practice Guidelines for Management of the Difficult Airway: An Updated Report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2013, 118(2):251-270.**

Updated (and largely unchanged) recommendations on “Practice guidlines for postanesthetic care”. Of

note, it was determined that there is insufficient new literature to further assess and refine the general

recommendations that “periodic assessment and monitoring of airway patency, respiratory rate and oxygen

saturation” be done during emergence and recovery. One new RCT corroborates the original findings/guidelines

that administration of supplemental oxygen during patient transportation or in the recovery room reduces the

incidence of hypoxemia, although the experts were equivocal as to whether such oxygen administration should be

routine for patients who are not deemed to be at high risk for hypoxemia

*Related Content*Law JA, Broemling N, Cooper R, Drolet P, Duggan L, Griesdale D, Hung O, Jones P, Kovacs G, Massey S *et al*: The difficult airway with recommendations for management – Part 1 – Difficult tracheal intubation encountered in an unconscious/induced patient. *Can J Anesth* 2013, 60(11):1089-1118.Law JA, Broemling N, Cooper R, Drolet P, Duggan L, Griesdale D, Hung O, Jones P, Kovacs G, Massey S *et al*: The difficult airway with recommendations for management – Part 2 – The anticipated difficult airway. *Can J Anesth* 2013, 60(11):1119-1138.

([76](#_ENREF_76)) Arenkiel B, Smitt M, Olsen KS: The duration of fibre-optic intubation is increased by cricoid pressure. A randomised double-blind study. *Acta anaesthesiologica Scandinavica* 2013, 57(3):358-363.

This study double-blind, cross-over RCT (N=50) evaluated the effect of cricoid pressure (CP) on the duration of fibre-optic intubation in non-obstetric patients. Three (3) intubations without CP and 13 with CP failed (i.e., were not completed in 180 s). The durations of intubation with/without CP were 59 s (34-144 s) and 75 s (43-179 s), respectively (P < 0.001). The study showed that CP prolongs the duration of fibre-optic intubation in patients with Mallampati grades 1-2.

**(**[**77**](#_ENREF_77)**) Yoo KY, Kang DH, Jeong H, Jeong CW, Choi YY, Lee J: A dose-response study of remifentanil for attenuation of the hypertensive response to laryngoscopy and tracheal intubation in severely preeclamptic women undergoing caesarean delivery under general anaesthesia. *Int J Obstet Anesth* 2013, 22(1):10-18.**

This RCT (N=75 women with severe preeclampsia) assigned severe preeclamptic patients to 1 of 5 remifentanil dose groups (0.25, 0.50, 0.75, 1.0, or 1.25mcg/kg) given before induction of anesthesia with thiopental 5mg/kg and suxamethonium 1.5mg/kg, then measured hypertensive response. ED(50) and ED(95) were 0.6 (95% CI 0.5-0.7) mcg/kg and 1.3 (1.0-2.2) mcg/kg, respectively. Norepinephrine concentrations remained unaltered following intubation but increased significantly at delivery, with no differences between the groups. Apgar scores and umbilical arterial, venous pH and blood gas values were comparable among the groups. The determined ED(95) of remifentanil for attenuating the hypertensive response to tracheal intubation during induction of anesthesia in severely preeclamptic patients undergoing CD under GA was 1.34 mcg/kg.

Postpartum Hemorrhage

([78](#_ENREF_78)) Heesen M, Hofmann T, Klohr S, Rossaint R, M VDV, Deprest J, Straube S: Is general anaesthesia for caesarean section associated with postpartum haemorrhage? Systematic review and meta-analysis. *Acta Anaesth Scand* 2013, 57(9):1092-1102.

This meta-analysis of 18 articles (N=12,330 parturients) reviewed the effect of general (GA) vs. neuraxial anesthesia on estimated blood loss and transfusion requirements after CD. Analysis of non-randomized trials found a significantly higher transfusion requirement after GA (RR=5.1 [95% CI 2.5-10.3] P<0.00001) but the heterogeneity of the studies was very high. In the few RCTs, the difference was not statistically significant. As such, these findings are of unclear clinical significance.

Intraoperative Awareness

([79](#_ENREF_79)) Mashour GA, Kent C, Picton P, Ramachandran SK, Tremper KK, Turner CR, Shanks A, Avidan MS: Assessment of Intraoperative Awareness with Explicit Recall: A Comparison of 2 Methods. *Anesth Analg* 2013, 116(4):889-891.

This single institution patient cohort study (N=18,836) investigated the whether the modified Brice interview (MBI) was superior to quality assurance (QA) techniques for detecting intraoperative awareness with explicit recall (AWR) under GA. Review of completed MBIs, 28-30 days post-op, revealed a 0.1% incidence of AWR. A review of QA records for the same period revealed a 0.02% incidence of AWR reported on routine post-op for a statistically significant difference. The MBI provided a better detection of AWR (P<0.0001) suggesting that that prior data from QA measures may have underestimated rates due to methodological issues. Although variation in interview timing may have influenced results, previous research suggests that this would not account for the magnitude of difference demonstrated in this study.

***TAP Blocks***

**(**[**80**](#_ENREF_80)**) Singh S, Dhir S, Marmai K, Rehou S, Silva M, Bradbury C: Efficacy of ultrasound-guided transversus abdominis plane blocks for post-cesarean delivery analgesia: a double-blind, dose-comparison, placebo-controlled randomized trial. *Int J Obstet Anesth*2013, 22(3):188-193.**

This double-blind, RCT (N=60) investigated the impact of adding either high-dose (HD) ropivacaine (3mg/kg), low-dose (LD) ropivacaine (1.5mg/kg) or no ultrasound-guided TAP block to standard multimodal therapy for CD. Neither HD nor LD TAP blocks as part of a multimodal analgesia regimen which included intrathecal morphine, improved pain scores with movement at 24 hr (primary outcome). The mean pain scores with movement at 6 hr and 12 hr were lower in the HD TAP group vs. the LD and placebo groups (P=0.009) and (P=0.011), respectively (secondary outcomes). There were no differences in pain scores at rest or in breakthrough opioid consumption.

([81](#_ENREF_81)) Lee AJ, Palte HD, Chehade JM, Arheart KL, Ranasinghe JS, Penning DH: Ultrasound-guided bilateral transversus abdominis plane blocks in conjunction with intrathecal morphine for postcesarean analgesia. *J Clin Anesth* 2013, 25(6): 475-485.

This double-blinded, RCT (N=51 women) sought to determine whether TAP blocks with ropivacaine as an adjunct to intrathecal morphine (CSE anesthetics) offered superior analgesia for post CD pain when compared to intrathecal morphine alone. Although the ropivacaine group reported better short term pain management at 2 hr (P < 0.001); by 24 hr, the two groups were similar in pain scores and analgesia consumption. At 48 hr, the ropivacaine group received more analgesics for moderate pain (P = 0.04) whereas the placebo group received more analgesics for severe pain (P = 0.01). The data was not supportive of TAP blocks providing additional analgesia relief beyond the 2 hr post-operative time interval.

**(**[**82**](#_ENREF_82)**) Griffiths JD, Le NV, Grant S, Bjorksten A, Hebbard P, Royse C: Symptomatic local anaesthetic toxicity and plasma ropivacaine concentrations after transversus abdominis plane block for Caesarean section. *Br J Anesth* 2013, 110(6):996-1000.**

This interventional study (N = 30) assessed total and free serum ropivacaine concentrations in parturients undergoing bilateral TAP blocks (2.5 mg/kg of ropivacaine diluted to 40 ml) and spinal anesthesia for CD. The mean (standard deviation) peak total concentration of ropivacaine occurred at 30 min post-injection and was 1.8 (0.69) mcg/ml (max= 3.8 mcg/ml, at 10 min post-injection). Three patients reported symptoms of mild neurotoxicity with elevated mean peak levels. TAP blocks can result in elevated plasma ropivacaine concentrations in patients undergoing CD which may be associated with neurotoxicity.

**PREGNANCY: POSTPARTUM**

**Maternal Morbidity/Mortality**

***Postpartum Hemorrhage and Hemostasis***

Epidemiology/Risk Stratification of Post Partum Hemorrhage

([83](#_ENREF_83)) Dilla AJ, Waters JH, Yazer MH: Clinical validation of risk stratification criteria for peripartum hemorrhage. *Obstet Gynecol* 2013, 122(1):120-126.

This retrospective cohort study (N = 10,134) aimed to validate the California Maternal Quality Care Collaborative (CMQCC) risk groups prediction of PPH and the need for peripartum pretransfusion testing. By identifying 5 novel RF for PPH not present in the preexisting CMQCC framework, investigators were able to re-categorize and capture 85% of the women who ultimately had PPH into a modified high- risk group. Women in this high-risk group are particularly suitable for peripartum pretransfusion testing.

([84](#_ENREF_84)) Mhyre, JM, Shilkrut A, Kuklina EV, Callaghan WM, Creanga AA, Kaminsky S, Bateman, BT: Massive blood transfusion during hospitalization for delivery in New York State, 1998-2007. *Obstet Gynecol* 2013, 122(6): 1288-1294.

This retrospective state-based review of delivery hospitalizations (N = 690,742) found that massive blood transfusion (MBT) complicated 6 per 10,000 deliveries, with cases observed even in the smallest facilities. RF having the strongest independent associations with MBT included abnormal placentation, placental abruption, severe preeclampsia, and intrauterine fetal demise. The most common etiologies of MBT were abnormal placentation, uterine atony, abruption, and PPH associated with coagulopathy (ranging 27% to 15%). A disproportionate number of women who received a MBT experienced severe morbidity including renal failure, acute respiratory distress syndrome, sepsis, and in-hospital death. In the presence of known RF, women should be duly informed, should ideally deliver in a well-resourced facility and receive appropriate blood product preparation and venous access before delivery.

**(**[**85**](#_ENREF_85)**) Kramer MS, Berg C, Abenhaim H, Dahhou M, Rouleau J, Mehrabadi A, Joseph KS: Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. *Amer J Obstet Gynecol* 2013, 209(5):449 e441-447.**

In this U.S. population-based retrospective study (N = 8,571,209 deliveries), a growing rate of severe PPH from 1.9 to 4.2 per 1,000 deliveries was noted from 1999 to 2008. The increases included atonic and nonatonic PPH, in particular PPH with transfusion but also with hysterectomy. RF were CD, multiple pregnancy, fibroids, and advanced maternal age. Changes related to known RF accounted for only of the 5.6% increase. The contributions of labor augmentation, obesity, or stillbirth timing couldn’t be assessed and may play a major role.

*Associated Content: Clinical Opinion*Gibbins KJ, Albright CM, Rouse DJ: Postpartum hemorrhage in the developed world: whither misoprostol? *Amer J Obstet Gynecol* 2013, 208(3):181-183.

Prevention/Management of Postpartum Hemorrhage

**(**[**86**](#_ENREF_86)**) Tuncalp O, Souza JP, Gulmezoglu M: New WHO recommendations on prevention and treatment of postpartum hemorrhage. *Int J Obstet Gynecol* 2013, 123(3):254-256.**

An overview of the most recent WHO guidelines for prevention and treatment of PPH, with an emphasis on key messages and changes aimed at achieving the Millennium Development Goal 5. Strategies include usual prevention and treatment of PPH (oxytocin 10 U IV/IM proceeding to 2nd and 3rd line agents, intrauterine balloon tamponade, uterine artery ligation, and surgical intervention if persistent) and, if needed, temporizing measures (e.g. bimanual uterine compression, external aortic compression, non-pneumatic anti-shock garments).

**(**[**87**](#_ENREF_87)**) Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, Fries D, Gorlinger K, Haas T, Imberger G *et al*: Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2013, 30(6):270-382.**

These Guidelines from the European Society of Anesthesiology task force with graded evidence address the management of severe perioperative bleeding, reflecting research updates from 20,664 articles published between 2000-2012. Comprehensive sections are provided on gynecologic and obstetric bleeding which include the role of fibrinogen measurement in predicting PPH, transfusion thresholds, blood product and factor replacement, and the use of adjuncts (e.g. tranexamic acid and cell saver).

*Associated Content: Editorial*
Butwick AJ: Postpartum hemorrhage and low fibrinogen levels: the past, present and future. *Int J Obstet Anesth* 2013, 22(2):87-91.

([88](#_ENREF_88)) Abdel-Aleem H, Alhusaini TK, Abdel-Aleem MA, Menoufy M, Gulmezoglu AM: Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trial. *J Matern Fetal Neonatal Med* 2013, 26(17):1705-1709.

In this RCT (N = 740, women for elective CD at term), the intervention group (N = 373) that received 1 g tranexamic acid (TA) 10 min prior to CD were compared to a control group without TA (N = 367) for measured blood loss during and for two hr after delivery. Mean total blood loss was significantly less in TA vs. control group (241.6 [standard error = 6.8] vs. 510 [7.7]). Mild side effects (e.g. headache, nausea, vomiting) were more common in the TA group; however other complications, medications, and change in vital signs did not differ between groups. This intervention could prove particularly valuable to anemic women or those who refuse blood transfusion in the context of CD*.* We await the results of the WOMAN trial (an international randomized, double blind, placebo controlled trial [N>11,000] investigating TA for the treatment of PPH) for more definitive elucidation of this topic.

([89](#_ENREF_89)) Deneux-Tharaux C, Sentilhes L, Maillard F, Closset E, Vardon D, Lepercq J, Goffinet F: Effect of routine controlled cord traction as part of the active management of the third stage of labour on postpartum haemorrhage: multicentre randomised controlled trial (TRACOR). *Br Med J* 2013, 346:f1541.

This multicenter RCT investigated the impact of controlled cord traction (CCT) (N=2,005) and standard placenta expulsion (SPE) (N=2,008) on PPH outcome. The incidence of PPH and other markers of maternal blood loss did not differ between groups (9.8% vs 10.3% in the CCT vs SPE group, respectively), thus calling into question the appropriateness of routine CCT practice for PPH in high-resource settings. However, in the CCT group, the need for manual removal of the placenta was markedly less (RR = 0.7, 95% CI: 0.5-0.9), and those women also reported less pain/discomfort.

([90](#_ENREF_90)) Chen M, Chang Q, Duan T, He J, Zhang L, Liu X: Uterine massage to reduce blood loss after vaginal delivery: a randomized controlled trial. *Obstet Gynecol* 2013, 122(2 Pt 1):290-295.

This multicenter RCT compared whether random allocation of 10 U oxytocin immediately after VD of the baby’s shoulder plus 30 mins sustained transabdominal uterine massage after delivery of the placenta (N= 1,170) vs. 10 U of oxytocin alone (N = 1,170) influenced blood loss. No difference was found in the primary outcome of blood loss > 400 mL in 2 hrs, nor in any secondary outcomes. This result suggests that the routine practice of uterine massage as a preventative strategy for PPH may be ineffective and unnecessary, depending on available alternatives.

([91](#_ENREF_91)) Elagamy A, Abdelaziz A, Ellaithy M: The use of cell salvage in women undergoing cesarean hysterectomy for abnormal placentation. *Int J Obstet Anesth* 2013, 22(4):289-293.

This case series (N = 15) reports no amniotic fluid embolism, hypotension, sepsis or coagulopathy in women who received autologous blood after cell salvage in cesarean hysterectomy for placenta accreta and lends further support to its use.

([92](#_ENREF_92)) Rogers WK, Wernimont SA, Kumar GC, Bennett E, Chestnut DH: Acute Hypotension Associated with Intraoperative Cell Salvage Using a Leukocyte Depletion Filter During Management of Obstetric Hemorrhage Due to Amniotic Fluid Embolism. *Anesth Analg* 2013, 117(2):449-452.

This single case presentation describes an experience using of cell salvage in the resuscitation of a patient who had sustained an amniotic fluid embolus (AFE) during CD. Cell salvage with a leukocyte depletion filter was instituted at a time of relative hemodynamic stability, immediately after which the patient became profoundly hypotensive and desaturated. She was ultimately resusitated (rFVIIa was employed). This case raises the question of the safety of cell salvage in the setting of AFE.

***Identifying Who’s Sick***

**(**[**93**](#_ENREF_93)**) Saucedo M, Deneux-Tharaux C, Bouvier-Colle MH, French National Experts Committee on*Maternal*Mortality:** **Ten years of confidential inquiries into maternal deaths in France, 1998-2007. *Obstet Gynecol* 2013, 122(4):752-60.**

This retrospective review (French Confidential Enquiry into Maternal Deaths examined maternal deaths; N=660 maternal deaths; 1998-2007). Among maternal deaths identified, there was similar maternal mortality ratios in two 5-year periods: 8.8 per 100,000 live births (95% CI: 7.8-9.8) for 1998-2002 and 8.4/100,000 live births (95% CI 7.6-9.4) for 2003-2007. The distributions of maternal age, nationality, and of cause of death (COD) did not change: hemorrhage was the leading COD (18%), followed by amniotic fluid embolism, thromboembolism, HDP, and cardiovascular conditions (10-12%, each). Anesthesia complications accounted for 0.9 and 1.5% of deaths during the two time periods. Suboptimal care decreased from 70% in 1998-2002 to 60% in 2003-2007 (P<0.03). Half of all deaths were considered avoidable and this proportion was unchanged. The most frequent contributory factor was inadequate management, calling for improvements in care by all of involved providers.

*Associated Content: Editorial*

Main EK, Menard MK: Maternal Mortality: Time for National Action. *Obstet Gynecol* 2013, 122(4):735-736

**(**[**94**](#_ENREF_94)**) Foo L, Bewley S, Rudd A: Maternal death from stroke: a thirty year national retrospective review. *Eur J Obstet Gynecol Reprod Biol* 2013, 171(2):266-270.**

This retrospective study (UK confidential enquiries into maternal death; 1979-2008) investigated maternal mortality from stroke. Of 21,514,457 total maternities, there were 347 maternal stroke deaths (139 cases were “direct”, i.e., pregnancy-related). The incidence of fatal stroke was relatively constant at 1.61 per 100,000 maternities, with a 13.9% (95% CI: 12.6–15.3) mortality rate. Intracranial hemorrhage was the single greatest cause of maternal death from stroke. Sub-standard care involved poor management of dangerously high systolic BP levels. These findings highlight how improved education in managing rapid-onset hypertension and superimposed coagulopathies is paramount.

([95](#_ENREF_95)) Wanderer JP, Leffert LR, Mhyre JM, Kuklina EV, Callaghan WM, Bateman BT: Epidemiology of Obstetric-Related ICU Admissions in Maryland: 1999-2008. *Crit Care Med* 2013, 41(8):1844-1852.

This retrospective state-based study (N=2,927 ICU admissions; 1999-2008) examined the epidemiology of pregnancy-related ICU admissions. The rates of ICU utilization were 162.5, 202.6, and 54.0 per 100,000 deliveries for the antepartum, delivery, and postpartum periods, respectively. The leading diagnoses associated with ICU admission were HDP (29.9%), hemorrhage (18.8%), cardiomyopathy/other cardiac disease (18.3%), genitourinary infection (11.5%), complications from ectopic pregnancies and abortions (10.3%), non-genitourinary infection (10.1%), sepsis (7.1%), cerebrovascular disease (5.8%), and pulmonary embolism (3.7%). Assessment of changes over time found rising rates of sepsis (10.1 per 100,000 deliveries to 16.6 per 100,000 deliveries, p = 0.003) and trauma (9.2 per 100,000 deliveries to 13.6 per 100,000 deliveries, p = 0.026) with decreasing rates of anesthetic complications (11.3 per 100,000 to 4.7 per 100,000, p = 0.006). The overall frequency of obstetric-related ICU admission and the rates for other indications remained relatively stable.

**(**[**96**](#_ENREF_96)**) Bauer ME, Bateman BT, Bauer ST, Shanks AM, Mhyre JM: Maternal sepsis mortality and morbidity during hospitalization for delivery: temporal trends and independent associations for severe sepsis. *Anesth Analg* 2013, 117(4):944-950.**

This retrospective population-based study (National Inpatient Sample; N = 44,999,260 delivery hospitalizations; 1998 -2008) investigated peripartum sepsis. Sepsis complicated 1 per 3,333 (95% CI= 1:3,151-1:3,540) deliveries, severe sepsis (i.e. sepsis with acute organ dysfunction, hypotension, or hypoperfusion) complicated 1 in 10,823 (1:10,000-1:11,792) deliveries, and sepsis-related death complicated 1 in 105,263 (1:83,333-1:131,579) deliveries. While the overall frequency of sepsis was stable (P = 0.95), the risk of severe sepsis and sepsis-related death increased during the study period. Independent associations for severe sepsis, (with aOR and lower bound 95% CI > 3) include congestive heart failure, chronic liver disease, chronic renal disease, systemic lupus erythematous, and rescue cerclage placement. Since severe sepsis often occurs in the absence of recognized RF, we must develop systems of care that increase early disease detection as well as early treatment in patients with associated conditions and warning signs for sepsis.

**(**[**97**](#_ENREF_97)**)** **Lipman SS, Wong JY, Arafeh J, Cohen SE, Carvalho B: Transport decreases the quality of cardiopulmonary resuscitation during simulated maternal cardiac arrest. *Anesth Analg* 2013, 116(1):162-167.**

This simulation study (26 teams, 2 providers) investigated whether the quality of CPR for maternal cardiac arrest suffered during transport to the operating room (OR). The median (IQR) % of correctly rendered compressions in the multidisciplinary OR “transfer group” was 32% (10%-63%) vs. 93% (58%-100%) in the labor room “stationary” group, (P = 0.002). Interruptions in CPR were observed in 92% of transport and 7% of stationary drills (P < 0.001). Median (IQR) tidal volume was 270 (166-430) mL in the transport group and 390 (232-513) mL in the stationary group (P = 0.03). These data suggest that transport negatively affects the quality of resuscitation and strengthen recommendations that perimortem CD should be performed at the site of maternal cardiac arrest.

([98](#_ENREF_98)) American College of Obstetrics and Gynecology: Practice Bulletin No. 138: Inherited Thrombophilias in Pregnancy. *Obstet Gynecol* 2013, 122(3): 706-716.

This document provided a review on common thrombophilias and their association with maternal venous thromboembolism risk, and accompanying guidelines for screening and managing these conditions across the pregnancy continuum. Highlights include detection methods for Factor V Leiden and Prothombin G20210A mutations as well as protein C and antithrombin deficiencies; suggested prophylaxis for high risk women including compression boots/stockings and substitution to unfractionated heparin at 36 weeks to permit neuraxial anesthesia; and recommendations for continued therapy and monitoring 6 weeks postpartum.

***Anesthetic Complications/Side Effects***

Respiratory Depression

**(**[**99**](#_ENREF_99)**) Crowgey TR, Dominguez JE, Peterson-Layne C, Allen TK, Muir HA, Habib AS: A retrospective assessment of the incidence of respiratory depression after neuraxial morphine administration for postcesarean delivery analgesia. *Anesth Analg* 2013, 117(6):1368-1370.**

This single-center retrospective study (N= 5,036; mean BMI = 34) investigated respiratory depression events after neuraxial morphine administration for women undergoing CD. Most patients received either morphine 3 mg (epidural) or 1.5 mg (intrathecal). Patients also received non-steroidal anti-inflammatory drugs and Percocet (1-2 tablets) every 3-4 hr, as needed, for break-through pain. The majority of patients were obese. There were no instances of respiratory depression requiring naloxone administration or rapid response team involvement within 48 hr. Minor hypoventilation or desaturations were not measured. The upper 95% confidence limit for respiratory depression in this study was 0.07% (1 event per 1429 cases).

Local Anesthetic Toxicity

([100](#_ENREF_100)) Kuo I, Akpa BS: Validity of the lipid sink as a mechanism for the reversal of local anesthetic systemic toxicity: a physiologically based pharmacokinetic model study. *Anesthesiology* 2013, 118(6):1350-1361.

The authors generated a physiologically-based, pharmacokinetic model to quantitatively probe the merits of a lipid “sink” mechanism, exploring the binding action of plasma lipid. Lipid infusion after a simulated IV overdose was predicted to cause an increase in total plasma concentration, a decrease in unbound concentration, and a decrease in tissue content of bupivacaine. The model was validated in healthy human volunteers with nontoxic doses and then extended to the simulated conditions. Results suggest that the timescale on which tissue content is reduced varies among organs doesn’t fully match the effects observed in practice. This preliminary study suggests that the lipid “sink” is insufficient to fully explain reversal of systemic toxicity. Other mechanisms may include a positive ionotropic and/or metabolic effect of the lipid.

Epidural Hematomas

([101](#_ENREF_101)) Bateman BT, Mhyre JM, Ehrenfeld J, Kheterpal S, Abbey KR, Argalious M, Berman MF, Jacques PS, Levy W, Loeb RG *et al*: The risk and outcomes of epidural hematomas after perioperative and obstetric epidural catheterization: A report from the multicenter perioperative outcomes group research consortium. *Anesth Analg* 2013, 116(6):1380-1385

This multicenter retrospective observational study (Multicenter Perioperative Outcomes Group Consortium; N = 62,450) evaluated risks and outcomes for epidural hematomas in patients undergoing perioperative epidural catheterizations for OB or surgical indications. Seven (7) patients developed hematomas requiring surgical evacuation (event rate = 11.1x10-5 [95% CI: 4.5 x10-5 to 23.1x10-5]); none were OB patients (upper 95% CI: 4.6 x10-5 , P = 0.003). This corresponds to a rate of neurological injury of 1 per 12,000 epidural catheterizations. Of note, 4/7 cases had anticoagulation/antiplatelet therapy deviating from American Society of Regional Anesthesia guidelines on safety for neuraxial anesthesia. Data are lacking on hematomas managed non-operatively or from failed/aborted epidural placement. Findings supports that epidural hematoma is a rare but serious complication, especially in the OB population, and is often associated with inappropriate perioperative anticoagulant management or high risk patients.

*Associated Content: Editorial*Horlocker T, Kopp S: Epidural Hematoma After Epidural Blockade in the United States: It's Not Just Low Molecular Heparin Following Orthopedic Surgery Anymore. *Anesth Analg* 2013, 116(6):1195-1197

([102](#_ENREF_102)) Pumberger M, Memtsoudis SG, Stundner O, Herzog R, Boettner F, Gausden E, Hughes AP: An Analysis of the Safety of Epidural and Spinal Neuraxial Anesthesia in More Than 100,000 Consecutive Major Lower Extremity Joint Replacements. *Reg Anesth Pain Med* 2013, 38(6):515-519.

This retrospective study (N=100,027; 2000-10) analyzed the frequency of spinal/epidural hematomas in patients undergoing orthopedic joint arthroplasty under neuraxial anesthesia. Ninety-seven patients underwent imaging studies to evaluate perioperative neurologic deficits (1.0 per 1,000 [95% CI 0.8–1.2 per 1,000]). Eight patients were identified with findings of an epidural blood or gas collection (0.1 per 1,000 [0.02–0.1per 1,000]). No patients receiving only spinal anesthesia were affected. All patients diagnosed with hematoma took at least 1 anticoagulant. No patient incurred persistent nerve damage. The incidence of epidural/spinal complications found in this consecutive case series is relatively low but higher than previously reported in the non-OB population.

Post Dural Puncture Headache

([103](#_ENREF_103)) Heesen M, Klohr S, Rossaint R, Walters M, Straube S, van de Velde M: Insertion of an intrathecal catheter following accidental dural puncture: a meta-analysis. *Int J Obstet Anesth* 2013, 22(1):26-30.

This systematic literature search and meta-analysis (9 reports) pursued the efficacy of intrathecal catheter insertion after accidental dural puncture to prevent PDPH. Intrathecal catheter insertion reduced the risk for an epidural blood patch (RR=0.6 [95% CI 0.5-0.8], P=0.001), but not for developing a PDPH (P=0.06). However, there was high heterogeneity in the studies for the PDPH subgroup, and moderate heterogeneity for EBP subgroup. Additional benefits of intrathecal catheter insertion after accidental dural puncture include potentially avoiding a repeat dural puncture, rapid onset of action and use for anesthesia.

([104](#_ENREF_104)) Bradbury CL, Singh SI, Badder SR, Wakely LJ, Jones PM: Prevention of post-dural puncture headache in parturients: a systematic review and meta-analysis. *Acta Anaesth Scand* 2013, 57(4):417-430.

This systematic review and meta-analysis (40 RCTs; N = 11,536 CSE) evaluated 5 methods of reducing PDPH: prophylactic epidural blood patch (4 trials, median quality score = 2, risk difference (RD)= -0.5 [95% CI: -0.9 to -0.09]), lateral positioning of the epidural needle bevel upon insertion (1 trial, quality score = 1), Special Sprotte needles (1 trial, quality score = 5, RD = -0.44 [-0.67 to -0.21]), epidural morphine (1 trial, quality score = 4, RD = -0.36 [-0.59 to -0.13]), and cosyntropin [1 trial, quality score = 5, RD = -0.36 [ -0.55 to -0.16]). Special Sprotte needles, epidural morphine, and cosyntropin are thus far each supported by a single, good quality trial. Prophylactic blood patches are supported by 3 trials, but with flawed methodology. Most trials were of limited quality, and additional well-conducted, larger trials are needed.

**(**[**105**](#_ENREF_105)**)** **Basurto Ona X, Uriona Tuma SM, Martinez Garcia L, Sola I, Bonfill Cosp X: Drug therapy for preventing post-dural puncture headache. *Cochrane Db Syst Rev* 2013, 2:CD001792.**

This Cochrane review with intention-to-treat analysis (10 trials; N=1,611; 72% parturients) addressed the efficacy and safety of drugs for preventing PDPH in adults and children. Meta-analysis was not performed because of the heterogeneity of the studies. Epidural morphine and IV cosyntropin (1 mg) showed some effectiveness for preventing PDPH, especially in patients at high risk (i.e. OB patients with inadvertent dural puncture) compared to placebo. IV Aminophylline also reduced PDPH severity after a lumbar puncture vs. placebo when compared in patients undergoing elective CD. Neuraxial morphine increased the number of participants affected by side effects (e.g., pruritus, nausea, vomiting). IV Dexamethasone increased the risk of PDPH after spinal anesthesia for CD and oral caffeine increased insomnia. These conclusions should be interpreted carefully given the small sample sizes and the inability to correct for risk of bias.

Nausea/Vomiting

([106](#_ENREF_106)) Du BX, Song ZM, Wang K, Zhang H, Xu FY, Zou Z, Shi XY: Butorphanol prevents morphine-induced pruritus without increasing pain and other side effects: a systematic review of randomized controlled trials. *Can J Anaesth* 2013, 60(9):907-917.

This systematic review (16 RCT; N=795 patients) investigated the efficacy of butorphanol for preventing neuraxial morphine-induced pruritus. IV (infusion) and epidural butorphanol reduced pruritus with RR=0.2 (95% CI 0.1-0.4) and RR=0.2 (0.2-0.4), respectively. Epidural butorphanol decreased the number of patients requesting rescue treatment for pruritus (RR=0.6 [0.4 to 0.8]) (low heterogeneity) and reduced postoperative nausea and vomiting (RR=0.4 [0.2 to 0.7]) (moderate heterogeneity). Butorphanol also decreased postoperative pain intensity without increasing respiratory depression, somnolence, or dizziness.

([107](#_ENREF_107)) Habib AS, George RB, McKeen DM, William D, Ituk US, Megalla SA, Allen TK: Antiemetics Added to

Phenylephrine Infusion During Cesarean Delivery: A Randomized Controlled Trial. *Obstet Gynecol* 2013,

121(3):615-623.

This multicenter RCT (N = 300) investigated whether the addition of metoclopramide (given before spinal placement) or its

combination with ondansetron (given after cord clamping) to a prophylactic phenylephrine infusion provides improved

intraoperative nausea and vomiting (IONV) prophylaxis during CD. Intra-operative nausea and vomiting (IONV) occurred in 49%,

31%, and 23% of patients in the placebo, metoclopramide, and combination groups, respectively (P =0.001). Postop nausea and

vomiting were reduced in the combination (vs. placebo) at 2 hrs (39% vs. 20%; p<0.017) but not thereafter. Notably, surgical

factors (e.g., exteriorization of the uterus, surgical duration) contributed to a significant difference in IONV between the 2

centers but the results were still significant.

 **Postoperative Pain**
 ***Predictive Tools***

**(**[**108**](#_ENREF_108)**) Pan PH, Tonidandel AM, Aschenbrenner CA, Houle TT, Harris LC, Eisenach JC: Predicting acute pain after**

**cesarean delivery using three simple questions. *Anesthesiology* 2013, 118(5): 1170-1179.**

This study presented the development (N=200 women) and validation (N=151) of a predictive model of acute post-CD pain after spinal anesthetic for CD based a simple 3-item preoperative questionnaire documenting: 1) anticipated anxiety? (scale: 0-100), 2) anticipated pain? (scale: 0-100), and 3) anticipated pain medicine need? (scale: 0-5). Responses from these questions correlated moderately with 24 hr evoked pain intensity (r = 0.2-0.3, P < 0.001). Rating of intensity of audio tones contributed uniquely, but only minimally, and therefore was not included in the model. As constructed, the sensitivity and specificity for identifying patients in the top 20% for activity associated pain were both 0.69. Given the large variability in pain with activity after CD and the tendency to use a standard postoperative pain regimen for all patients, having a simple, predictive tool may be clinically meaningful.

*Associated Content: Editorial*Flood P, Wong CA: Chronic pain secondary to childbirth: Does it exist? *Anesthesiology* 2013; 118:16–8.

([109](#_ENREF_109)) Carvalho B, Zheng M, Aiono-Le Tagaloa L: Evaluation of experimental pain tests to predict labour pain and epidural analgesic consumption. *Br J Anaesth* 2013, 110(4):600-606.

This prospective, case-controlled study (N=50) determined whether experimental pain tests (EPTs) using heat, pressure, and IV cannulation (pre-induction of labor) reliably predicted epidural analgesic use and pain intensity during labor. Heat tolerance was significantly correlated with worst labor pain (r=0.3, P=0.025) and pain with IV cannulation was correlated with time to epidural request (r=0.33, P=0.025). Multiple linear regression analysis found that labor pain could be predicted with suprathreshold heat VAS, heat and pressure tolerance. Pre-labor EPTs were not reliable at predicting the labor pain experience, but pain rating during IV cannulation showed some utility as an EPT.

*Related Content: Editorial*
Carvalho B, Cohen SE: Measuring the labor pain experience: delivery still far off. *Int J Obstet Anesth* 2013, 22(1):6-9.

***Biological Profiles***

([110](#_ENREF_110)) Landau R, Liu SK, Blouin JL, Carvalho B: The Effect of OPRM1 and COMT Genotypes on the Analgesic Response to Intravenous Fentanyl Labor Analgesia. *Anesthesia and analgesia* 2013, 116(2):386-391.

This study (N=106) investigated whether Asn/Asn-Met/Met combination alters the analgesic response to IV Fentanyl compared to other combinations of these 2 genetic polymorphisms. The combined effect of the single-nucleotide polymorphisms rs1799971 (c.118A/G, p. 40Asn/Asp) of the micro-opioid receptor gene (OPRM1) and rs4680 (c.472G/A, p.158Val/Met) of the catechol-O-methyltransferase (COMT) gene are known from previous work to influence pain perception and opioid response in carriers. IV analgesic success was 6% in women with the combination Asn/Asn-Met/Met (N = 17) vs. 20% in all other women combined. Met/Met158 (n = 31) versus Met/Val or Val/Val of COMT was associated with a smaller decrease in Numerical Verbal Pain Scale (24 + 18 vs. 37 +23; P = 0.005). Unfortunately, this study was underpowered to draw clear conclusions on the influence of OPRM1 and COMT genotypes on labor analgesia with IV fentanyl.
 ***Chronic Pain***

([111](#_ENREF_111)) Liu TT, Raju A, Boesel T, Cyna AM, Tan SG: Chronic pain after caesarean delivery: an Australian cohort. *Anaesth Inten Care* 2013, 41(4):496-500.

This prospective study (N=426) investigated the incidence of and RF for persistent pain after CD. The incidence of persistent abdominal wound pain at 2 months was 14.6% and decreased to 4.2% at 12 months. Whereas at 2 months, pain was constant or daily in 7.8% of patients, by 12 months, only 1.1% had constant or daily mild pain. There was no apparent increased incidence of persistent pain associated with type of anesthesia, emergency vs. elective procedure, higher acute pain scores, or history of previous CD. By 12 months, <1% of women had pain requiring analgesia or disrupting mood/sleep.

*Related Content:*

Landau R, Bollag L, Ortner C: Chronic pain after childbirth. *Int J Obstet Anesth* 2013, 22(2):133-145.

([112](#_ENREF_112)) Eisenach JC, Pan P, Smiley RM, Lavand'homme P, Landau R, Houle TT: Resolution of pain after childbirth. *Anesthesiology* 2013, 118(1):143-151.

This study (N=1,223, both CD and VD patients) investigated predictors of pain 2 months after CD, and the incidence of pain at 6 and 12 months. As documented by telephone interview, pain that began at delivery was present in 9.8% of participants in 2 months, but was rare 6 and 12 months later: 1.8% and 0.3% [upper 95% CI, 1.2%], respectively. Of note, the 3 patients with pain 12 months after delivery had all experienced VD and had an Edinburgh postpartum depression index consistent with depression. Past history of pain and degree of tissue damage at delivery accounted for 7.0% and 16.7%, respectively, of the variability in acute post-delivery pain and were not associated with incidence of pain 2 months later. Women appear to have a low incidence of new pain that begins at delivery that is still present 12 months later, despite the substantial degree of tissue trauma.

([113](#_ENREF_113)) Gutierrez S, Liu B, Hayashida K, Houle TT, Eisenach JC: Reversal of peripheral nerve injury-induced hypersensitivity in the postpartum period: role of spinal oxytocin. *Anesthesiology* 2013, 118(1):152-159.

This animal model (N=168 rats) explored pregnancy’s effect on chronic pain by testing hindpaw hypersensitivity to mechanical stimuli induced by peripheral nerve injury after intrathecal oxytocin, atosiban, and naloxone administration during mid-pregnancy and 1 day postpartum. Pregnancy did not alleviate experimentally induced hypersensitivity but delivery and postpartum association with pups were shown to confer less hypersensitivity to painful stimuli. Separation of the pups from the mother on the first postpartum day interfered with this decrease in hypersensitivity. Reversal of this protective effect was achieved by intrathecal injection of an oxytocin receptor antagonist (atosiban) but not nalaxone. Supraspinal oxytocin increase after delivery may be at least partially responsible for prevention of chronic postpartum pain.

*Associated Content: Editorial*
Flood P, Wong CA: Chronic pain secondary to childbirth: Does it exist? *Anesthesiology* 2013; 118(1):16–8.

***Other***

**(**[**114**](#_ENREF_114)**) Chooi CS, White AM, Tan SG, Dowling K, Cyna AM: Pain vs comfort scores after Caesarean section: A randomized trial. *Br J Anaesth* 2013, 110(5):780-787.**

This RCT (N=300 women) investigated whether language used by hospital staff influences the patient’s pain experience after CD. The median (IQR) pain scores were higher than comfort scores at rest (p=0.001) and movement (p=0.001). The Group “P” women (where “0” was “no pain” and “10” was “worst pain imaginable”) were more likely to be bothered by their CD, had greater ‘Bother’ scores (4 vs. 1, P<0.001), and perceived post-op sensations as ‘unpleasant’ (RR= 3.1 [95% CI 2.2-4.2], p<0.001) and a product of tissue damage rather than of healing and recovery (RR 2.0 [1.3-3.2], p=0.001) compared with the Group “C” (“0” was least comfortable and “10” was most comfortable). These findings suggest that asking about pain and pain scores after CD adversely affects patient reports of their post-op experience, and staff and patients may benefit from using more positive language.

([115](#_ENREF_115)) Macintyre PE, Russell RA, Usher KA, Gaughwin M, Huxtable CA: Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. *Anaesth Inten Care* 2013, 41(2):222-230.

This retrospective cohort study (N=51) investigated pain relief and opioid requirements in the first 24 hrs post-operatively, in buprenorphine opioid substitution therapy (BOST) and methadone opioid substitution therapy (MOST) patients prescribed patient-controlled analgesia (PCA). There were no significant differences in pain scores, treatment-requiring nausea or vomiting, or sedation between patient groups or within groups whether they had or had not received BOST or MOST on the day after surgery. There were also no significant differences in PCA requirements between patient groups overall, or between MOST patients with or without postoperative therapy. However, BOST patients without BOST therapy the day after surgery (and in most cases, the day of surgery) used more PCA opioid than these patients with their BOST therapy (P=0.02) which suggests that buprenorphine should be continued perioperatively.

**FETAL COMPLICATIONS/OUTCOMES**

 **Timing of Delivery**

***Guidelines***

**(**[**116**](#_ENREF_116)**) American College of Obstetrics and Gynecology: Committee opinion no 579: definition of term pregnancy. *Obstet Gynecol* 2013, 122(5): 1139-1140.**

In recognition that neonatal outcomes vary during the broad interval (37-42 weeks) that was once considered to be “term”, this ACOG Consensus statement designates new nomenclature: “Early Term” (37 0/7 – 38 6/7 weeks); “Full Term” (39 0/7 – 40 6/7 weeks); “Late Term” (41 0/7 – 41 6/7 weeks); and “Postterm” (42 0/7 weeks – beyond).

**(**[**117**](#_ENREF_117)**) American College of Obstetrics and Gynecology: Committee opinion no. 561: Nonmedically indicated early-term deliveries. *Obstet Gynecol* 2013, 121(4): 911-915.**

The ACOG Committee on Obstetric Practice and Society for Maternal-Fetal Medicine cites evidence to support the recommendation that nonmedically indicated early term delivery (<39 weeks) is not appropriate.

***Fetal Outcomes***

([118](#_ENREF_118)) Chiossi G, Lai Y, Landon MB, Spong CY, Rouse DJ, Varner MW, Caritis SN, Sorokin Y, O'Sullivan M J, Sibai BM *et al*: Timing of delivery and adverse outcomes in term singleton repeat cesarean deliveries. *Obstet Gynecol* 2013, 121(3):561-569.

This multicenter prospective study (N=23,794) examined composite maternal (pulmonary edema, cesarean hysterectomy, pelvic abscess, thromboembolism, pneumonia, transfusion, or death) and neonatal risk (respiratory distress, transient tachypnea, necrotizing enterocolitis, sepsis, ventilation, seizure, hypoxic-ischemic encephalopathy, NICU admission, 5-min Apgar of < 3, or death) of elective repeat CD at different gestational ages. Elective delivery at 37 weeks of gestation had significantly higher risks of adverse maternal outcome (OR = 1.6 [95% CI: 1.1 -2.3]), whereas elective delivery at 39 weeks of gestation was associated with better maternal outcome vs. pregnancy continuation (OR = 0.5 [0.4 -0.7]). Elective repeat CD at 37 and 38 weeks of gestation had significantly higher risks of adverse neonatal outcome (37 weeks OR = 2.0 [1.7-2.4]; 38 weeks OR = 1.4,[1.2-1.5]), whereas delivery at 39 and 40 weeks of gestation presented better neonatal outcome as opposed to pregnancy continuation (39 weeks OR = 0.8 [0.7-0.9]; 40 weeks OR = 0.6 [0.4-0.8]). Thirty nine (39) weeks gestation is the optimal time for repeat CD for both mother and neonate, unless otherwise indicated.

([119](#_ENREF_119)) Serenius F, Kallen K, Blennow M, Ewald U, Fellman V, Holmstrom G, Lindberg E, Lundqvist P, Marsal K, Norman M *et al*: Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden. *JAMA* 2013, 309(17):1810-1820.

This population-based prospective cohort (N=1157) evaluated the neurodevelopmental outcome of consecutive extremely preterm (EPT) infants born <27 weeks of gestation compared to matched full term controls. Overall, 42% (99% CI, 36%-48%) of EPT children had no disability, 31% (99% CI, 25%-36%) had mild disability, 16% (99% CI, 12%-21%) had moderate disability, and 11% (99% CI, 7.2%-15%) had severe disability. Moderate or severe overall disability decreased with gestational age at birth (22 weeks, 60%; 23 weeks, 51%; 24 weeks, 34%; 25 weeks, 27%; and 26 weeks, 17%; P for trend < 0.001). Thus, of children born EPT and receiving active perinatal care, 73% had mild or no disability and neurodevelopmental outcome improved with each week of gestational age. These results are relevant for clinicians counseling families facing EPT birth.

**(**[**120**](#_ENREF_120)**) Stenson BJ, Tarnow-Mordi WO, Darlow BA, Simes J, Juszczak E, Askie L, Battin M (BOOST Study) *et al*: Oxygen saturation and outcomes in preterm infants. *N Engl J Med* 2013, 368(22):2094-2104.**

These 3 international RCTs (N= 2,448) evaluated the effect of targeting an O2 saturation of 85-89% vs. 91-95% on disability-free survival at 2 yrs in infants born <28 weeks' gestation. There was a change in oximeter-calibration algorithm mid-study which resulted in heterogeneity for the mortality outcome. The rate of death was significantly higher in the lower-target group (LTG) than in the higher-target group (HTG) (23.1% vs. 15.9%; RR in LTG = 1.5; 95% CI: 1.2- 1.8; P=0.002). Recruitment was stopped early when interim analysis showed increase rate of death in the LTG group. In the larger sample, infants with LTG had significantly reduced rates of retinopathy of prematurity and increased rates of necrotizing enterocolitis. There were no significant between-group differences in other outcomes or adverse events.

 *Associated Content: Editorial*

Polin RA and Bateman D: Oxygen-saturation targets in preterm infants. *N Engl J Med* 2013, 368(22): 2141-2142.

**Perinatal Exposures**

***Anesthetics***

([121](#_ENREF_121)) Bong CL, Allen JC, Kim JTS: The Effects of Exposure to General Anesthesia in Infancy on Academic Performance at Age 12. *Anesth Analg* 2013, 117(6):1419-1428

In this pilot observational cohort study (N=100 subjects), researchers sought to determine whether children exposed to general anesthesia for minor surgery during infancy exhibited differences in academic achievement at age 12 years as evidenced by lower aggregate scores in the Singapore standardized Primary School Leaving Examination (PSLE) and formally diagnosed learning disability (LD) vs. unexposed children (N=106). There was no difference in mean PSLE scores between groups. The presence of formally diagnosed LD was 15% and 3.7% in the exposed vs. unexposed groups (P< 0.001). The OR for LD diagnosis if exposed to GA vs. controls = 4.5 (95% CI: 1.4–14.1)). The study’s validity was challenged in the accompanying editorial due to the lack of rigor in the definition and verification of learning disabilities, gender differences between cases and controls, small sample sizes, and bias in parental recall.

*Associated Content: Editorial*Crosby G and Davis PJ: General Anesthesia in Infancy Is Associated with Learning Disabilities—or Not.  *Anesth Analg* 2013*,* 117(6): 1270-1272.

([122](#_ENREF_122)) Yonamine R, Satoh Y, Kodama M, Araki Y, Kazama T: Coadministration of Hydrogen Gas as Part of the Carrier Gas Mixture Suppresses Neuronal Apoptosis and Subsequent Behavioral Deficits Caused by Neonatal Exposure to Sevoflurane in Mice. *Anesthesiology* 2013, 118(1):105-113.

This mouse model assessed whether hydrogen gas attenuates neuronal apoptosis in response to sevoflurane exposure. Western blot analysis (N=3-6 per group) showed that hydrogen gas significantly reduced the level of neuronal apoptosis with neonatal exposure to 3% sevoflurane coadministered with 1.3% hydrogen gas to approximately 40% (*P* < 0.001), and immunohisto­chemical analysis (N= 8-10) showed that hydrogen reduced oxidative stress induced by neonatal sevoflurane exposure. Behavioral deficits were not apparent in mice co-administered hydrogen. There may potentially be a protective effect of hydrogen mixed in with the carrier gas for general anesthesia exposure in neonates.

([123](#_ENREF_123)) Dalal PG and Berlin C: Safety of the breast-feeding infant after maternal anesthesia. *Ped Anesth* 2013, Advanced publish online; doi: 10.1111/pan.12376.

This review addresses the available literature on the safety of breast feeding during the perioperative period in light of the American Academy of Pediatrics recommendations promoting increased breast feeding among mothers. It reiterates the recommendation to use regional anesthesia and short-acting agents when feasible, and to minimize agents with active metabolites. The conclusion is that although most drugs can transfer into the breast milk, the quantities are clinically insignificant and pose minimal risk to the full term, healthy infant.

***Other Maternal Medications***

([124](#_ENREF_124)) Orbach H, Matok I, Gorodischer R, Sheiner E, Daniel S, Wiznitzer A, Koren G, Levy A: Hypertension and antihypertensive drugs in pregnancy and perinatal outcomes. *Am J Obstet Gynecol* 2013, 208(4):301 e301-306.

This population based retrospective cohort study (N=100,029 deliveries, 1,964 pregnant women with chronic HTN and 620 neonates exposed to at least one antihypertensive) studied the fetal effects of *in utero* exposure to therapy (methyldopa or atenolol). Neonates exposed in the 3rd trimester had 2-4 times higher rates of IUGR, small for gestational age, and PTD. The findings were similar when comparing women with chronic HTN who were not treated during pregnancy vs. those with no chronic HTN and no medication exposure. However, chronic HTN with or without treatment is an independent RF for adverse perinatal outcomes and therefore represents an example of confounding by indication.

*Associated Content: Discussion Article*
Macones GA, Odibo A, Cahill A: Discussion: 'Hypertension and antihypertensives in pregnancy,' by Orbach et al. *Am J Obstet Gynecol* 2013, 208(4):e1-2.

**(**[**125**](#_ENREF_125)**) Stephansson O, Kieler H, Haglund B, Artama M, Engeland A, Furu K, Gissler M, Norgaard M, Nielsen RB, Zoega H *et al*: Selective serotonin reuptake inhibitors during pregnancy and risk of stillbirth and infant mortality. *JAMA* 2013, 309(1):48-54**

This population-based cohort study from all Nordic countries (N=1,633,877; 1996-2007) explored the association between maternal SSRI use and risk of stillbirth and infant mortality. The risk of stillbirth and post-neonatal death were higher for the exposed group in the initial model; however all associations lost statistical significance in the multivariable models controlling for maternal characteristics and prior psychiatric hospitalizations. Thus, women exposed to an SSRI do not appear to be at higher risk for stillbirth, neonatal mortality, or post-neonatal mortality.

**(**[**126**](#_ENREF_126)**) Pasternak B, Svanstrom H, Hviid A: Ondansetron in pregnancy and risk of adverse fetal outcomes. *N Engl J Med* 2013, 368(9):814-823.**

Using a historical cohort (N= 608,385 pregnancies) in Denmark, investigators compared the risk of adverse fetal outcome with women given ondansetron during pregnancy vs. those who were not (1:4 ratio), while accounting for nausea severity and use of other antiemetics. Findings show that ondansetron exposure was not associated with a significantly increased risk of spontaneous abortion, stillbirth, any major birth defect, PTD, delivery of a low-birth-weight infant or small-for-gestational age infant, and therefore should be considered safe during pregnancy regarding severe fetal outcomes.

**(**[**127**](#_ENREF_127)**) Yazdy M, Mitchell A, Tinker S, Parker S, Werler, M: Periconceptional Use of Opioids and the Risk of Neural Tube Defects. *Obstet Gynecol* 2013, 122(4): 838-844.**

This case-control study (Slone Epidemiology Center Birth Defects Study data; 1998-2010) investigated the relationship between periconceptional use of opioids and neural tube defects. Data was gathered from interviews of mothers with babies born with relevant defects. A higher percentage (3.9%, N=305) of mothers of babies with neural tube defects reported using an opioid medication than those in the non-malformed control group (1.6%, N=7,125) and those in the malformed control group (2.0%, N=13,405) with OR = 2.2 (95% CI 1.2-4.2) and 1.9 (1.0-3.4), respectively. However, there are concerns of recall bias which are addressed in this study.

**Effect of Delivery Mode**

**(**[**128**](#_ENREF_128)**) Barrett JFR, Hannah ME, Hutton EK, Willan AR, Allen AC, Armson BA, Gafni A, Joseph KS, Mason D, Ohlsson A *et al*: A Randomized Trial of Planned Cesarean or Vaginal Delivery for Twin Pregnancy. *N Engl J Med* 2013, 369(14):1295- 1305.**

This multicenter, international RCT (N = 2,804 women) considered perinatal outcomes in planned VD vs. CD for twins (32 weeks 0 days-38 weeks 6 days). Rate of CD was 90.7% in planned CD group and 43.8% in planned VD group There was no significant difference in the primary outcome of composite fetal/neonatal death or serious neonatal morbidity between groups (2.2 vs. 1.9%, OR = 1.16 for CD; 95%CI 0.7-1.7). This research expands the evidence that planned CD may not increase or decrease the risk of fetal/neonatal death or serious morbidity; however there was a high rate of CD in the planned VD group. There may be varying degrees of obstetric provider comfort with delivering second twins vaginally that have non-cephalic presentations.

([129](#_ENREF_129)) Werner EF, Han CS, Savitz DA, Goldshore M, Lipkind HS: Health outcomes for vaginal compared with cesarean delivery of appropriately grown preterm neonates. *Obstet Gynecol* 2013, 121(6):1195-1200.

This retrospective cohort study (N=20,231) compared the outcomes for preterm, appropriate for gestational age weight neonates and adverse neonatal outcome by mode of delivery. Of singleton, live-born, cephalic neonates, 69.3% had VD and 30.7% were delivered by CD. CD compared with VD delivery was associated with increased odds of respiratory distress (39.2% vs. 25.6%, OR = 1.7 [95% CI: 1.6-1.9]) and 5-min Apgar score < 7 (10.7% vs. 5.8%, OR = 2.0 [1.8 -2.4]). In this preterm cohort, CD was not protective against poor outcomes but rather increased risk of respiratory distress and low Apgar score compared with VD.

([130](#_ENREF_130)) Walsh CA, Robson M, McAuliffe FM: Mode of delivery at term and adverse neonatal outcomes. *Obstet Gynecol* 2013, 121(1):122-128.

This 10-year single center retrospective study (N = 64,555) in term neonates reaching the 2nd stage of labor assessed the rate of peripartum death, neonatal encephalopahy, intracranial hemorrhage by delivery mode. Compared with neonates delivered by 2nd stage CD, there were no differences in the rates of peripartum neonatal death or neonatal encephalopathy after operative VD. No significant differences in adverse neonatal outcomes were demonstrated between vacuum-assisted and forceps-assisted deliveries, although sub-analysis is limited by the small numbers of serious adverse outcomes. The absolute risk of neonatal death secondary to intracranial hemorrhage is 3 to 4 per 10,000 operative VD for both instruments.

**Fetal Heart Monitoring**

**(**[**131**](#_ENREF_131)**) Alfirevic Z, Devane D, Gyte GM: Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour.[Update of Cochrane Database Syst Rev. 2006; 3:CD006066; PMID: 16856111]. *Cochrane Db Syst Rev* 2013, 5: CD006066.**

This Cochrane meta-analysis (13 RCTs; N = 37,000 women) compares the efficacy of continuous cardiotocography (CTG) with and without fetal blood sampling with no fetal monitoring, intermittent auscultation, or intermittent CTG. Only 2 trials were judged to be of high quality. Compared with intermittent auscultation, CTG showed no significant improvement in overall perinatal death rate or CP, but was associated with fewer neonatal seizures (RR=0.5 [95% CI: 0.3 to 0.8], N = 32,386; 9 trials). There was a significant increase in CD associated with CTG (RR = 1.6 [1.3 to 2.1], N = 18,861; 11 trials and instrumented VD (RR = 1.2 [1.0 to 1.3], N = 18,615; 10 trials). Access to fetal blood sampling did not appear to influence the difference in neonatal seizures nor any other pre-specified outcome.

**(**[**132**](#_ENREF_132)**) Clark SL, Nageotte MP, Garite TJ, Freeman RK, Miller DA, Ricesimpson K, Belfort MA, Dildy GA, Parer JT, Berkowitz RL *et al*: Intrapartum management of category II fetal heart rate tracings- Towards standardization of care. *Am J Obstet Gynecol* 2013, 209(2):89-97.**

These authors propose an algorithm for the management of category II fetal heart rate patterns synthesized from the available evidence and current scientific thought. They highlight the timeliness of anticipated delivery, re-evaluation every 30 min, and re-application of algorithm if FHR parameters change significantly. Use of this algorithm may help clinician to comply with this standard of care, and may enhance the ability to further assess the implications of intrapartum fetal heart rate monitoring in research and clinical practice.

([133](#_ENREF_133)) Moaveni DM, Birnbach DJ, Ranasinghe JS, Yasin SY: Review article: fetal assessment for anesthesiologists: are you evaluating the other patient? *Anesth Analg* 2013, 116(6):1278-1292.

This review article outlined the current antepartum and intrapartum expert guidelines and fetal assessment modalities (nonstress test, biophysical profile, Doppler velocimetry, electronic fetal heart rate monitoring, fetal electrocardiogram (STAN-ST waveform analysis), and fetal pulse oximetry), their physiologic basis, and the available evidence regarding their utility in clinical practice. The authors empower the obstetric anesthesiologist to be an informed member of the perioperative, multidisciplinary care team.

**TOOLS OF OUR TRADE**

 **Technology**

***Ultrasound***

([134](#_ENREF_134)) Arzola C, Carvalho JA, Cubillos J, Ye X, Perlas A: Anesthesiologists’ learning curves for bedside qualitative ultrasound assessment of gastric content: a cohort study. *Can J Anesth* 2013, 60(8):771-779.

This cohort study (N = 6 anesthesiologists, N = 180 assessments) measured the amount of training necessary for an anesthesiologist to achieve competence in ultrasound (US) technique for assessing gastric content. Anesthesiologists underwent a teaching intervention (didactic and interactive workshop) followed by a formative assessment; learning curves were then constructed after diagnosis gastric content in healthy volunteers. Results imply that with appropriate training and supervision, it is estimated that anesthesiologists will achieve a 95% success rate in bedside qualitative US assessment after performing approximately 33 exams. As demonstration of competency has become an integral part of our specialty’s credentialing process, studies such as these can serve as the basis for developing faculty education programs.

**(**[**135**](#_ENREF_135)**) Sahota JS, Carvalho JC, Balki M, Fanning N, Arzola C: Ultrasound estimates for midline epidural punctures in the obese parturient: paramedian sagittal oblique is comparable totransverse median plane. *Anesth Analg* 2013, 116(4):829-835.**

This prospective study of term obese women (N = 60; mean BMI = 39.6) receiving labor epidural analgesia (LEA) or CSE anesthesia for CD investigated whether ultrasound (US) scanning in the paramedian sagittal oblique (PSO) plane vs. the transverse median (TM) plane yielded a more precise estimate of the actual skin-epidural space measurement. The estimated US needle depth in the PSO and TM planes and the actual needle depth were 6.5 (1.2) cm, 6.5 (1.1) cm, and 6.6 (1.3) cm with minimal skin compression. The quality of imaging was rated as good in the PSO and TM planes in 86.7% and 68.3% cases, respectively (P = 0.028). The estimates of the US-determined distance to the epidural space in the PSO and the TM planes in obese patients are comparable, but the option to use both views for midline punctures may prove useful in certain patients.

**(**[**136**](#_ENREF_136)**)** **Shaikh F, Brzezinski J, Alexander S, Arzola C, Carvalho JC, Beyene J, Sung L: Ultrasound imaging for lumbar punctures and epidural catheterisations: systematic review and meta-analysis. *Br Med J* 2013, 346:f1720.**

This systematic review and meta-analysis (14 RCT; N=674 in the ultrasound (US) group and 660 in the control group) compared US imaging to standard palpation methods to reduce the risk of failed lumbar punctures or epidural catheterizations, traumatic procedures, insertion attempts, and/or needle redirections (included both obstetric and non-obstetric studies). US reduced the risk of failed procedures (RR=0.2, P<0.001, low heterogeneity): risk reduction was similar when subgroup analysis was performed for lumbar punctures (0.2, P=0.002) or epidural catheterizations (0.23, P=0.003). US also significantly reduced the risk of traumatic procedures (0.3, P=0.005, low heterogeneity) the number of insertion attempts (mean difference -0.4, P<0.001, high heterogeneity) and the number of needle redirections (mean difference -1.0, P<0.001, high heterogeneity).

*Associated Content: Comment On*Rizzoli P: Taking the sting out of lumbar puncture. *Br Med J* 2013, 346:f1734**.**

***Videotaping***

([137](#_ENREF_137)) Friedman Z, Siddiqui N, Mahmoud S, Davies S: Video-assisted structured teaching to improve aseptic technique during neuraxial block. *Br J Anaesth* 2013, 111(3):483-7.

This interventional study (N= 29 residents, each videotaped 3-4 times) compared epidural aseptic technique performance by novice operators after a targeted teaching intervention that included a video assessment and demonstration. The median aseptic technique scores for the rotation period were significantly higher in the post-intervention group (27.6 [IQR: 22.3–29.5] vs. 16.6 [13.3–22.0], p < 0.001) with high inter-rater reliability. Similar results were seen when scores were analyzed for low, moderate, and high levels of experience. Video recording may provide a valuable tool for improving aseptic practice and other manual techniques by novice trainees as part of procedure-specific teaching, especially when based on commonly observed mistakes among the trainees.

**Publications**

([138](#_ENREF_138)) Vintzileos WS, Ananth CV, Vintzileos AM: External funding of obstetrical publications: citation significance and trends over 2 decades. *Am J Obstet Gynecol* 2013, 209(2):150e151-156.

This retrospective study determined that 61% (27/44) of the research presented in the “citation classics” (100 most frequently cited articles) within *Obstet & Gynecol* and *Am J Obstet Gynecol* were externally funded (34% through the NIH). Relative to 1989, in 2012 there was a 34.8% decrease in the number of OB-related published manuscripts (10,175 manuscripts reviewed), a 59.6% decrease in the number of non-funded manuscripts, but a 6.8% increase in the number of funded manuscripts with an 8.2% increase in the number of NIH-funded publications. This highlights the importance for securing NIH-or other funding for academic physicians.