

### **ABSTRACT TITLE**

# Cancer Risk in Children Conceived by Assisted Reproductive Technology

# ABSTRACT AUTHORS AND AFFILIATIONS

Marte Myhre Reigstad, Norwegian National Advisory Unit on Women's Health, Oslo University Hospital, Norway; Inger Kristin Larsen, The Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo, Norway; Tor Åge Myklebust, The Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo, Norway; Trude Eid Robsahm, The Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo, Norway; Nan Birgitte Oldereid, Section for Reproductive Medicine, Department of Gynecology, Oslo University Hospital, Rikshospitalet, Oslo, Norway; Louise A. Brinton, National Cancer Institute, Division of

# **ABSTRACT TEXT**

#### Background and objectives:

As children conceived by assisted reproductive technology (ART) are ageing into adulthood, the potential long term effects on their health is of interest. The aim of the study is to compare cancer risk in children conceived by ART to that in children conceived without.

Method:

Data, including exposure to ART, on all children born between 1984 and 2011 were obtained from the Medical Birth Registry of Norway. Cancer diagnoses were obtained by linkage with the Cancer Registry of Norway. Person years were accrued from date of birth, and until the first cancer diagnosis, death or emigration, or 31st December 2011. A Cox proportional hazards model was used to calculate hazard ratios (HR) and 95% confidence intervals (CI) of overall cancer risk, as well as risk of all childhood cancer types, for ART children compared to non-ART children. Results:

The study cohort comprised 1 628 658 children, of which 25 782 were ART children. There were 51 cancers in the ART group, and 4503 in the non-ART group. Although no increased risk of overall cancer was found, HR 1.21 (95% CI 0.90-1.63), the risk of leukemia was significantly elevated for ART children compared to non-ART children, HR 1.67 (95% CI 1.02-2.73). An elevated risk of Hodgkin lymphoma was found for ART children, HR 3.63 (95% CI 1.12-11.72), although this estimate was based on only three cases in the ART group.

This population-based cohort study detected elevated risk of leukemia and Hodgkin lymphoma in children born after ART.



### **ABSTRACT TITLE**

Caesarean section rates in the Nordic Countries using the Robson grouping – what has changed from 2000 to 2011?

# ABSTRACT AUTHORS AND AFFILIATIONS

Authors: Pyykönen A 1, Gissler M 2, Klungsøyr K 14,15, Skjeldestad FE 16, Løkkegaard E 4, Rasmussen S 4, Berholdt T 4, Bjarnadóttir R 5, Másdóttir BB 6, Smarason A 7, Fagerberg MC 8, Gottvall K 9,10, Källén K 9,11, Albrechtsen S 12,13, Tapper A-M 1

#### Affiliations:

1. Helsinki University Central Hospital, Department of Obstetrics and Gynecology, Helsinki, Finland

### **ABSTRACT TEXT**

Object: Report on the trends in the Caesarean section (CS) rates in the Nordic countries using the Robson ten-group classification system.

Design and Setting: Retrospective population-based register study with data from national medical birth registries.

Population 3 398 586 deliveries consisting of all parturients in the five Nordic countries (Denmark, Finland, Iceland, Norway, Sweden) from 2000 to 2011.

Methods The Robson group profile of the study population was reported for four time periods. Both the crude and the age- and Robson group-adjusted CS rates were analyzed for four time periods and compared over time using the first time period as a reference.

Results After 2000, CS rates in the Nordic countries have a bell shaped curve with a significantly lower total CS rate in 2009 to 2011 than in the beginning of the decade, when adjusted by age and Robson groups (case-mix). The contribution of different Robson groups to the total number of CS has changed over time; most significantly for the Robson group 5, women with a previous Caesarean, with steadily increasing contribution.

Conclusions In the Nordic countries, the total CS rates adjusted by case-mix are decreasing. The changes in the obstetric population are clearly shown by the use of the Robson classification system. In order to reduce the CS rates further, it is highly important to focus on preventing the first Caesarean section.



# Levonorgestrel-releasing intrauterine system and the risk of breast cancer

# ABSTRACT AUTHORS AND AFFILIATIONS

Tuuli Soini, Department of Obstetrics and Gynecology/Hyvinkää Hospital, Finland; Ritva Hurskainen, Department of Obstetrics and Gynecology, Hyvinkää Hospital, Finland; Seija Grénman, Department of Obstetrics and Gynecology/Turku University Hospital, and University of Turku, Finland; Johanna Mäenpää, School of Medicine/ University of Tampere, and Department of Obstetrics and Gynecology/Tampere University Hospital, Finland; Jorma Paavonen, Department of Obstetrics and Gynecology/Helsinki University Hospital, and University of Helsinki, Finland; Heikki Joensuu, Department of Oncology, Comprehensive Cancer Center/Helsinki University

## **ABSTRACT TEXT**

Background: Prolonged steroid hormone therapy has been reported to increase the risk of breast cancer, especially the risk of lobular cancer. The levonorgestrel-releasing intrauterine system (LNG-IUS) is widely used for heavy menstrual bleeding but its effect on the breast cancer risk is controversial. We explored the risk of breast cancer and its histological subtypes in LNG-IUS users. Material and methods: A cohort of women who had received reimbursement for the LNG-IUS purchase prescribed for heavy menstrual bleeding at the age of 30 to 49 in 1994-2007 in Finland was identified from the national Medical Reimbursement Registry (n=93,843). The cohort of LNG-IUS users was followed for incident breast cancers through the Finnish Cancer Registry up to the age of 55 and to the end of 2012. Standardized incidence ratios (SIRs) were calculated by dividing the observed number of cancer cases by the expected number of cancer cases.

Results: A total of 2,015 women had breast cancer diagnosed in the cohort during follow-up of 1,032,767 women-years. The LNG-IUS users had an increased risk for both ductal breast cancer (SIR 1.20, 95% confidence interval [CI] 1.14-1.25) and for lobular breast cancer (SIR 1.33, 95% CI 1.20-1.46). The SIR for lobular cancer among LNG-IUS users who purchased the device at least twice was 1.73 (95% CI 1.37-2.15).

Conclusions: The use of LNG-IUS was associated with an elevated risk for breast cancer, especially the lobular type.



Lifestyle intervention in obese pregnant women can reduce hsCRP.

# ABSTRACT AUTHORS AND AFFILIATIONS

Kristina Martha Renault, Dept of Obstetrics and Gynecology, Hvidovre Hospital, University of Copenhagen and Obstetric Clinic, JMC, Rigshospitalet, University of Copenhagen; Emma Malchau Carlsen, Dept of Pediatrics, Hvidovre Hospital, University of Copenhagen; Sofie Hædersdal, Center for Diabetes Research, Gentofte Hospital, University of Copenhagen; Lisbeth Nilas, Dept of Obstetrics and Gynecology, Hvidovre Hospital, University of Copenhagen; Niels Jørgen Secher, JMC, Rigshospitalet, University of Copenhagen; Jesper Eugen-Olsen, Clinical Research Centre, Hvidovre Hospital, University of Copenhagen, Sjurdur F Olsen; Centre for Fetal Programming,

## **ABSTRACT TEXT**

Background: Offspring of obese mothers have increased risk of developing obesity and related short and long-term disease. The cause is multifactorial and may partly be explained by the unfavourable intrauterine environment.

Objective: To assess the effect of lifestyle intervention on markers of maternal metabolism and inflammation in "the TOP (Treatment of Obese Pregnant Women) -study", a randomized controlled trial. And to examine which dietary components may account for any changes as result of the intervention.

Methods: In the TOP-study 425 participants with BMI≥30 kg/m2 were randomised 1:1:1 to intervention with diet and physical activity assessed by pedometer (D+PA), physical activity alone (PA) or control (C). Of 389 participants completing the study 376 had available blood samples. Outcome measures were OGTT 2-hour-value, se-insulin, c-peptide, lipid profile, Leptin, hsCRP, and suPAR in week 18-20 and 28-30. Diet was assessed in gestational week 11-14 and 36-37 using a validated Food Frequency Questionnaire.

Results: Median levels of hsCRP in gestational week 28-30 were lower in each of the intervention groups (8.3mg/l in goup PA+D and 8.8mg/l in group PA) compared to the control group (11.5mg/l) (D +PA vs C: P=0.03 and PA vs C: P=0.007). In week 28-30 hsCRP was positively and inversely associated with maternal glycemic load and protein intake respectively.

There were no differences in lipid profile or any of the metabolic parameters in week 28-30.

Conclusions: Lifestyle intervention in obese women can reduce hsCRP representing a marker of inflammation during pregnancy. The effect may partly be mediated by changes in intake of protein and glycaemic load.



# Adverse obstetric outcomes among early-onset cancer survivors in Finland

# ABSTRACT AUTHORS AND AFFILIATIONS

Johanna Melin, Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland; Sirpa Heinävaara, Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland; Nea Malila, Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland; Aila Tiitinen, Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; Mika Gissler, National Institute for Health and Welfare, Helsinki, Finland; Laura Madanat-Harjuoja, Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer

## **ABSTRACT TEXT**

OBJECTIVE: To evaluate risk of adverse obstetric outcomes and operative deliveries in female cancer survivors (diagnosed younger than 35 years of age) compared with their female siblings.

METHODS: Nationwide cancer and birth registries were merged to identify 1,800 first postdiagnosis deliveries of female cancer survivors and 7,137 first deliveries of female siblings between January 1987 and December 2013. Multiple unconditional logistic regression models were used to estimate the risk for adverse obstetric outcomes and operative deliveries adjusting for maternal age, year of delivery, gestational age (not in preterm delivery) and smoking.

RESULTS: We found a significantly elevated risk for induction of labor, 19.1% in survivors and 15.6% in siblings (odds ratio [OR] 1.17, 95% confidence interval [CI] 1.02–1.35), cesarean delivery, 23.6% in survivors and 18.6% in siblings (OR 1.15, 95% CI 1.01–1.31) and preterm delivery, 8.0% in survivors and 5.3% in siblings (OR 1.48, 95% CI 1.21–1.82) among cancer survivors compared with female siblings. The risks of instrumental vaginal delivery, malpresentation, placental pathologies, and postpartum hemorrhage were not, however, elevated among cancer survivors. The highest risks of adverse obstetric outcomes were seen among women treated in their childhood (aged 0–14 years). CONCLUSION: Cancer survivors have a small but statistically increased risk for induction of labor, cesarean delivery and preterm delivery compared with siblings without a history of cancer. Our findings indicate that pregnancies in cancer survivors are typically uncomplicated and cancer survivors should not be discouraged to have children after their cancer is cured.



# Immediate insertion of the levonorgestrel-releasing intrauterine system after medical abortion

# ABSTRACT AUTHORS AND AFFILIATIONS

Riina Korjamo, University of Helsinki, Helsinki University Hospital; Maarit Mentula, Helsinki University Hospital;
Oskari Heikinheimo, University of Helsinki, Helsinki University Hospital

## **ABSTRACT TEXT**

OBJECTIVE: An intrauterine device (IUD) is conventionally inserted in a few weeks after medical abortion. However, up to half the women fail to attend the follow-up appointment. An immediate initiation of IUD at the time of medical abortion could result in a higher uptake of effective intrauterine contraception and a lower rate of recurrent abortion. The primary outcome of the present randomized trial was to assess the expulsion rates of IUD after immediate vs. delayed IUD insertion after medical abortion. The secondary outcomes were the rates of various complications.

METHODS: Altogether 267 women were randomised at the time of medical abortion to immediate vs. delayed insertion of the levonorgestrel-releasing intrauterine system (LNG-IUS). In the immediate group the LNG-IUS was inserted within 3 days (when gestational age was ≤63 days), or before leaving hospital (gestational age between 64-140 days) after the abortion. In the delayed group the LNG-IUS insertion occurred after 2 to 4 weeks. Expulsions and complications were recorded at follow-up visits at 2 to 4 weeks and 3 months after the abortion.

RESULTS: Expulsion rates were 2.3% in the immediate, and 1.5% in the delayed insertion groups (p=1.00, OR 1.49, 95%Cl 0.24-9.06). Partial expulsion was diagnosed in 17.3%, and 1.5% of women (p<0.0001, OR 13.49, 95%Cl 3.11 to 58.49), respectively. No cases of uterine perforation occurred. Clinically diagnosed infections receiving antibiotic treatment were diagnosed 12.8% vs. 9.2% (p=0.432) in the group of immediate vs. delayed insertion.

DISCUSSION: Our results show that the policy of immediate post-abortal insertion of LNG-IUS is feasible and safe, and should be liberally offered at the time of medical abortion.



# Platelet alloantibodies in mothers of newborns with intracranial hemorrhage

# ABSTRACT AUTHORS AND AFFILIATIONS

Erle Refsum, Dept. of Laboratory Medicine, Karolinska Institutet; Stellan Håkansson, Dept. of Clinical Sciences, Pediatrics, Umeå University; Anette Mörtberg, Dept. of Laboratory Medicine, Karolinska Institutet and Clinical Immunology and Transfusion Medicine, Karolinska University Hospital; Petter Höglund, Dept. of Medicine Huddinge, Center for Hematology and Regenerative Medicine (HERM), Karolinska Institutet and Clinical Immunology and Transfusion Medicine, Karolinska University Hospital; Agneta Wikman, Dept. of Laboratory Medicine, Karolinska Institutet and Clinical Immunology and Transfusion Medicine, Karolinska University Hospital;

## **ABSTRACT TEXT**

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a rare condition, with an estimated incidence of 1:1-2000 live births. Predominantly, FNAIT is due to maternal alloantibodies that target paternally derived human platelet antigen (HPA) 1a on fetal platelets. The most feared complication is an intracranial hemorrhage (ICH). Using the Swedish Neonatal Quality Register, the aim of this study is to investigate the prevalence of maternal platelet alloantibodies in a retrospective cohort of neonates born after 32 weeks of gestation and diagnosed with ICH in Sweden from 2003 until 2012. The study is still ongoing: Out of 286 registered neonates, 278 mothers were contacted and invited to donate peripheral blood for antibody analyses. Of the 120 who provided samples, only two (1.7%) were negative for HPA-1a antigen, a frequency similar to an unselected population. Preliminary antibody analyses (n=60) revealed one mother (1.7%) with anti-HPA-1a antibodies, and one mother (1.7%) with both anti-HPA-5b and anti-HPA-15a antibodies. Sixteen mothers (27%) tested positive for anti-HLA class I antibodies, a frequency similar to women with a history of pregnancy in other materials. Investigation of the clinical data (n=286) showed a variety of associated diagnoses; the most frequent were asphyxia (30%, n=86), infections (18%, n=51) and birth-related trauma (21%, n=61). Seizures were present in 51% (n=147) of cases, and 8.4% (n=24) of the neonates were registered as deceased. Our cohort revealed a wide range of factors associated with ICH in neonates born close to term, and suggests platelet alloimmunisation to be a minor contributor.



# Increased risk of premature death after teenage pregnancy in Finland

# ABSTRACT AUTHORS AND AFFILIATIONS

Eerika Holma MD, Dept Ob&Gyn, Päijät-Häme central hospital and University of Helsinki

Oskari Heikinheimo Professor, chief physician, Dept Ob&Gyn, University of Helsinki and Kätilöopisto hospital, Helsinki University Central Hospital

## **ABSTRACT TEXT**

Background: Teenage pregnancy appears to increase the risk of premature death but it is not clear how socioeconomic status or the outcome of pregnancy (delivery or induced abortion) affects this risk. The objective of the study was to determine the association between adolescent pregnancy and premature death.

Materials and methods: This is a prospective population-based register study. All Finnish nulliparous teenagers who got pregnant in 1987 – 1989 and had induced abortion (n=6652) or delivery (n=7040) and controls without teenage pregnancy (n=41058) were included. Data on women's socioeconomic status was obtained from the National Institute for Health and Welfare. Participants were born in 1966 – 1975 and they were followed up to 2013 for a possible death and it's cause. Adjusted mortality rate ratios and 95 % confidence intervals (CI) were calculated.

Results: Women with teenage pregnancy were more likely to die than controls (RR=1.5, 95 % CI 1.3 - 1.8, p<0.01). The increased risk was most evident for deaths from injuries (2.0, 1.6 - 2.5, P<0.01), alcohol related diseases (2.0, 1.3 - 3.2, P<0.01), suicide (2.5, 1.8 - 3.3, p<0.01) and vascular diseases (1.8, 1.1 - 2.8, p=0.02). The risk of dying from cardiovascular diseases was higher in women who gave birth when compared to women who had an induced abortion (3.1, 1.3 - 7.7, P=0.01). There was no statistically significant difference in other causes of death between these groups.

Conclusions: Teenage pregnancy increases the risk of premature death and especially the risk of dying from cardiovascular diseases when the pregnancy ends in delivery.



Mode of delivery and risk of anal incontinence later in life

– a long term population based follow up study

# ABSTRACT AUTHORS AND AFFILIATIONS

Berit Schei, Department of Public Health and General Practice, Norwegian University of Science and Technology (NTNU) /Department of Gynecology, St Olavs Hospital, Trondheim, Norway; Anne Kjersti Daltveit, Department of Public Health and Primary Health Care, University of Bergen, Norway; Kathrine Rømmen, Department of Public Health and General Practice, NTNU; Abdul H Sultan, Croydon University Hospital, Croydon, UK/ St.George's University of London, UK; Astrid Rydning, Department of Surgery, St. Olavs Hospital, Trondheim, Norway; Siv Mørkved, Department of Public Health and General Practice, NTNU / Clinical Service, St. Olavs Hospital

## **ABSTRACT TEXT**

Background The impact of perineal rupture during delivery is considered an important risk factor for anal incontinence (AI) in the post- partum period. However, anal incontinence increases with age, and competing non-obstetric causes will affect the occurrence of AI, potentially reducing the impact of the obstetrical events. Aims To assess the association between mode of delivery, later self- reported anal incontinence. Methods Data on mode of delivery and perianal tears were collected from the Norwegian Medical Birth Registry (MBR) and merged with information on self-reported Al collected as part of a large population-based health survey in Nord-Trøndelag 2006-2008 (HUNT 3). Results A total of 12 998 women were included; 10 616 women who had only vaginal deliveries (VD only group) reported AI at approximately 20 years after last delivery, and 1091 women with only caesarean section deliveries (CS only group) reported AI at approximately 14 years since last delivery. The nulliparous (Control - group) consisted of 1291 women who were identified in HUNT 3 but had no records of deliveries in MBR. Prevalence of AI was 18.0% (95% CI 17.3-18.8) in the VD only group, compared to 16.9% (95%CI 14.6-19.1) in the CS only group, and 16.9% (95%CI 14.8-18.9) in the PO group. After adjusting for age, parity, age at first delivery, body-mass index and years between last delivery and reporting AI, the pattern remained the same. Conclusion: Mode of delivery did not have a significantly impact on the occurrence of anal incontinence in a long time perspective.



Rates of cesarean section and complete uterine rupture: A population-based Nordic study.

# ABSTRACT AUTHORS AND AFFILIATIONS

Lotte B. Colmorn (1). Jens Langhoff-Roos (1). Maija Jakobsson (2). Anna-Maija Tapper (3). Mika Gissler (4,5). Pelle Lindqvist (6). Karin Källen (7,8). Karin Gottval (9). Kari Klungsoyr (10). Per E. Børdahl (11). Ragnheidur I. Bjarnadottir (12). Lone Krebs (13)

1. Department of Obstetrics, Rigshospitalet, University of Copenhagen, Denmark 2. Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Helsinki, Finland

### **ABSTRACT TEXT**

Objective: To investigate the impact of CS rates and intended mode of delivery on the rates of complete uterine rupture. To assess predictors, symptoms and maternal complications in women with complete uterine rupture.

Design: A population-based study

Population: Women giving birth in the Nordic countries between April 2009 and August 2012 (n=666 306).

Methods: Cases with complete uterine rupture were continuously collected using a web- or paper-based data collection form and retrospectively validated from the national medical birth registers. Data of all women giving birth in the Nordic countries during the study period were retrieved from the national medical birth registers. Results were stratified by previous cesarean section. Main outcome measures: Population-based incidences, relative risk estimates.

Results: We identified 335 complete uterine ruptures (5.5/10 000 deliveries). The adjusted OR of uterine rupture was 93 3 (95%CL 57 8-150 5) with previous cesarean section.

the dentified 335 complete uterine ruptures (5.5/10 000 deliveries). The adjusted OR of uterine rupture was 93.3 (95%CI 57.8-150.5) with previous cesarean section, 26.6 (95%CI 9.73-70.89) for trial of labor after cesarean section and 1.77 (95%CI 1.36-2.30) for labor induction in women with previous cesarean section. For women with no history of cesarean section the odds increased with maternal age ≥35 years (aOR 3.96, 95%CI 1.76-8.90), multiple pregnancies (twins or more) (aOR5.59, 95%CI 1.43-21.79) and labor induction (aOR 3.62, 95%CI 1.56-8.44). Complications to complete uterine rupture were more frequent in women attending vaginal delivery with no history of cesarean section.

Conclusion: High national rates of complete uterine rupture were not associated to high national rates of previous CS in the Nordic countries. Most important predictors were intended vaginal delivery and induction of labor. In one fifth of the women there was no suspicion of uterine rupture prior to cesarean section.



# Long-term mortality in mothers with perinatal losses

# ABSTRACT AUTHORS AND AFFILIATIONS

Frode Halland, MD/ University of Bergen; Nils-Halvdan Morken, MD, PhD/ University of Bergen; Lisa deRoo, PhD/ University of Bergen, National Institutes of Health:NIEHS; Kari Klungsøyr, MD, PhD/ University of Bergen, Norwegian Institute of Public Health; Allen J Wilcox, MD, PhD/ National Institutes of Health:NIEHS; Rolv Skjærven, PhD/ University of Bergen, the Medical Birth Registry of Norway.

## **ABSTRACT TEXT**

Objective: To assess the association between maternal long-term mortality and perinatal losses and effect modification by surviving children and attained education.

Methods: A population-based cohort study of mothers registered in the Medical Birth Registry of Norway (1967–2009). Using Cox proportional hazard models, we calculated age specific (40-69 years) cardiovascular and non-cardiovascular mortality. We estimated mortality in mothers with perinatal losses, compared to mothers without, and mortality in mothers with one loss by number of surviving children in strata of mothers' attained education, low (less than 11 years) and high (11 or greater years).

Results: Mothers with perinatal losses had increased crude mortality compared to mothers without (cardiovascular: hazard ratio (HR) 1.8, 95% confidence interval (CI) 1.5-2.2, non-cardiovascular: HR 1.3 (1.2-1.4)). Mothers with one perinatal loss without surviving children had increased mortality compared to mothers with one birth and no loss (cardiovascular: low education; HR 2.7, 95% CI 1.7-4.3, high education; HR 0.91 (0.13-6.5), non-cardiovascular: low education; HR 1.6 (1.3-2.2), high education; HR 1.8 ( 1.08-2.9). Mothers with one perinatal loss, surviving children and high education had no increased mortality, whereas corresponding mothers with low education had slightly increased mortality (cardiovascular: two surviving children; HR 1.7 (1.2-2.4), three surviving children; HR 1.6 (1.05-2.4), non-cardiovascular: one surviving child; HR 1.2 (1.00-1.5), two surviving children; HR 1.2 (1.06-1.4)).

Conclusions: Mothers with a perinatal loss without surviving children had increased mortality. In mothers with surviving children, the association between a perinatal loss and increased mortality was only found in mothers with low education.



# **ABSTRACT TITLE**

# Thyroid function in pregnant PCOS women randomized to metformin / placebo

# ABSTRACT AUTHORS AND AFFILIATIONS

Anastasia Trouva, Department of Molecular Medicine and Surgery, Karolinska Institutet, Centre for Clinical Research Sörmland, Uppsala University, Eskilstuna, and Department of Endocrinology, Internal Medicine Clinic, Eskilstuna Hospital, Sweden; Jan Calissendorff, Department of Clinical Science and Education, Södersjukjuset, Karolinska Institutet, Stockholm, Sweden; Angelica Lindén Hirschberg, Department of Women's and Children's Health, Karolinska Institutet and Department of Obstetrics and Gynecology, Karolinska University Hospital, Stockholm, Sweden and; Eszter Vanky, Institute of Laboratory Medicine, Children's and Women's Health,

# **ABSTRACT TEXT**

#### Context:

Both polycystic ovary syndrome (PCOS) and hypothyroidism are associated with adverse pregnancy outcome. Little is known about the effect of PCOS on thyroid function in pregnancy. This is the first study on possible metformin influence on thyroid function in pregnant women with PCOS.

To investigate 1) the prevalence of overt and sub-clinical hypothyroidism in PCOS pregnancies, 2) the effect of metformin on serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4) at each trimester in women with PCOS.

#### Patients/Methods:

Analysis of the thyroid status at each trimester of 287 women with PCOS, singleton pregnancies, aged 18-42 years, participating in two RCTs.

Intervention: 1700 - 2000 mg metformin daily or placebo.

#### Results:

The prevalence of overt and sub-clinical hypothyroidism in the first trimester was 1.5% and 8.6% respectively among non-levothyroxine-treated patients but among all participants the prevalence of hypothyroidism was 15%. The mean level of TSH during pregnancy was comparable between the metformin and placebo groups. The mean level of FT4 in the 2nd and 3rd trimester was higher (but within the normal range) in the metformin compared to placebo group (p<0.001, p<0.05 respectively). Among the 15 patients on levothyroxine treatment, mean FT4 in the 3rd trimester was higher in the metformin group compared to placebo (p<0.05).

#### Conclusions:

Hypothyroidism was highly prevalent among pregnant women with PCOS in our study. This should be taken into consideration when managing this patient group in early pregnancy. The clinical significance of higher FT4 levels in the metformin group needs to be further investigated.



# **ABSTRACT TITLE**

# Fertility treatment and subfertility: offspring intelligence and academic performance

# ABSTRACT AUTHORS AND AFFILIATIONS

Bjørn Bay, Post Doc (a, b),; Erik Lykke Mortensen, Professor (c); Susan Golombok, Professor (b); Lena Hohwü, Post Doc (d, e); Carsten Obel, Professor (d, e); Tine Brink Henriksen, Professor (f); Ulrik Schiøler Kesmodel, Professor (g)

a) The Fertility Clinic, Dept. of Obstetrics and Gynecology, Institute of Clinical Medicine, Aarhus University & Region Hospital Horsens, Denmark; b) Centre for Family Research, University of Cambridge, United Kingdom;

## **ABSTRACT TEXT**

### Objective

To study whether fertility treatment, subfertility, or pregnancy planning are related to long-term intellectual development.

#### Methods

Danish register-based cohort study with follow-up on children born in the Aarhus Birth Cohort 1990-1992. A total of 5,032 singletons were followed up to a mean age of 19 years. These children were born as a result of fertility treatment (n=210), had subfertile parents who took more than 12 months before conceiving naturally (n=334), had fertile parents who conceived naturally within 12 months (n=2,661), or had parents who reported the pregnancy as unplanned (n=1,827). The outcome measures were parent reported school difficulties at age 9-11, register-based school grades at age 16, 17, and 19, and conscription intelligence test scores at age 19.

### Results

We found no evidence of school difficulties in childhood, impaired school performance in adolescence, or lower intelligence in young adulthood in multivariate analyses adjusted for parental age, educational level, maternal parity, pre-pregnancy body mass index, smoking and alcohol intake in pregnancy, cohabitation status, child gender, and age.

### Conclusion

In the longest follow-up of cognitive development of children conceived after fertility treatment or by subfertile parents conducted so far, this study did not show any association between pregnancy planning, subfertility, or fertility treatment and cognitive ability or academic performance.



# SNP-based chromosomal microarrays identify microdeletion syndromes in miscarriage samples

# ABSTRACT AUTHORS AND AFFILIATIONS

Melissa K. Maisenbacher, Natera Inc., San Carlos, CA; Katrina Merrion, Natera Inc., San Carlos, CA; Styrmir Sigurjonsson, Natera Inc., San Carlos, CA; Michael Young, Natera Inc., San Carlos, CA; Zachary Demko, Natera Inc., San Carlos, CA; Kimberly Martin, Natera Inc., San Carlos, CA; Barbara Pettersen, Natera Inc., San Carlos, CA

# **ABSTRACT TEXT**

BACKGROUND: Submicroscopic chromosomal losses (microdeletions) cause multiple developmental and congenital anomalies; however, their involvement in causing fetal demise is not well understood. The first step in determining if these copy number variants contribute to the cause of miscarriage is evaluating the frequency of their occurrence in this population. We focused our initial analysis on five common microdeletion syndromes (live birth rate): 1p36 deletion, 1/5000; Cri du Chat, 1/20,000; Angelman, 1/12,000; Prader-Willi, 1/10,000; and 22q11.2 deletion, 1/2000–1/4000.

AIM: To examine the incidence and size of five common microdeletions (at the 1p36, 5p-, 15q11-q13, and 22q11.2 regions) in POC samples.

METHODS: 17,424 fresh POC samples and maternal blood samples genotyped using Illumina CytoSNP-12b microarrays were retrospectively analyzed.

RESULTS: Fetal results were found in 14,824 (84%) cases, of which 31 (0.2%) had one of the above microdeletion syndromes: 6 cases with 1p36 deletion (1/2,470), 12 cases with Cri du Chat (1/1,253), 2 cases with Angelman (1/7,412), 3 cases with Prader-Willi (1/4,941), and 8 cases with 22q11.2 deletion (1/1,853). 15/31 cases had additional findings, which may be related to the cause of the loss, or may be incidental.

CONCLUSIONS: Higher incidences of syndromic microdeletions were found in this study of POC samples compared to reported live birth rates. Future research focusing on the size of the deleted region, syndromic phenotypic variability by gestational age and relationship to the causality of miscarriage is warranted. This data may allow better recurrence risk counseling for families with a pregnancy affected with one of these syndromes.



# Cesarean delivery in induced term pregnancies in the Nordic countries.

# ABSTRACT AUTHORS AND AFFILIATIONS

Løkkegaard E1, Rasmussen S1, Pyykönen A2, Tapper A-M2, Bjarnadóttir RI3, Másdóttir BB3, Smarason A4, , Klungsøyr K5,6, Albrechtsen S7,8, Fagerberg MC9, Gottvall K 10, Källén K10, Skjeldestad FE11, Gissler M12, Bergholt T13

Department of Obstetrics and Gynecology, Nordsjællands Hospital, University of Copenhagen, Denmark
 Helsinki University Central Hospital, Department of Obstetrics and Gynecology, Finland
 The Icelandic Birth Registry, National University Hospital of Iceland, Iceland

## **ABSTRACT TEXT**

The present study aimed to evaluate the association between induction of labor and the risk of cesarean delivery in women with a single cephalic presentation at term without a history of cesarean section.

Method: A Nordic collaborative study was initiated using data from the national birth registries from 2000 to 2011. Multiple logistic regression analyses were performed.

Results: In the five Nordic countries during 2000-2011 there were total 3,398,586 deliveries of which 196,220(5.8%) were nulliparous women and 188,158(5.5%) multiparous with a single cephalic presentation induced at term.

The induction rate increased with maternal age. The gestational age (GA) for induction decreased during the observation period.

Overall the cesarean delivery rate among induced were 25.0% in nulliparous and 5.5% in multiparous. The risk of cesarean delivery augmented with increasing maternal age as compared to 25-29 years old the risk was 1.28(1.25-1.32), 1.74(1.68-1.80) and 2.30(2.16-2.44), in 30-34, 35-39 and > 40 years old nulliparous women, respectively. There was increasing risk of caesarean delivery with increasing GA. After week 41 the risk was 1.20(1.18-1.23) in nulliparous with induced cephalic term pregnancies GA 39-41 weeks as reference. The risk of cesarean delivery among induced term cephalic pregnancies had a u-formed relation with birth weight. Similar results concerning maternal age, GA and birth weight yielded in induced multiparous women. Lowest risk of cesarean delivery in induced term cephalic pregnancies was found in Finland, especially among multiparous.

Conclusion: Maternal age and gestational age are important risk factors for cesarean delivery in induced term singleton cephalic pregnancies in the Nordic countries.



# Natural history of urinary incontinence in nulliparous women aged 25-65 years

# ABSTRACT AUTHORS AND AFFILIATIONS

Maria Gyhagen Department of Obstetrics and Gynecology, Södra Älvsborgs Hospital, Borås, Sahlgrenska Academy at Gothenburg University, Gothenburg; Jwan Al-Mukhtar Othman Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg; Ida Nilsson Department of Obstetrics and Gynecology, Södra Älvsborgs Hospital, Borås; Sigvard Åkervall Department of Surgery, Södra Älvsborgs Hospital, Borås; Ian Milsom Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg

## **ABSTRACT TEXT**

#### Aim

To describe the age-related occurrence, type, severity, impact, and treatment of urinary incontinence (UI) in nulliparous women in order to provide the most suitable control group for the evaluation of the effect of pregnancy and childbirth on pelvic floor function.

#### Method

The study population was identified in 2014 by the Central Bureau of Statistics and comprised Swedish women that had not given birth and were aged 25-64 years. The self-administered questionnaire included questions about UI, its frequency, volume, severity, subjective impact, treatment etc. Incontinence was defined according to the International Continence Society.

#### Result

The cohort comprised 9197 women (response rate 52.0%). Overall prevalence of UI was 16.7% (95% Confidence Interval 15.9-17.4%). The prevalence more than doubled from 11.7% in the youngest (25-34yrs.) to 24.9% in the oldest age group (55-64 yrs.). A majority of incontinent women had stress (40.3%), followed by mixed (29.7%), and urge incontinence (17.9%). Other UI occurred in 12.1%. Mixed UI doubled from 21.8% to 41.1% whereas stress UI decreased from 43.7% to 33.3% in the youngest compared with the oldest group. UI  $\geq$  once/week occurred in every third (31.9%) of the youngest to every second (53.1%) among the oldest. Bothersome UI was experienced by 28.1%, although only a negligible number had received treatment (<7%).

#### Conclusion

Nulliparity does not imply normality of urinary continence. Most parameters of UI increased with age, however to different degrees. This fact is of vital importance for the estimation of the effects of pregnancy and childbirth, using nulliparous women as controls.



# The risk of uterine leiomyosarcomas (LMS) in anticipated benign conditions

# ABSTRACT AUTHORS AND AFFILIATIONS

Marit Lieng M.D., Ph.D.(1,2), Espen Berner M.D., Ph.D (1), Bjorn Busund M.D (1)

(1) Department of Gynaecology, Oslo University Hospital, Oslo, Norway. (2) Institute of Clinical Medicine, University of Oslo, Oslo, Norway.

## **ABSTRACT TEXT**

#### Study Objective:

To evaluate the incidence of uterine LMS and identify the risk of morcellating LMS in a gynecological department that offers laparoscopic supracervical hysterectomy (LSH) and laparoscopic myomectomy using an electromechanical morcellator.

#### Design:

Retrospective trial in a Norwegian university teaching hospital.

#### Patients:

Women referred for an anticipated benign condition, diagnosed with uterine LMS and the total population of women who underwent surgical treatment for uterine fibroids in the period January 1st 2000 to December 31st 2013.

### Interventions:

The women underwent LSH, subtotal abdominal hysterectomy, total laparoscopic hysterectomy, total abdominal hysterectomy, laparoscopic myomectomy, abdominal myomectomy or hysteroscopic resection of fibroids

### Measurements and Main Results:

In total, 4.791 women were included in this trial. A morcellator was used in 1.846 of 1.957 laparoscopic procedures performed. Uterine LMS was diagnosed in 26 women, mean age 61.2 (SD=12.3) years. For six women, the LMS was diagnosed preoperatively. In 14 women with uterine LMS, the initial treatments were according to suspicion of a malignant condition. Consequently, six women with uterine LMS were treated according to anticipated benign fibroids. The incidence of uterine LMS in the population of women with anticipated benign fibroids was 0.0054 (1 in 183 women). The rate of unintended morcellation of LMS was 0.0002 (1 in 4791 women).

#### Conclusion:

The incidence of uterine LMS was comparable with the incidence found in the literature. The risk of unintended morcellation of uterine LMS after a preoperative selection of women with fibroids appears to be very low.



### **ABSTRACT TITLE**

# Peripartum cardiomyopathy in Denmark 2004-2015 - a nationwide registry-based cohort study.

# ABSTRACT AUTHORS AND AFFILIATIONS

Anne S. Ersbøll, Finn Gustafsson, Niels Vejlstrup, Peter Damm, Marianne Johansen.

Center for Pregnancy and Heart Disease, Rigshospitalet University of Copenhagen, Faculty of Health and Medical Sciences Denmark

### **ABSTRACT TEXT**

#### Background:

Peripartum cardiomyopathy (PPCM) is a rare disease presenting with heart failure in late pregnancy or in the first 6 months postpartum. The incidence varies around the world ranging from 1:300 in Haiti to 1:20.000 in Japan, but no population-based estimates of the incidence in European countries have been published. We aimed to estimate the incidence and report outcomes of PPCM in Denmark in 2004-2015 using data from nationwide registries and patient records.

#### Method:

The Danish National Birth Registry and the Danish National Patient Registry were linked and searched for the ICD-10 diagnoses "peripartum cardiomyopathy" or "heart failure" or "cardiomyopathy" in relation to a delivery from January 2004 to May 2015. All diagnoses were validated according to the EURObservational Research Programme PPCM Registry's inclusion criteria, and additional data were extracted from original medical records.

#### Results:

We searched 619.084 deliveries and identified 65 women who meet the inclusion criteria, equaling 1:9524 deliveries. There were 70 live born babies and one case of perinatal death. A total of 30 women (46.1%) had a hypertensive disorder of pregnancy in the index pregnancy. Four women needed mechanical cardiac support and two of these women underwent heart transplantation. There were three maternal deaths (4.6%).

#### Conclusion:

The incidence of peripartum cardiomyopathy in Denmark in 2004-2015 was 1:9524 deliveries based on validated national registry data. This is the first European incidence estimate based on nationwide registry-data. Major adverse events (death, transplantation and mechanical cardiac support) were comparable to other American and European cohorts.



# **ABSTRACT TITLE**

# **Preimplantation Genetic Diagnosis: A National Multicentre Obstetrical and Neonatal Follow-up**

# ABSTRACT AUTHORS AND AFFILIATIONS

Bjørn Bay (1,2); Hans Jakob Ingerslev(1); Josephine Lemmen (3) Birte Degn (1); Iben Anne Rasmussen (4); Ulrik Schiøler Kesmodel (1, 5)

1The Fertility Clinic and Center of Preimplantation genetic diagnosis, Department of Obstetrics and Gynecology, Aarhus University Hospital, Denmark; 2 Department of Gynecology and Obstetrics, Regionhospital Horsens, Denmark; 3The Fertility Clinic, Rigshospitalet, Denmark; 4The Fertility clinic, Department of Gynecology and Obstetrics, Odense University Hospital, Denmark; 5The Fertility Clinic, Herlev and Gentofte Hospital, Denmark.

### **ABSTRACT TEXT**

### Objective

Do women conceiving after preimplantation genetic diagnosis (PGD) and their children have greater risk of adverse pregnancy and birth outcomes compared to children conceived spontaneously or after vitro fertilization (IVF) with or without intra-cytoplasmatic sperm injection (ICSI).

#### Methods

Prospective cohort study based on medical records from all PGD centers in Denmark and the national IVF Registry and Medical Birth Register. The study included all deliveries after PGD treatment (n=126 deliveries/149 children), IVF/ICSI treatment (n=30,418 deliveries/36,115 children), and spontaneous conception (n=896,448 deliveries/909,624 children) in Denmark during the period 1999 to 2013.

#### Results

Compared to spontaneously conceived pregnancies PGD-pregnancies were at significantly increased risk of placenta praevia (adjusted OR (ORa)=9.1 (3.4; 24.9)), caesarian section (ORa=2.0 (1.3; 2.9)), preterm birth (ORa=1.6 (1.0; 2.7)), shorter gestation (-3.4 days (-5.7; -1.1)), and longer neonatal admission (24 days (17; 30)), whereas the risk of malformations was not significantly increased (ORa=1.1 (1.0; 1.2)). When analyses took into account the indication of PGD, adverse obstetrical and neonatal outcomes were only present in children conceived by PGD due to parental monogenetic disorder. The risks were comparable to those of children born to parents with monogenic disorders conceiving without PGD, except for a higher risk of placenta previa.

#### Conclusion

Compared to spontaneously conceived pregnancies PGD-pregnancies were at significantly increased risk of placenta praevia, caesarian section, preterm birth, shorter gestation, and longer neonatal admission. However, the risk seems to be related to the underlying parental condition rather than the PGD procedure.



# Long-term pelvic floor disorders after two consecutive sphincter injuries

# ABSTRACT AUTHORS AND AFFILIATIONS

Ida Nilsson Department of Obstetrics and Gynecology, Södra Älvsborgs Hospital, Borås; Jwan Al-Mukhtar Othman Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg; Sigvard Åkervall Department of Surgery, Södra Älvsborgs Hospital, Borås; Ian Milsom Department of Obstetrics and Gynecology, Sahlgrenska Academy at Gothenburg University, Gothenburg; Maria Gyhagen Department of Obstetrics and Gynecology, Södra Älvsborgs Hospital, Borås, Sahlgrenska Academy at Gothenburg University, Gothenburg;

## **ABSTRACT TEXT**

#### Aim

To survey the prevalence of symptomatic pelvic floor disorders (PFD) in 2-para women who suffered an obstetric anal sphincter injury (OASI) at each of two vaginal deliveries (VD).

#### Method

The Swedish Medical Birth Register identified all 2-para women with two VDs, each complicated by an OASI, during 1987-2000. Register data was combined with a self-administered questionnaire on PFDs distributed in 2015. Thus the follow-up time after the last VD was a minimum 15 years. The 40-item questionnaire included questions about urinary (UI) and fecal incontinence (FI), genital prolapse (sPOP), etc.

#### Results

In total, 324 women were included (response rate 69.0%). Mean (SD) age was 51(4) years. Time since last VD was 19(3) years. Infant birthweight (IBW)  $\geq$ 4.0 kg occurred in 27.2% at 1st and in 47.7% at 2nd delivery. 14.2% of babies at 2nd birth weighted  $\geq$  4.5 kg. The mean (95% confidence limits) for the prevalence of the main PFDs were: FI 36.1% (30.9-41.4%); UI 37.7% (32.4-43.0%); sPOP 16.4% (12.3-20.4%); any PFD 58.6% (53.3-64.0%); and overactive bladder (OAB) 28.5% (23.5-33.4%).

### Conclusion

Approximately two decades after two OASIs almost two-thirds of the women had one or more PFDs. FI was remarkably high, afflicting more than every third woman. For comparison, in the SWEPOP-1 study, performed in primipara with a similar follow-up time, the FI rate was 13.3% after one spontaneous VD, 27.8% after one VD with OASI, and 30.2% after vacuum extraction with an OASI. IBW ≥4.5 kg was strongly overrepresented at 2nd birth.



# Episiotomy affects the risk of OASIS in vacuum-assisted deliveries

# ABSTRACT AUTHORS AND AFFILIATIONS

Ninna Sønderby Lund, MD, Department of Gynecology and Obstetrics, Herning Hospital, Herning, Denmark; Lisa Kristine Grange Persson, Department of Gynecology and Obstetrics, Hvidovre Hospital, Copenhagen, Denmark; Hanna Jangö, MD, Department of Gynecology and Obstetrics, Herlev Hospital, Copenhagen, Denmark; Ditte Gommesen, RM, MHSc, Department of Gynecology and Obstetrics, Odense University Hospital, Odense, Denmark; Hanne Brix Westergaard, MD, PhD, Department of Gynecology and Obstetrics, North Zealand Hospital, Hillerød, Denmark.

## **ABSTRACT TEXT**

Background: The risk of obstetric anal sphincter injury (OASIS) is increased in vacuum-assisted delivery. Episiotomy might affect this risk. In Scandinavian countries, the use of episiotomy in vacuum-assisted delivery varies greatly. The objective of this study was to assess whether episiotomy affects the risk of OASIS in vacuum-assisted delivery among primiparous women in Scandinavian populations.

Materials and methods: A systematic review and meta-analysis was performed (PubMed, Cochrane library and Embase databases). Scandinavian studies investigating the risk of OASIS for primiparous women in vacuum-assisted deliveries with and without the use of episiotomy (median episiotomy excluded) were considered for inclusion. We assessed risk of bias of the included studies using the Scottish Intercollegiate Guideline Network (SIGN) quality score.

Results: Seven Scandinavian studies were included (n=91,943). Episiotomy significantly reduced the risk of OASIS in vacuum-assisted deliveries in primiparous women (OR 0.67 (95% CI 0.49-0.93)), NNT 13.8 (95% CI 13.1-14.5), i.e. 14 episiotomies have to be performed to avoid one case of OASIS in vacuum-assisted deliveries.

Conclusions: Mediolateral or lateral episiotomy can protect against OASIS and should be considered in vacuum-assisted delivery among primiparous women. The optimal episiotomy frequency is yet to be defined, and adverse effects of the procedure should be weighed against the benefits.



# **Cell based Non-invasive Prenatal Testing (NIPT)**

# ABSTRACT AUTHORS AND AFFILIATIONS

Niels Uldbjerg, Dep Obstet Gynecol, Aarhus University Hospital, Denmark; Ripudaman Singh, Arcedi Biotech ApS, Denmark; Lotte Hatt, Arcedi Biotech ApS, Denmark; Ida Vogel, Dep Clin Genet, Aarhus University Hospital, Denmark, Else Marie Vestergaard, Dep Clin Genet, Aarhus University Hospital, Denmark; Rikke Christensen, Dep Clin Genet, Aarhus University Hospital, Denmark; Palle Schelde, Arcedi Biotech ApS, Denmark; Steen Kølvraa, Arcedi Biotech ApS, Denmark.

# **ABSTRACT TEXT**

NIPT, based on circulating cell free fetal DNA in maternal plasma (cffNIPT) has a good screening-performance

concerning Downs syndrome. Recently, however, a number of publications have indicated that cffNIPT has only

limited clinical utility for subchromosomal abnormalities. However, if fetal cells – which is known to circulate in

maternal blood in extremely low numbers – could be isolated in pure form, it would be possible using whole

genome amplification to get pure fetal DNA in sufficient amounts to do microarray analysis or NGS without

contaminating maternal DNA. We therefore hypothesize that NIPT based on amplified DNA from fetal cells

circulating in maternal blood (fcmb-NIPT) will make it possible to detect subchromosomal aberrations. In the present study we present a robust method for isolation of fetal cells from maternal blood. We find a

mean number of fetal cells of 13 per 30 ml whole blood (range 2-45 cells per 30 ml whole blood. Furthermore, we have so far obtained fetal cells from every participant. Using blood samples from women

carrying a male fetus we have in addition investigated the fetal cell specificity of our marker combination by

using Y chromosome FISH signals as verification of a fetal cell. We here find a 100% fetal cell specificity of our

marker combination. We also find that fetal cells are stable in blood samples stored up to 48 hours. The performance of this method will be exemplified by cases.

We conclude that fcmb-NIPT deserves full attention concerning research and clinical validation.



### **ABSTRACT TITLE**

A new clinically applicable age-specific comorbidity index for preoperative risk assessment of ovarian cancer patients

# ABSTRACT AUTHORS AND AFFILIATIONS

Mette Calundann Noer, Department of Gynecology, Rigshospitalet, Copenhagen, Denmark; Cecilie Dyg Sperling, the Danish Cancer Society, Copenhagen, Denmark; Sofie Leisby Antonsen, Department of Gynecology, Rigshospitalet, Copenhagen, Denmark; Bent Ottesen, Department of Gynecology, Rigshospitalet, Copenhagen, Denmark; Ib Jarle Christiensen, Department of Pathology, Herlev University Hospital, Herlev, Denmark; Claus Høgdall, Department of Gynecology, Rigshospitalet, Copenhagen, Denmark

## **ABSTRACT TEXT**

Objective: To develop and validate a new feasible comorbidity index based on self-reported information suited for preoperative risk assessment of ovarian cancer patients.

Methods: The study was based on patient self-reported data from ovarian cancer patients registered in the Danish Gynecological Cancer Database between January 1, 2005 and December 31, 2012. The study population was divided into a development cohort (n=2020) and a validation cohort (n=1975). Age-stratified multivariate Cox regression analyses were conducted to identify comorbidities significantly impacting five-year overall survival in the development cohort, and regression coefficients were used to construct a new weighted comorbidity index. The index was applied to the validation cohort, and its predictive ability in regard to overall and cancer-specific five-year-survival was investigated. Finally, the performance of the new index was compared to that of the Charlson comorbidity index.

Results: Regression coefficients of age and five comorbidities (atherosclerotic cardiac disease, chronic obstructive pulmonary disease, diabetes, dementia and hypertension) were included in the new comorbidity index. The validation study found the new index to be significantly associated to both overall survival (HR 1.44, p=0.013) and cancer-specific survival (HR 1.51, p=0.017) in multivariate analyses adjusted for other prognostic factors. The index was a significantly better predictor than the Charlson comorbidity index.

Conclusion: This new age-specific comorbidity index based on self-reported information is a significant predictor of overall and cancer-specific survival in ovarian cancer. It can be used to quickly identify those ovarian cancer patients requiring special attention in terms of preoperative optimization and postoperative care.



# Higher-intensity physical activity in mid-pregnancy is predictive of improved glucose tolerance

# ABSTRACT AUTHORS AND AFFILIATIONS

Helga Medek1,3, Thorhallur Halldorsson2,3, Ingibjörg Gunnarsdottir2,3, Reynir T. Geirsson1,3 1Department of Obstetrics and Gynecology, 2 Unit for Nutrition Research, Landspitali University Hospital, Reykjavik, 3School of Health Sciences, University of Iceland, Reykjavik, Iceland.

## **ABSTRACT TEXT**

Introduction: Physical activity is recommended as therapeutic for patients with impaired glucose tolerance, including those overweight and obese. Whether such recommendations are also justified for pregnant women is not as well established. We investigated the association between physical activity among pregnant women and maternal glucose tolerance.

Material and methods: A non-selective sample of 217 pregnant women was recruited at a routine 20 week ultrasound examination. Participants answered the International Physical Activity Questionnaire (IPAQ) about frequency, intensity and duration of daily physical activity during the last 7 days and underwent oral glucose tolerance testing (OGTT) between 24-28 weeks. A subset of 72 overweight/obese pregnant women wore a pedometer for one week to assess IPAQ score and pedometric correlations to this.

Results: Of the sample 177 attended for OGTT; 51% were overweight or obese. The mean (SD) fasting glucose was 4.4 (0.4) mmol/l, and 13% had GDM. Only one-third engaged in vigorous physical activity . After adjustment for pre-pregnancy BMI, age and parity, those engaging in vigorous physical activity had significantly lower fasting glucose levels (by 0.15 mmol/l, 95%CI: 0.03-0.27) compared to those not vigorously active. This decrease was similar in both normal and overweight/obese women. The number of GDM cases was lower (p=0.03) among those vigorously active (3/57; 5%), compared to those who were not (19/120; 16%). No association with glucose tolerance was observed for physical activity of moderate intensity.

Conclusions: Only vigorous physical activity appears beneficial with respect to maternal glucose tolerance, both among normal, overweight and obese women.



### **ABSTRACT TITLE**

Risk of postnatal depression in women treated with selective serotonin reuptake inhibitors that discontinue use before pregnancy or receive treatment during pregnancy

### ABSTRACT AUTHORS AND AFFILIATIONS

Julie Glavind, MD, PhD 1, Anne S. Ferreira, MD 2,3, Poul Videbech, MD, DMSc, Professor 4, Niels Uldbjerg, MD, DMSc, Professor 2, Lars Henning Pedersen, MD, PhD, Associate Professor 2

1 Perinatal Epidemiology Research Unit, Institute for Clinical Medicine, Aarhus University Hospital, Denmark

2 Dep. Obstetrics and Gynecology, Aarhus University Hospital, Denmark

3 Regional Center for Child and Adolescent Psychiatry, Aarhus University Hospital, Denmark

4 Center for Neuropsychiatric Depression Research, Mental Health Center Glostrup, Denmark

### **ABSTRACT TEXT**

#### **OBJECTIVE**

To investigate the risk of postpartum depression among women treated with selective serotonin reuptake inhibitors (SSRI) that do or do not discontinue the drug before pregnancy.

#### **METHODS**

From the Aarhus Birth Cohort information was obtained on women giving birth from Jan 2011 to Sep 2012. Exposure to SSRIs was estimated by linkage to The Danish National Health Service Prescription Database. Edinburgh Postnatal Depression Scale (EPDS), obtained as part of routine screening, was used to measure symptoms of postpartum depression. We included 108 mothers who had used SSRIs during pregnancy (group 1), 210 mothers who discontinued SSRI within the last 6 months before conception (group 2), and 5,991 women with no SSRI use between 6 months prior to conception and parturition (group 3). Regression models were used to estimate adjusted odds ratios (aOR) of an EPDS score above 13 and to compare EPDS scores in the groups.

#### **RESULTS**

Preliminary results suggest different distributions of EPDS-scores in the groups: Median scores were 6, 5, and 3 among women in groups 1 to 3, respectively (p<0.001). The aOR for EPDS>13 was 13.1 (95% CI 7.0-24.5) in group 1 and aOR 3.0 (95% CI 1.5-5.9) in group 2 compared with group 3. The EPDS in the groups 1 and 2 had larger variances compared with the unexposed, suggesting a high heterogeneity in risk.

### CONCLUSION

Both women treated with SSRI during pregnancy and women who stopped treatment before pregnancy have a significantly increased risk of postpartum depression and should receive special care during and after pregnancy.



### **ABSTRACT TITLE**

# Reduced risk of breast cancer mortality in women using postmenopausal hormone therapy: A Finnish nationwide comparative study

# ABSTRACT AUTHORS AND AFFILIATIONS

Tomi S Mikkola, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, and Folkhälsan Research Center; Hanna Savolainen-Peltonen, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, and Folkhälsan Research Center; Pauliina Tuomikoski, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology; Fabian Hoti, EPID Research Oy; Pia Vattulainen, EPID Research Oy; Mika Gissler, National Institute for Health and Welfare, Information Services Department; Olavi Ylikorkala, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, Helsinki, Finland.

## **ABSTRACT TEXT**

Data are controversial on the impact of postmenopausal hormone therapy (HT) on breast cancer mortality. We analyzed nationwide Finnish data on breast cancer mortality risk in women using HT consisting of estradiol alone (ET) or estradiol plus progestogen combination (EPT).

In total 489 105 women using HT in 1994-2009, traced from the nationwide reimbursement register, were followed from the HT initiation (3.3 million cumulative exposure years) to breast cancer death (n=1578 women). The observed deaths were compared with those in the age-standardized background population using standardized mortality ratio (SMR) with 95% CI.

The breast cancer mortality risk was reduced in all HT users with exposure for ≤5 years (SMR 0.56; CI 0.52-0.60), >5 to 10 years (0.46; 0.41-0.51), or >10 years (0.62; 0.56-0.68). A significantly larger risk reduction was detected in the 50-59 years age group (0.33; 0.29-0.37) as compared to 60-69 (0.64; 0.59-0.70) or 70-79 (0.78; 0.69-0.87) years age groups. The death risk reductions in ET users tended to be larger in all age groups as compared to EPT users, with a significant difference only in the 70-79 years age group (0.66; 0.57-0.76 vs. 0.88; 0.77-1.00). The age at HT initiation, regardless whether ET or EPT, showed no association with breast cancer mortality.

In the Finnish unselected population breast cancer is fatal in one out of 10 patients. Our data imply that this risk in patients with a history of HT use is one out of 20 patients. This is an important message for women considering or already using HT.



# Histopathological characteristics of retained placenta: a prospective case-control study

# ABSTRACT AUTHORS AND AFFILIATIONS

Nikos Papadogiannakis, Department of Laboratory Medicine, Division of Perinatal Pathology, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; Margit Endler, Karolinska Institutet, Södersjukhuset, Department of Clinical Science and Education, Division of Obstetrics and Gynecology, Stockholm Sweden; Sissel Saltved, Karolinska Institutet, Södersjukhuset, Department of Clinical Science and Education, Division of Obstetrics and Gynecology, Stockholm Sweden.

## **ABSTRACT TEXT**

Introduction: Retained placenta is a potentially fatal obstetric disorder due to postpartum hemorrhage, its pathophysiology is however unknown. We aimed to assess if retained placenta was associated with increased macroscopic and histological signs of placental maternal underperfusion, a pattern otherwise seen in preeclampsia and other disorders of defective placentation. Methods: This was a case-control study of retained (n=49) and non-retained (n=47) placentas, collected from full-term singleton and otherwise healthy pregnancies, carried out at a tertiary level obstetric department. Macroscopic and histological analysis was performed. Signs of maternal placental underperfusion and signs of placental inflammation, fetal vascular thrombo-occlusive disease and increased placental attachment were recorded in a primary and secondary analysis respectively. Variables were compared groupwise using unconditional logistic regression or comparison of median or mean values. Results: Compared to non-retained placentas retained placentas had a significantly smaller surface area (p=0.05), were more oblong in shape (OR 5.24 95% CI:1.34-20.21) and showed overall more signs of maternal underperfusion (OR 2.52 95% CI: 1.07-5.87). There was no significant difference in signs of placental inflammation, fetal vascular thrombo-occlusive disease or placenta accreta but basal plate myometrial fibers were more common among retained placentas. Conclusion: In regard to shape, surface area and histological signs of maternal placental underperfusion, retained placentas showed a histological pattern similar to that seen in preeclamptic placentas.



### **ABSTRACT TITLE**

# Effects of free-of-charge provision of LARC-methods – a population based study

# ABSTRACT AUTHORS AND AFFILIATIONS

Frida Gyllenberg, MD, University of Helsinki, City of Vantaa; Tuire Karjalainen, MD, City of Vantaa; Satu Suhonen, MD, PhD, City of Helsinki, Mika Gissler, PhD, National Institute of Health and Welfare; Oskari Heikinheimo, MD, PhD, University of Helsinki, The Hospital District of Helsinki and Uusimaa.

# **ABSTRACT TEXT**

#### Background

The Long-Acting Reversible Contraceptive (LARC) methods, i.e. intrauterine devices and contraceptive implants outclass other commonly used methods in contraceptive efficacy. Large studies indicate that liberal provision of LARC methods result in high uptake and effective prevention of unplanned pregnancies.

#### Method

With 210 000 inhabitants, Vantaa is one of three large communities in the Helsinki metropolitan area (population 1,1 million). Since 2013 Vantaa has offered women their first LARC method free-of-charge at the public family planning clinics. We studied the abortion rates in Vantaa before and after this intervention, and compared with national rates using the Finnish national register on induced abortions.

#### Results

In 2003–2012 the mean annual abortion rate in Vantaa was 11.4/1000 women aged 15 – 49. Since the beginning of the intervention, 4160 women have received a LARC method free-of-charge and the abortion rate has declined to 10.2/1000 in 2013, 9.8/1000 in 2014 and 8.8/1000 in 2015. The corresponding decline in the number of abortions is 20% from approximately 550 abortions annually before the intervention to 439 in 2015. The calculated number-needed-to-treat in prevention of one unplanned pregnancy is 20. The overall abortion rate in Finland remained at a level just under 9/1000 (8.8/1000 in 2012, 8.7/1000 in 2013, 8.5/1000 in 2014).

#### Conclusions

The provision of LARC methods at no-cost was associated with reduced abortion rates in Vantaa. Further studies aim to reveal who chooses a LARC method when provided free-of-charge, if the provision can be further optimized and whether this intervention is cost-effective.



Endometrial cancer: Is the current follow-up routine essential?

# ABSTRACT AUTHORS AND AFFILIATIONS

Mette Moustgaard Jeppesen, Dpt. of Gynecology and Obstetrics, Odense University Hospital (OUH), University of Southern Denmark; Pernille Tine Jensen, Dpt. of Gynecology and Obstetrics, OUH, University of Southern Denmark; Dorte Gilså Hansen, The National Research Center of Cancer Rehabilitation, Research Unit of General Practice, University of Southern Denmark; Maria lachina, The Research Unit of Clinical Epidemiology, University of Southern Denmark; Malene Korsholm, Dpt. of Gynecology and Obstetrics, OUH, University of Southern Denmark; Ole Mogensen, Dpt. of Gynecology and Obstetrics, OUH, University of Southern Denmark

## **ABSTRACT TEXT**

#### Background:

Considerable controversy remains as to the optimal organization of endometrial cancer follow-up. Objectives: In a nation-wide cohort to: i) characterize disease recurrence in early stage endometrial cancer, ii) analyze the role of symptoms in the detection of disease recurrence.

#### Material and Methods:

All Danish women diagnosed with stage I and II endometrial cancer from 2005-2009 were included in a large national population-based historical cohort. The population was created using the Danish Gynecologic Cancer Database. Disease recurrences up to three years after the primary diagnosis were identified using a combination of national registries and chart reviews.

#### Results:

The resulting cohort consisted of 2612 women. Of these, 183 (7.0 %) women relapsed within three years after the primary diagnosis. Recurrence localization significantly impacted on overall survival with 5-year survival rates of 85.1 % in vaginal and 19.2 % in distant relapse, respectively. Among the 183 women with disease recurrence, 116 (63.4%) had a symptomatic relapse. One third of these were vaginal symptoms as a sign of vaginal recurrence. Examination was postponed until the next follow-up visit in 37.1 % of the women. Asymptomatic recurrence was found in less than 2.5 % of the 2612 women, and the asymptomatic recurrence was situated in the vaginal vault in 1.6 %.

#### Conclusion:

Understanding the nature of endometrial cancer relapse is the first step in evaluating the need of follow-up examinations. The majority of disease recurrences were symptomatic suggesting a superior role of symptoms compared to traditional follow-up visits in the detection of recurrence.



### **ABSTRACT TITLE**

# Pediatric respiratory morbidity after early term or term caesarean delivery: two-year follow-up from a randomized trial

# ABSTRACT AUTHORS AND AFFILIATIONS

Julie Glavind, MD, PhD 1, Ioanna Milidou, MD, PhD 1,2, Niels Uldbjerg, MD, DMSc, Professor 3, Tine Brink Henriksen, MD, PhD, Professor 1,2

1 Perinatal Epidemiology Research Unit, Institute for Clinical Medicine, Aarhus University Hospital, Denmark
2 Dep. Pediatrics, Aarhus University Hospital, Denmark
3 Dep. Obstetrics and Gynecology, Aarhus University Hospital, Denmark

# **ABSTRACT TEXT**

#### **OBJECTIVE**

To compare long-term respiratory morbidity after randomization to elective caesarean delivery (CD) at 38+3 weeks versus 39+3 weeks of gestation.

#### **METHODS**

Two-year follow-up from a randomized trial. From March 2009 to June 2011 1274 women from 7 Danish tertiary delivery wards were randomized to elective CD at 38 weeks 3 days (early term) or 39 weeks 3 days (term). Information on pediatric hospitalizations and ICD-10 diagnoses was retrieved from the Danish National Patient Registry. Information on any bronchodilator or inhaled steroid prescription in the children was obtained from the National Prescription Database. The primary outcome was any hospitalization with a respiratory diagnosis between 28 days and 2 years of age. Risk estimates, expressed as adjusted odds ratios (aOR) with 95% confidence intervals (CI), were calculated using logistic regression.

#### **RESULTS**

From 1271 children included in the analyses, 132/635 children with 710 admissions were registered in the early term group compared to 134/636 children with 683 hospital admissions in the term group. Thirty-one children in the early term group versus 38 in the term group had at least one admission with a respiratory diagnosis (aOR 1.05, 95% CI 0.82-1.34). Two-hundred-and-three children randomized to early term versus 214 to term CD had at least one prescription of inhaled drugs (aOR 0.96, 95% CI 0.82-1.12), whereas 382 early term versus 378 term children had at least one systemic antibiotic prescription (aOR 0.91, 95% CI 0.71-1.17).

### CONCLUSION

Within two years of birth, we found no significant difference in respiratory morbidity in children randomized to CD at early term as compared to term gestation.



# The maternal brain in preeclampsia, evidence for magnesium-deficiency: a 31P-MRS study.

# ABSTRACT AUTHORS AND AFFILIATIONS

Maria Nelander ,Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; Jan Weis, Department of Surgical Sciences, Radiology Unit, Uppsala University, Uppsala, Sweden; Lina Bergman, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden, Sweden Center for Clinical Research, Dalarna, Sweden; Anna-Karin Wikström, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden, Department of Medicine, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden;

## **ABSTRACT TEXT**

Background: Magnesium sulfate (MgSO4) is used as a prophylaxis for eclamptic seizures. The exact mechanism of action is not fully established.

Aim: Our aim was to study the maternal brain in preeclampsia with phosphorus magnetic resonance spectroscopy (31P-MRS) with particular interest in magnesium (Mg).

Methods: This cross-sectional study comprised 28 women with preeclampsia, 30 women with normal pregnancies in corresponding gestational week (range: 23-41 weeks) and 11 non-pregnant healthy controls. All women underwent 31P-MRS of the brain and were interviewed about cerebral symptoms. Results are presented as mean mmol/L ± standard deviation. Differences between groups were calculated by ANOVA and Tukey post hoc test.

Results: Mg levels in the maternal brain were significantly lower in preeclampsia,  $0.12\pm0.02$ , compared to normal pregnancy,  $0.14\pm0.03$  (p=0.044). Non-pregnant and normal pregnant women did not differ in Mg levels (p=0.98). Those in the preeclampsia group with visual symptoms had lower Mg than those without,  $0.11\pm0.02$  vs  $0.13\pm0.03$ , p=0.046.

Conclusions: Women with preeclampsia have lower levels of Mg in the brain which could explain the potent anti-seizure prophylactic properties of MgSO4. Within the preeclampsia group, women with visual disturbance had lower levels of Mg.



# **ABSTRACT TITLE**

# Estrogen metabolism in premenopausal breast adipose tissue – differences between women with or without breast cancer

# ABSTRACT AUTHORS AND AFFILIATIONS

Hanna Savolainen-Peltonen, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, and Folkhälsan Research Center; Feng Wang, Folkhälsan Research Center; Veera Vihma, Folkhälsan Research Center; Esa Hämäläinen, HUSLAB, Helsinki University Hospital; Ursula Turpeinen, HUSLAB, Helsinki University Hospital; Marjut Leidenius, University of Helsinki and Helsinki University Hospital, Breast Surgery Unit; Matti J Tikkanen, Folkhälsan Research Center; Tomi S Mikkola, University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, and Folkhälsan Research Center, Helsinki, Finland

# **ABSTRACT TEXT**

In premenopausal women circulating estrogens show cyclic variation during the menstrual cycle. Previous data suggest that these hormonal changes may affect breast tumor biology. Little is known about local estrogen metabolism in premenopausal breast adipose tissue and if there are differences between women with or without breast cancer.

We collected serum and breast sc adipose tissue samples from premenopausal women undergoing mastectomy due to an estrogen receptor-positive breast tumor (n=11) and from women undergoing breast reduction mammoplasty (n=17). Estradiol (E2), and estradiol fatty acyl ester (E2-FAE) concentrations were determined by liquid chromatography-tandem mass spectrometry. mRNA expression levels of estrogen-converting enzymes were analyzed by qRT-PCR.

Adipose tissue E2 concentrations fluctuated significantly during menstrual cycle, in line with serum concentrations, whereas E2-FAE concentrations remained unchanged. Adipose tissue E2 (median 584 pmol/kg vs. 350 pmol/L, P<0.01) and E2-FAE levels (112 vs. 11, P<0.01) were higher than the respective serum levels. Furthermore, adipose tissue E2 concentration was lower in the follicular than the luteal phase of menstrual cycle in women with cancer (404 vs. 889, P<0.05) but not in controls. In the follicular phase, the relative expressions of 17 $\beta$ -hydroxysteroid dehyrdogenase type 1 and CYP19A1 mRNA were also significantly lower in women with breast cancer than in controls.

Our findings indicate that both E2 and E2-FAE are present in higher concentrations in breast sc adipose tissue compared to serum of premenopausal women. Adipose tissue estradiol synthesis is actively regulated during the menstrual cycle, and may be different in women with or without cancer.



# **ABSTRACT TITLE**

# Normo- and hyperandrogenic PCOS-women exhibit an adverse metabolic profile through life.

# ABSTRACT AUTHORS AND AFFILIATIONS

Pekka Pinola 1,2, Katri Puukka 2,3, Terhi T. Piltonen 1,2, Johanna Puurunen 1,2, Eszter Vanky 4,5, Inger Sundström-Poromaa 6, Elisabet Stener-Victorin 7, Angelica Lindén Hirschberg 8, Marianne Skovsager Andersen 9, Dorte Glintborg 9, Jan Roar Mellembakken 10, Aimo Ruokonen 2,3, Juha S. Tapanainen 2,11 and Laure C. Morin-Papunen 1,2

1 Department of Obstetrics and Gynecology, Oulu University Hospital, Finland

## **ABSTRACT TEXT**

Introduction: Women with polycystic ovary syndrome (PCOS) exhibit several metabolic risk factors such as obesity, insulin resistance, dyslipidemia, chronic inflammation, and impaired glucose tolerance. Studies on age-related metabolic risk profiles in PCOS are scarce.

Objective: To compare the metabolic profile in normoandrogenic (NA-PCOS) and hyperandrogenic (HA-PCOS) women with controls throughout reproductive life in a Nordic population.

Subjects and Methods: 1526 PCOS women (NA-PCOS N=684 and HA-PCOS N=842) and 447 controls from eight study sites in the Nordic countries were divided into three age groups (<30, 30-39 and >39 years). The variables were assayed according to the routine methods used in the laboratories of the different study centers.

Results: NA-PCOS and HA-PCOS women had increased serum levels of insulin (after fasting and during oral glucose tolerance test), triglycerides, LDL, and lower HDL and higher blood pressure (all p<0.001) independent of body mass index (BMI) compared with the controls already from early adulthood until menopause. HA-PCOS women had higher BMI and waist circumference compared with NA-PCOS women, whereas other metabolic risk factors were comparable. The prevalence of metabolic syndrome was 2-5-fold higher in women with PCOS compared with controls, and the highest prevalence was observed in HA-PCOS women (42.4% vs. 19.5% in the NA-PCOS women, P=0.03 and 18.2% in the controls, P=0.01) in their late reproductive age.

Conclusions: When evaluating metabolic risks in women with PCOS, androgenic status, obesity and age should be taken into account, which would allow a tailored management of the syndrome already from early adulthood on.



# Effect of a national cardiotocography education program on birth hypoxia

# ABSTRACT AUTHORS AND AFFILIATIONS

Thellesen L(1), Bergholt T(1), Sorensen JL(1), Rosthoej S(2), Hedegaard M(1)

(1) Department of Obstetrics, The Juliane Marie Centre for Children, Women, and Reproduction, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

(2) Section of Biostatistics, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

## **ABSTRACT TEXT**

#### Introduction

Literature indicates an association between errors in management of electronic fetal monitoring (CTG) and hypoxic brain injuries. We aimed to examine whether the introduction of a national CTG education program was associated with a decrease in incidence of birth hypoxia.

### Method

A national obstetric safety project was introduced in 2012, consisting of a mandatory CTG education program and three checklists for admission, oxytocin augmentation, and assisted vaginal delivery to be implemented at all 24 Danish maternity units.

Study population: Liveborn singleton cephalic term infants, born at a Danish maternity unit 2008-2015. Data retrieved from the Medical Birth Register and the National Patient Register.

Birth hypoxia measured as Apgar score <7/5, umbilical cord pH <7.00, and the need for therapeutic hypothermia. Time trend analyses using logistic regression were performed.

#### Preliminary results

343.538 infants were included. Overall incidence of low Apgar score, low umbilical cord pH, and therapeutic hypothermia was 0.57 percent, 0.45 percent, and 0.05 percent, respectively. Incidence of both low Apgar and low pH was 0.08 percent. Minor variations were detected in the outcome incidences over time. A temporary rise in the incidence of emergency cesarean sections and an unchanged decreasing trend in assisted vaginal deliveries were detected.

#### Conclusion

Birth hypoxia is a rare adverse event and we did not detect a decreasing trend after a national CTG education program. We observed a temporary increase in cesarean sections and a continuous decreasing trend in assisted vaginal deliveries. The vast majority of infants with low cord pH had Apgar scores≥7/5.



# Older women are at highest risk of cervical cancer in Denmark

# ABSTRACT AUTHORS AND AFFILIATIONS

Anne Hammer (1,2), Johnny Kahlert (3), Anne Rositch (4), Lars Pedersen (3), Patti Gravitt (5), Jan Blaakær (1,2) Mette Søgaard (3)

1. Department of Obstetrics and Gynecology, Aarhus University Hospital, Denmark. 2. Department of Clinical Medicine, Aarhus University, Denmark. 3. Department of Clinical Epidemiology, Aarhus University Hospital. 4. Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, USA. 5. Department of

## **ABSTRACT TEXT**

Hysterectomy is a common gynecological procedure. Previous studies have shown that failing to remove hysterectomized women from the at-risk denominator when calculating the cervical cancer incidence rate may result in an underestimation of the cervical cancer incidence and in misleading age-specific comparisons.

Using data from nationwide registries, we calculated the cervical cancer incidence rate in Denmark during 2000-2011. Uncorrected rates were calculated by dividing the number of cervical cancers with the person-years of the at-risk female population. Hysterectomy corrected rates were calculated by subtracting the post hysterectomy women years from the at-risk denominator.

The overall cervical cancer incidence rate increased from 17.8/100,000 person-years (95% confidence interval (CI) 17.3 –18.3) to 19.3/100,000 person-years (95% CI 18.8 –19.9) after correcting for hysterectomy, equivalent to an 8.4% increase. The highest uncorrected cervical cancer incidence rate was seen in women aged 35-39 years (24.4/100,000 person years ; 95% CI 22.5 – 26.5), whereas the highest hysterectomy corrected incidence rate was observed in women aged 75-79 years, (29.4/100,000 person-years ; 95% CI 26.0 – 33.2). Over the study period, women  $\geq$  60 years had the highest hysterectomy corrected cervical cancer incidence compared to women < 60 years, although this difference was less remarkable in recent years.

In conclusion, correction for hysterectomy shifted the peak in cervical cancer incidence from women aged 35-39 years to women aged 75-79 years when screening is no longer recommended. Thus, evaluation of the current recommendations on the age for cessation of routine cervical cancer screening may be warranted.



# Delineating the association between mode of delivery and postpartum depression symptoms

# ABSTRACT AUTHORS AND AFFILIATIONS

Patricia Eckerdal<sup>1</sup>, Marios K. Georgakis<sup>2</sup>, Anastasia Kollia<sup>3</sup>, Anna-Karin Wikström<sup>1</sup>, Ulf Högberg<sup>1</sup>, Alkistis Skalkidou<sup>1</sup>

<sup>1</sup> Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden
<sup>2</sup> Department of Hygiene, Epidemiology and Medical Statistics, School of Medicine, National and Kapodistrian University of Athens, Greece

<sup>3</sup> Department of Biostatistics, Harokopio University, Athens, Greece

### **ABSTRACT TEXT**

Background: Postpartum depression (PPD) has a multifactorial genesis. The role of obstetric factors and specifically mode of delivery is still unclear.

Main Objective: To explore the association between mode of delivery and PPD taking into account the potentially mediating role of sociodemographic factors, psychiatric history, fear of childbirth, delivery experience, delivery complications and subjective postpartum symptoms.

Methods: In a longitudinal study of 3,888 Swedish childbearing women, the effect of delivery mode (spontaneous vaginal [VaD], vacuum extraction [VE], elective caesarean section [EICS] or emergency caesarean section [EmCS]) on PPD assessed by Edinburgh Postnatal Depression scale (EPDS) at six weeks postpartum was investigated. EPDS≥12 was defined as PPD. Information was collected through self-reported web-based questionnaires and medical records. Logistic regression models were designed and path-analysis using Generalized Structural Equation Modelling was conducted.

Results: Women who delivered by EmCS were at higher risk for PPD at six weeks postpartum compared to those who delivered spontaneous vaginally in the crude analysis (OR 1.45, [1.04-2.01]). No significant association between mode of delivery and PPD emerged in the multivariate analysis, but depression history, fear of delivery, negative delivery experience, delivery complications and subjective postpartum symptoms independently increased the odds of PPD. Many of these variables had a statistically significant mediating effect on the association between EmCS and PPD in the path-analysis. Diverse patterns emerged in the path-analyses for EICS and VE/EmCS versus VaD.

Conclusions: Mode of delivery has no direct impact on PPD. Still, several modifiable and non-modifiable mediators are present in this association.



#### **ABSTRACT TITLE**

# Prealbumin is a marker of nutritional risk in Hyperemesis Gravidarum

### ABSTRACT AUTHORS AND AFFILIATIONS

Olga Zybkina, School of Nutrition, Department of Clinical Medicine, University of Bergen; Anne Lise Bjørke Monsen, Institute of Clinical Science, University of Bergen; Jutta Dierkes, Department of Clinical Medicine, Section of Nutrition, University of Bergen; Jone Trovik, Institute of Clinical Science, University of Bergen and Department of Gynecology and Obstetrics, Haukeland University Hospital, Bergen, Norway

#### **ABSTRACT TEXT**

Objective: Hyperemesis gravidarum (HG) affects 1% of pregnancies and is potentially harmful for mother and foetus. Prealbumin is a marker of nutritional status. We wanted to investigate if Prealbumin level was associated with severity and nutritional risks of NVP (nausea and vomiting in pregnancy). Methods: A case-control study including 76 hospitalized patients with HG and 36 healthy controls. Serum Prealbumin was correlated to clinical and biochemical nutritional parameters, including 24h recall food-diary.

Results: HG patients had longer gestational length than controls, median 8.6 versus 7.0 weeks, p=0.001. The groups were similar regarding pre-pregnant weight, BMI, parity and proportion of patients with earlier hyperemesis pregnancies. The Prealbumin levels were significant lower in HG patients, median 0.19 mg/dL (95% CI 0.18-0.20) versus 0.23 in the control group (95% 0.19-0.24, p=0.003). Compared to the control group HG patients had significantly lower 24h energy intake, median 720 kcal versus 1646 (p=0.017), larger weight-change at inclusion, median –3 kg versus +1 kg (p<0.001), higher percentage of ketonuria +3-4 (69% versus 3%, p<0.001) and higher PUQE-score (Pregnancy Unique Questionnaire of Emesis and nausea) median 13 (95% CI 13-14) versus 7 (95% CI 6-9). Prealbumin level , 24 h caloric and protein intake significantly decreased while weight-loss and ketonuria increased across severity of NVP as classified by the three-tiered PUQE-score <6, 7-12 and 13-15 (all p <=0.013). Prealbumin level was significantly correlated to 24 h protein intake, Pearson Correlation =0.339 (p=0.008).

Conclusion: Prealbumin-measuring validates patients with severe NVP/HG as being at high nutritional risk.



# Prophylactic tranexamic acid in benign hysterectomy, a randomized placebo-controlled trial

### ABSTRACT AUTHORS AND AFFILIATIONS

Märta Topsoee, Department for Obstetrics and Gynecology, North Zealand Hospital, University of Copenhagen, Dyrehavevej 29, 3400 Hilleroed, Denmark; Thomas Bergholt, Department of Obstetrics, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen, Denmark; Bent Ottesen, The Juliane Marie Centre, Rigshospitalet, University of Copenhagen, Denmark, Blegdamsvej 9, 2100 Copenhagen, Denmark; Annette Settnes, Department for Obstetrics and Gynecology, North Zealand Hospital, University of Copenhagen, Dyrehavevej 29, 3400 Hilleroed, Denmark.

#### **ABSTRACT TEXT**

Objective: To investigate the anti-hemorrhagic effect of prophylactic tranexamic acid (TA) in elective benign hysterectomy.

Study design: A double-blinded randomized placebo-controlled trial was conducted at four Gynecological departments in Denmark from April 2013 to October 2014. A total of 332 women undergoing benign abdominal, laparoscopic or vaginal hysterectomy were included and randomized to either 1 g of intravenous TA or placebo at start of surgery.

Results: Intraoperative total blood loss was significantly reduced in the TA group compared to the placebo group when estimated both subjectively by the surgeon and objectively by weight (98.4 ml vs 134.8 ml, P = .006 and 100.0 ml vs 166.0 ml, P = .004). The incidence of blood loss  $\geq$ 500 ml was also significantly reduced (6 vs 21, P = .003), as well as the use of open-label TA (7 vs 18, P = .024). Furthermore, the risk of reoperations due to postoperative hemorrhage was significantly reduced in the TA group compared to the placebo group (2 vs 9, P = .034). This corresponded to an absolute risk reduction of 4.2% and number-needed-to-treat of 24. No incidence of thromboembolic events or death was observed in any of the groups.

Conclusion: Our results suggest that tranexamic acid reduces overall total blood loss, the incidence of substantial blood loss and the need for reoperations due to postoperative hemorrhage in relation to benign hysterectomy. This without increasing the risk of serious adverse events. Thus, TA should be considered as a prophylactic treatment prior to elective benign hysterectomy.



#### **ABSTRACT TITLE**

#### Preterm births in the Nordic countries 1997-2011

### ABSTRACT AUTHORS AND AFFILIATIONS

Kristín María Gudjonsdóttir (1), R Bjarnadóttir (2), BB Másdóttir (2), E Løkkegaard (3), S Rasmussen (3), T Bergholt (4), S Albrechtsen (5), K Klungsøyr (6), FEI Skjeldestad (7), MC Fagerberg (8), K Källén (9), K Gottvall (9), A-M Tapper (9), A Pyykönen (10), M Gissler (11), A Smárason (12).

- (1) Dept of Obstet and Gynecol, National University Hospital of Iceland, Iceland
- (2) The Icelandic Birth Registry, National University Hospital of Iceland, Iceland

#### **ABSTRACT TEXT**

Objective: To study the incidence of preterm births (<37 weeks gestation) in the Nordic countries from 1997-2011, changes over time and the distribution of Cesarean deliveries (CD) within Robson groups 6-10.

Design and setting: Retrospective, population-based study including all preterm births in 1997-2011 based on the Birth Registries in Iceland, Norway, Sweden, Finland and Denmark.

Methods: Crude rates of preterm deliveries and CD were calculated by country and Robsons groups (6-10).

Results: The incidence of preterm delivery was on average 5.62% and stable over time. Highest in Norway 6.27% and lowest in Iceland 5.11%. Of the preterm births 5.0% were in group 6 (nulliparous breech), 4.6% in group 7 (multiparous breech), 14.2% in group 8 (multiples), 0.9% in group 9 (transverse lie) and 72.3% were in group 10 (single cephalic). Denmark had more multiple preterm deliveries and Finland fewer preterm breech deliveries (groups 6 and 7).

Only 0.33% deliveries were at 22-27 weeks. The CD rate in group 10 was around 30% in all countries at the beginning of the study period and increased to 33.3% in Denmark and decreased to 27.3% in Iceland. For preterm births in groups 6, 7 and 8 the CD rates were on average 76.1%, 72.1% and 52.9%, respectively, and highest in Denmark and Sweden.

Conclusions: Of all births in the Nordic countries 5.62% were preterm. This was stable over the study period and with minor differences between the countries. Group 10 has 72% of the preterm births with 30% CD rate on average.



# Influence of oral contraceptives on sexuality: evidence from a randomized placebo-controlled trial

### ABSTRACT AUTHORS AND AFFILIATIONS

Angelica Lindén Hirschberg, Dept of Women's and Children's Health, Karolinska Institutet and Dept of Obstetrics and Gynecology, Karolinska University Hospital, Stockholm, Sweden;

Niklas Zethraeus, Dept of Learning, Informatics, Management and Ethics, Karolinska Institutet, Stockholm, Sweden;

Anna Dreber, Dept of Economics, Stockholm School of Economics, Stockholm, Sweden; Eva Ranehill, Dept of Economics, University of Zurich, Zurich, Switzerland;

#### **ABSTRACT TEXT**

#### Background:

There is a lack of knowledge about the effects of oral contraceptives (OC) on sexual function in women. We hypothesized that a widely used combined OC impairs sexual function. Methods:

We conducted a double-blind, randomized, placebo-controlled trial on a combined OC (150  $\mu$ g levonorgestrel and 30  $\mu$ g ethinylestradiol) in 340 young healthy women. Sexual function was evaluated before and after three months of treatment. The primary outcome measure was the aggregate score on the Profile of Female Sexual Function (PFSF total). Secondary outcome measures were the seven domains of the PFSF, the Sexual Activity Log, and the Personal Distress Scale. Changes in sexual function were related to changes in serum levels of testosterone in exploratory analyses. Results:

Overall sexual function (PFSF total) in the OC group changed in the hypothesized direction but did not reach statistical significance compared to placebo (-3.0 vs -0.4, P=0.094). However, the PFSF domains desire (-5.9 vs -1.4), arousal (-4.8 vs 0.2) and pleasure (-6.3 vs -1.2) were significantly reduced in comparison to placebo (P<0.05, for all). The mean frequency of satisfying sexual episodes (P=0.055) and personal distress (P=0.082) tended to change in the hypothesized direction. There were no significant correlations between changes in sexual function and changes in serum levels of testosterone in the OC group.

#### Conclusions:

This study suggests a negative impact of a levonorgestrel-containing OC on aspects of sexual function in young women. While the observed change on average can be considered small it should be clinically meaningful in some individual women.



# Late-week surgery of endometrial cancer is associated with worse survival

### ABSTRACT AUTHORS AND AFFILIATIONS

Tormund S. Njølstad, Department of Clinical Science, University of Bergen and KG Jebsen Centre for Gynecologic Cancer Research, Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway; Henrica M. Werner, Department of Clinical Science, University of Bergen and KG Jebsen Centre for Gynecologic Cancer Research, Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway; Janusz Marcickiewicz, Department of Gynecology, Sahlgrenska Academy, University of Gothenburg, Sweden; Solveig Tingulstad, Department of Gynecology, St. Olav's Hospital, Trondheim, Norway;

#### **ABSTRACT TEXT**

Objective: To explore weekday of surgery in relation to long-term outcome in endometrial cancer. Background: Surgery is the cornerstone in primary endometrial cancer treatment including total hysterectomy with bilateral salpingo-oophorectomy, and retroperitoneal lymph node dissection and omentectomy for high-risk patients. Recent reports from esophageal cancer reveals worse outcome after surgery performed later in the week.

Methods: Weekday of surgery was related to clinicopathological variables and outcome in 1366 endometrial cancer patients prospectively included in the MoMaTEC multicenter trial. Day of surgery was dichotomized as early-week (Monday-Tuesday) vs. late-week (Wednesday-Friday), and evaluated as a discrete variable.

Results: Adjusted for age, BMI, stage, and histology, late-week surgery was associated with an estimated 46.9% increased risk for all-cause death (p=0.043). In high-stage patients the 5-year disease-specific survival proportions were 53.0% and 40.7% for early-week and late-week operated patients, respectively (p=0.006). A multivariate analysis for the same patient groups revealed late-week surgery to correlate with an increased risk of disease-specific and all-cause death (85.3% and 74.3%, p<0.020). Analyzing separately patients undergoing more advanced surgical procedures (including lymphadenectomy), the prognostic effect of late-week surgery remained for both disease-related and all-cause death (HR 2.09 and HR 1.88, p<0.006).

Conclusion: Endometrial cancer surgery conducted late-week is associated with worse long-term outcomes. The trends are most evident among patients with high FIGO stages and patients who had undergone major surgical procedures. Our results indicate surgery on endometrial cancer patients with suspected advanced disease is better carried out early in the week.



# Mortality and causes of death in women with history of placental abruption

### ABSTRACT AUTHORS AND AFFILIATIONS

Outi Riihimäki, Dept. of Obstetrics and Gynecology, University of Helsinki; Jorma Paavonen, Dept. of Obstetrics and Gynecology, University of Helsinki; Tiina Luukkaala, Science Center, University of Tampere; Mika Gissler, THL National Institute for Health and Welfare, Helsinki, Finland; Marjo Metsäranta, Children's Hospital, University of Helsinki; Sture Andersson, Children's Hospital, University of Helsinki; Mika Nuutila, Dept. of Obstetrics and Gynecology, University of Helsinki; Eero Pukkala, Finnish Cancer Registry, Helsinki, Finland; Minna Tikkanen, Dept. of Obstetrics and Gynecology, University of

#### **ABSTRACT TEXT**

Objective: To find out whether mortality is increased among women with history of placental abruption.

Methods: Data on women with placental abruption diagnosed between 1969 and 2005 (n=7,805) were collected from the Finnish Hospital Discharge Register and the Finnish Medical Birth Register. A matched reference cohort consisted of three women without placental abruption for each case (n=23,523). The causes of death were retrieved from the Cause-of-Death Register. The main outcome measure was the hazard ratio (HR) of cause-specific mortality in women with history of placental abruption compared with the reference cohort. Standardized mortality ratios (SMRs) were calculated to compare the mortality in both cohorts with that in the general population.

Results: By the end of year 2013, 395 women with history of placental abruption and 863 women from the reference cohort had died. The overall mortality was increased in the abruption cohort when compared with the reference cohort (HR 1.39, 95% confidence interval [CI] 1.24–1.57). The abruption cohort had an increased risk to die from malignancies of larynx, trachea, bronchus and lung (HR 1.72, [1.05–2.82]), alcohol-related causes (HR 1.84, [1.25–2.72]), and external causes (HR 1.63, [1.19–2.22]), especially suicides (HR 1.71, [1.07–2.74]). The overall SMR was increased in the abruption cohort when compared with that in general population (1.13, [1.02–1.24], especially for malignancies of larynx, trachea, bronchus and lung (1.79, [1.16–2.64]).

Conclusion: Both the overall mortality and mortality from several specific causes are increased in women with history of placental abruption.



# Decidual Nrf2-mediated oxidative stress response in preeclampsia and fetal growth restriction

### ABSTRACT AUTHORS AND AFFILIATIONS

S. B. Mundal1,4, P. Basnet4,5, G. B. Silva1, B. Skei1, L. C. V. Thomsen1,2, L. Bjørge2,3, G. Acharya4,5, A. C. Iversen1

 Centre of Molecular Inflammation Research, Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology (NTNU), NO-7491 Trondheim, Norway
 Department of Gynecology and Obstetrics, Haukeland University Hospital, NO-5058 Bergen, Norway
 Centre for Cancer Biomarkers, Department of Clinical Science, University of Bergen, NO-5021 Bergen, Norway

#### **ABSTRACT TEXT**

Introduction: Oxidative stress and antioxidant incapability is part of placental dysregulation in preeclampsia and fetal growth restriction (FGR). The master-regulator of oxidative stress response is the transcription factor Nrf2. We have previously identified the Nrf2-driven canonical pathway to be significantly affected in a decidua transcriptional profile of preeclamptic pregnancies.

Objective: We aimed to investigate whether the transcriptional up-regulation of the Nrf2 pathway correlates with decidual oxidative stress and total antioxidant capacity in pregnancies complicated by preeclampsia and/or FGR.

Material and methods: Decidua basalis tissue was collected by vacuum aspiration of the placental bed during caesarean section from women with pregnancies complicated by preeclampsia and/or FGR and women with normotensive pregnancies. Total antioxidant capacity and oxidative stress levels were measured.

Results: There were 19 included pregnancies with preeclampsia, 15 with FGR, 37 with preeclampsia combined with FGR, and 57 normotensive pregnancies. The total antioxidant capacity in decidua was decreased in pregnancies complicated with preeclampsia combined with FGR compared to controls (p= 0,02), but did not differ between pregnancies with only FGR, only preeclampsia and controls. In the reanalyzed decidual transcriptional profile, seven Nrf2-associated transcripts were significantly affected in pregnancies with both preeclampsia and FGR.

Conclusion: Pregnancies complicated with both preeclampsia and FGR are associated with decidual up-regulation of Nrf2-associated transcripts and decreased antioxidant capacity.



Chronic hypertension after perinatal exposure to preeclampsia, SGA and prematurity.

### ABSTRACT AUTHORS AND AFFILIATIONS

Linda Lindström, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; Eva Bergman, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; Maria Lundgren, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; Kari Klungsøyr, Department of Global Public Health and Primary Care, Bergen, Medical Birth Registry of Norway, Norwegian Institute of Public Health, Bergen, Norway; Sven Cnattingius, Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden; Anna-Karin Wikström, Department of

#### **ABSTRACT TEXT**

Background: There is an established association between perinatal exposures, such as low birth weight, and chronic hypertension in adult life. However, different adverse perinatal exposures are often coexistent in the same pregnancy. The aim of the study was to investigate single and conjoint perinatal exposure to preeclampsia, being born small for gestational age (SGA) or preterm and the subsequent risk of chronic hypertension among women of fertile age.

Methods: The study population consisted of 751,155 primiparous women from Norway and Sweden registered in the Medical Birth Registers both as infants and as first time mothers from 1967 (Norway) and 1973 (Sweden) until 2010. Risks of chronic hypertension in early pregnancy were calculated in women perinatally exposed to preeclampsia, born SGA and/or preterm by unconditional logistic regression analysis and adjusted for age and socioeconomic factors and presented as odds ratio (OR); 95% confidence intervals (CI).

Results: The rate of chronic hypertension was 0.42%. Risks of chronic hypertension were independently associated with perinatal exposures to preeclampsia, born SGA and preterm (adjusted OR; 95% CI: 2.23 1.81-2.74; 1.19 1.05-1.34 and 1.24 1.03-1.50 respectively). The risk of chronic hypertension was further increased after conjoint exposures, almost 4-fold after perinatal exposure to preeclampsia and preterm birth. Additional adjustment for BMI and smoking in a subset of the cohort only had minor impact on the results.

Conclusions: Perinatal exposure to preeclampsia, being born SGA or preterm is associated with an increased risk of chronic hypertension, in particular exposure to preeclampsia with or without conjoint exposure.



# Estrone metabolism in subcutaneous and visceral adipose tissue in postmenopausal women

### ABSTRACT AUTHORS AND AFFILIATIONS

Natalia Bogdan, University of Helsinki and Helsinki University Hospital; Hanna Savolainen-Peltonen, Helsinki University Hospital; Esa Hämäläinen, HUSLAB; Ursula Turpeinen, HUSLAB; Mikko Haanpää, HUSLAB; Feng Wang, Folkhälsan Research Center; Matti J. Tikkanen, Folkhälsan Research Center; Veera Vihma, Folkhälsan Research Center; Tomi S. Mikkola, Helsinki University Hospital and Folkhälsan Research Center

#### **ABSTRACT TEXT**

Adipose tissue (AT) is important in estrogen synthesis and metabolism in postmenopausal women. Key enzymes include steroid sulfatase (STS), which hydrolyzes circulating estrone sulfate (E1S) to estrone (E1), and aromatase, which converts androstenedione to E1, and testosterone to estradiol (E2).

We studied STS activity in postmenopausal women by incubating whole subcutaneous and visceral AT homogenates with [3H]-E1S and using liquid-scintillation counting to measure [3H]-E1 liberated. Concentrations of E1 in AT and serum, and E1S in serum, were measured using LC-MS/MS. STS and aromatase-encoding CYP19A1 gene mRNA expression levels were quantified with real-time qPCR.

STS activity was similar in subcutaneous and visceral AT, 4.7 vs. 5.1 nmol/kg adipose tissue/h. E1 concentration was higher in visceral (960 pmol/kg) than in subcutaneous AT (721 pmol/kg, P=0.02) and serum (88 pmol/l, P<0.001). Serum E1S correlated strongly with serum E1 (r=0.76, P<0.001), and both showed positive correlations with subcutaneous (r=0.47, P=0.02) and visceral (r=0.69, P<0.001) AT E1 concentrations.

mRNA expression levels of STS and CYP19A1 were higher in subcutaneous than in visceral AT, P<0.01. STS mRNA expression in visceral AT correlated positively with E1 concentration in serum (r=0.59, P=0.01) and visceral AT (r=0.53, P=0.03). E1 concentration in visceral AT also correlated positively with body mass index (BMI) (r=0.40, P=0.03).

We show that STS is active in converting E1S to E1 in subcutaneous and visceral AT. E1 concentration in visceral AT correlated with and exceeded those in the serum and subcutaneous AT, suggesting an important role of visceral AT in peripheral estrone metabolism in postmenopausal women.



Simulate anywhere - 'in situ' versus 'off site' obstetric simulation

### ABSTRACT AUTHORS AND AFFILIATIONS

Jette Led Sørensen (1), Cees Van der Vleuten (2), Susanne Rosthøj (3), Doris Østergaard (4), Vicki LeBlanc (5), Marianne Johansen (1), Kim Ekelund (1), Charlotte Albrechtsen (1), Berit Woetman Pedersen(1), Bent Ottesen (1) (1)Juliane Marie Centre for Children, Women and Reproduction, Dep. of Obstetrics and Anaesthesiology, Rigshospitalet, University of Copenhagen, Denmark. (2) Dep. of Educational Development and Research, Faculty of Health, Maastricht University, Netherlands. (3) Section of Biostatistics, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark. (4) Copenhagen Academy for Medical Education and Simulation, Herlev

#### **ABSTRACT TEXT**

#### Introduction:

Simulation-based medical education has traditionally been conducted as off site simulations (OSS) in simulation centres or hospital facilities. Recently, in situ simulation (ISS) was introduced. ISS is conducted on the actual patient care site, and argued to have more authenticity and leading to improved learning. The aim of this study was to investigate the effect of ISS versus OSS on various individual, team and organisational outcomes.

Method:

Design: Randomised trial. Setting: Obstetric and anaesthesiology departments, Rigshospitalet, Denmark. One hundred staff-members were recruited and matched in authentic teams of ten (midwifes, auxiliary, anaesthesia and nurses, specialty trainees and consultant doctors). Intervention: Two simulations (management of an emergency Caesarean section and postpartum haemorrhage) conducted in the ISS and OSS settings. Primary outcome measures: Knowledge based multiple choice question (MCQ) test. Exploratory outcome (individual level): Safety Attitudes Questionnaire, stress measures (State-Trait Anxiety Inventory, Cognitive Appraisal, salivary cortisol), Intrinsic Motivation Inventory and questionnaire to evaluate perceptions; on team level: video assessment of team-performance, and on organisational level: practical and organisational changes suggested by participants.

#### Results:

No difference between the ISS versus OSS was found in the MCQ-test, safety attitudes, stress measurements, motivation, perceptions and video assessment of team performance. However, ISS was perceived to be more authentic than OSS. More ideas/suggestions for changes on the organisational level came from ISS participants.

#### Conclusion

Participants' perception of the authenticity differed significantly with ISS being conceived as more authentic however, the site of simulation (ISS vs OSS) did not affect other individual or team outcomes.

Literature:http://bmjopen.bmj.com/content/5/10/e008344.full.pdf+html



Aspects of women's health before and after a sexual assault.

### ABSTRACT AUTHORS AND AFFILIATIONS

Mie-Louise Larsen, Centre for Victims of Sexual Assault, Rigshospitalet, University of Copenhagen, Denmark.

Malene Hilden, Centre for Victims of Sexual Assault, Rigshospitalet, University of Copenhagen and Department of
Obstetrics and Gynaecology, Rigshospitalet, University of Copenhagen, Denmark.

Øjvind Lidegaard, Department of Obstetrics and Gynaecology, Rigshospitalet, University of Copenhagen,
Denmark.

#### **ABSTRACT TEXT**

Introduction. Sexual assault is a public health issue with many potential short- and long-term consequences for the victims. We aimed to investigate the pre and post-assault morbidity in female victims of sexual assault.

Materials and Methods. We included 2501 women who attended the Centre for Victims of Sexual Assault in Copenhagen, and 10004 control-women without a known assault experience. Diagnoses were retrieved from the National Health Registry and number of visits to general practitioners from the Danish Health Insurance Registry. Data were assessed during a five-year period before and after the assault. Sensitivity analysis was performed for previous sexual victimization.

Results. The relative risk of having one or more psychiatric diagnoses was 5.7 (95 % CI 5.1-6.4) for exposed versus non-exposed women before the assault and 5.6 (5.1-6.1) after the assault. For some specific somatic disorders the risk estimates before and after the assault were: disease of digestive system: 2.7 (2.4-3.2) and 2.6 (2.3-2.4); epilepsy: 2.9 (2.2-3.8) and 4.1 (3.0-5.6); disease of the liver: 3.5 (1.9-6.3) and 7.0 (4.4-11.1). The relative risk of laparoscopic surgery was 1.5 (0.9-2.5) before and 3.4 (2.3-5.0) after the assault. The number of visits to a general practitioner was also significantly higher for exposed women both before and after the assault. Complications associated with childbirth were not statistically different between the two groups.

Conclusions. Our results suggest increased psychiatric and somatic morbidity in women seen at a sexual assault center before as well as after the assault compared to controls.



#### **ABSTRACT TITLE**

Circulating Levels of TNF-Related Apoptosis Inducing Ligand are decreased in patients with large Adult-type Granulosa Cell Tumors

### ABSTRACT AUTHORS AND AFFILIATIONS

Anniina Färkkilä, Obstetrics and Gynecology and Children's Hospital/Univ of Helsinki and Helsinki University Hospital (1); Giorgio Zauli, University of Ferrara, Italy; Ulla-Maija Haltia, (1); Marjut Pihlajoki, Chilren's Hospital/University of Helsinki and Helsinki University Hospital; Leila Unkila-Kallio, Obstetrics and Gynecology/ University of Helsinki and Helsinki University Hospital; Paola Secchiero, University of Ferrara, Italy; Markku Heikinheimo, Chilren's Hospital/University of Helsinki and Helsinki University Hospital.

#### **ABSTRACT TEXT**

Background: Targeted treatments are needed for advanced adult-type granulosa cell tumors (AGCTs). We set out to assess tumor tissue and circulating levels of TNF-related apoptosis inducing ligand (TRAIL), a promising anti-cancer cytokine, in patients affected by AGCT.

Methods: We analyzed tissue expression of TRAIL in 127 AGCTs using immunohistochemistry or RT-PCR. Soluble TRAIL was measured by means of ELISA from 141 AGCT patient serum samples, as well as the conditioned media of 15 AGCT patient-derived primary cell cultures, and the KGN cell line. Tissue and serum TRAIL levels were analyzed in relationship with clinical parameters, and serum estradiol, FSH and LH levels.

Results: We found that AGCT samples expressed TRAIL mRNA and protein at levels comparable to normal granulosa cells, and that TRAIL protein was also strongly expressed in the tumor stroma. AGCT cells did not produce soluble TRAIL. TRAIL protein levels were decreased in tumors over 10cm in diameter (p=0.04). Consistently, circulating TRAIL levels correlated negatively to tumor dimension (p=0.01). Circulating TRAIL levels negatively associated with serum estradiol levels. In multiple regression analysis, tumor size was an independent factor contributing to the decreased levels of soluble TRAIL in patients with large AGCTs.

Conclusions: AGCTs associate with significantly decreased tumor tissue and serum TRAIL levels in patients with a large tumor mass. These findings encourage further study of agonistic TRAIL treatments in patients with advanced or recurrent AGCT.



## Teenage births in the Nordic countries

### ABSTRACT AUTHORS AND AFFILIATIONS

Løkkegaard E1, Rasmussen S1, Pyykönen A2, Tapper A-M2, Bjarnadóttir RI3, Másdóttir BB3, Smarason A4, , Klungsøyr K5,6, Albrechtsen S7,8, Fagerberg MC9, Gottvall K 10, Källén K10, Skjeldestad FE11, Gissler M12, Bergholt T13

Department of Obstetrics and Gynecology, Nordsjællands Hospital, University of Copenhagen, Denmark
 Helsinki University Central Hospital, Department of Obstetrics and Gynecology, Finland
 The Icelandic Birth Registry, National University Hospital of Iceland, Iceland

#### **ABSTRACT TEXT**

The purpose of the present study was to describe the teenage births by The Robson classification system and risk of cesarean delivery.

Method: A Nordic collaborative study was initiated using data from the national birth registries from 2000 to 2011.

Results: During the study period there were 3,398,586 births of which 68,480 (2%) were teenage births. The rate of teenage births decreased from 2.3% to 1.9% percent over the study years. Highest birth rates were found in Finland (3.8%), followed by Iceland (2.3%), Norway (2.3%), Sweden (1.7%) and Denmark (1.4%).

In total 70.8% of the teenage births had spontaneous onset (Robson 1) and 10.6% were induced at term (Robson 2 and 4). In total 2.5% had breech (Robson 6), 0.7% multiple pregnancies (Robson 8) and 5.9% preterm (Robson 10).

Overall the cesarean delivery rate was 10.9% among teenage birth. The rate increased slightly from 10.3% till 11.0% across study.

The cesarean delivery rates were 4.7% in Robson 1, 14.0 % in Robson 2, 78.9% in Robson 6, 45.5% in Robson 8, and 22.9% in Robson 10.

Conclusion: The rate of teenage pregnancies is slightly decreasing with some variation between the Nordic countries. They are associated with stable low rate of cesarean delivery around 10% compared to 20% among nulliparous non-teenage pregnancies. The pre-labor cesarean section rate is 1.6% compared to 2.8% in nulliparous non-teenage pregnancies.



# Labour induction: Outcomes and complications related to individual regimens.

### ABSTRACT AUTHORS AND AFFILIATIONS

Mette Hedegaard, MD,
Øjvind Lidegaard, professor in Obstetrics and Gynecology,
Charlotte Wessel Skovlund, data manager
Lina Steinrud Mørch, epidemiologist, and
Morten Hedegaard, head of dept. of obstetrics,
Rigshospitalet, Copenhagen, Denmark

### **ABSTRACT TEXT**

Objective. To assess rates of emergency caesarean section and perinatal death among pregnant women induced either with vaginal Dinoprostone, vaginal Misoprostol or oral Misoprostol.

Design. Register-based cohort study.

Setting. Denmark, 2009-2012.

Participants. Pregnant women >37 weeks gestation with a medically induced labour. Participants were divided according to method of induction: vaginal Dinoprostone, vaginal Misoprostol or oral Misoprostol.

Outcome measures. Odds ratio for emergency caesarean section and perinatal death adjusted for age, parity, plurality, BMI and smoking.

Results. Included were 224,363 pregnancies, of which 43,281 were medically induced. Labour induction from 37 weeks' gestation increased significantly from 15.7% in 2009 to 26.4% in 2012 (p < 0.001), which resulted in a corresponding decrease in post-term pregnancy. The use of vaginal Dinoprostone decreased during the study period from 50.0% in 2009 to 30.4% in 2012, whereas the use of oral Misoprostol increased tenfold from 5.1% in 2009 to 49.2% in 2012. The adjusted OR for emergency caesarean section was 0.83 (0.79-0.88) with vaginal Misoprostol and 0.63 (0.58-0.68) with oral Misoprostol using oral Dinoprostone as a reference. No significant results were found concerning perinatal death.

Conclusion. Labour induction with Misoprostol resulted in less emergency Caesarean sections compared to Dinoprostone. The risk was lowest with oral route of administration compared to vaginal administration. No difference in risk of perinatal death was found between the different types of labour induction.



## Obstetric self/home monitoring of maternal and fetal wellbeing

### ABSTRACT AUTHORS AND AFFILIATIONS

Olav Bjørn Petersen, Dept of Obstetrics and Gynecology, Aarhus University Hospital Skejby; Katrine Bach, Dept of Obstetrics and Gynecology, Aarhus University Hospital Skejby; Lone Holst, Dept of Obstetrics and Gynecology, Aarhus University Hospital Skejby;

#### **ABSTRACT TEXT**

#### Aim

To describe development, implementation, organizational changes and experience with obstetric self/home monitoring in complicated pregnancies at a university hospital

#### Introduction

Home-monitoring of fetal well-being is commercial available, but to our knowledge hitherto only used in uncomplicated pregnancies, and not as a complete obstetric management system.

#### Methods

As a part of a large-scale Danish telemedicine project (KIH), we have developed a complete obstetric management system, based on a freely available Open Source platform (OpenTele), using a standard Android tablet.

The patient system enables monitoring by a range of available devices:

- -Fetal and maternal heart rate and uterine activity
- -Vital parameters; BP, pulse, oxygen saturation
- -Weight
- -Blood glucose
- -CRP

The patient system also includes a questionnaire generator, enabling interactive questionnaires which could also include manually entered values, i.e urinary analysis, temperature etc.

All data are transferred to a central (XDS)server, accessible through a standard web-interface.

Self/home monitoring was implemented for selected patients instead of impatient care, or to reduce or replace frequent outpatient visits.

The indications for obstetric self/home monitoring were:

- -Preeclampsia
- -Diabetes (type 1 and 2 and GDM)
- -High risk of preeclampsia (i.e history, medical disease like SLE/kidney disease, FGR)
- -History of previous intrauterine or peripartum death

#### Results

To date, 240 patients has been included (will be updated at presentation), with up to 15 at a time Implementation was followed by a up to 77% reduction in used staff-time.

The patient- and clinician satisfaction is very high

During implementation, number of high-risk pregnancy beds has been reduced by 44%



# Cervical Intraepithelial Neoplasia and Spontaneous Preterm Birth: Genome wide association study (GWAS)

### ABSTRACT AUTHORS AND AFFILIATIONS

Kalliala Ilkka1, Cartwright Rufus3, Mitra Anita1,2, Rodriguez Alina3, Piltonen Terhi4, Morin-Papunen Laure4, Bennet Phillip1,2, Jarvelin Marjo-Riitta3, Kyrgiou Maria1,2

1 Institute of Reproduction and Developmental Biology, Department of Surgery & Cancer, Imperial College, London, UK

2Imperial Healthcare NHS Trust, London, UK

#### **ABSTRACT TEXT**

#### Background

A minority of women infected with HPV develop CIN or cervical cancer, suggesting the presence of innate factors predisposing to tumor development. CIN has been associated with spontaneous preterm delivery (PTB), but the causal pathway remains unclear. We conducted a genome-wide association study to identify underlying genetic risk variants possibly predisposing to both outcomes.

#### Methods

Using nationwide Registers and Northern Finland Birth Cohort 1966 (NFBC66) we identified 365 women with CIN or cervical cancer and 1678 controls without a history of any cytological abnormalites. In the first stage we conducted genome wide analyses for CIN or cervical cancer. In the second stage we tested the SNPs considered at least suggestive for CIN or cervical cancer separately for PTB (119 cases and 1813 controls).

#### Results

We identified eleven SNPs (p<5x10E-8) associated with increased risk of CIN or cervical cancer. Two of the top variants were associated with three protein-coding genes at the same locus: PIBF1, BORA and MZT1 all with roles in mitotic cell division and/or cancer development. Among the 234 SNPs analysed in the second stage, two remained significant for PTB and were associated with protein coding sites: at SEPT8 (associated with cellular polarity and carcinogenesis) and one at CAPN1 (associated with human carcinogenesis and low birth weight in animal models).

#### Interpretation

We observed variants significantly associated with CIN or cervical cancer as well as loci suggesting a presence of shared genetic susceptibility to both outcomes in this cohort. These results are promising but require external replication for confirmation.



## **First Steps in Placental Development**

### ABSTRACT AUTHORS AND AFFILIATIONS

Ganesh Acharya, MD, PhD, FRCOG UiT-The Arctic University of Norway and University Hospital of North Norway, Tromsø, Norway

#### **ABSTRACT TEXT**

After fertilization, a single cell zygote develops into embryo with all its organ systems consisting of different cell types, and two temporary supportive structures called the yolk sac and the placenta. Before implantation, the zygote must divide and differentiate into three distinct cell lines, i.e. trophectoderm, primitive endoderm and epiblast, which form the placenta, yolk sac and the embryo proper, respectively. Early placental development is controlled by genetic as well as environmental factors. The feto-placental circulation is established early in gestation and blood flow has a major role in determining placental growth. However, the early placenta develops under hypoxic conditions as the utero-placental circulation is established much later. Oxygen delivery and supply of nutrient substrates becomes increasingly important as the gestation advances.

In very early stages of development cell polarization, cell positioning, signaling pathways and transcription factors play important roles in defining lineage specification and driving further placental development. Advances in imaging and super-resolution microscopy (nanoscopy) have recently opened new possibilities in cell lineage tracing and studying subcellular structures. Combined with other conventional techniques, this method has a potential to provide important information on early stages of human placental development. The key concepts related to early placental development and growth will be discussed.



## **Cancer during pregnancy**

### ABSTRACT AUTHORS AND AFFILIATIONS

Frédéric Amant (MD, PhD)

#### Affiliations:

Gynecologic Oncology, University Hospitals Leuven, and Division of Oncology, KU Leuven, Leuven, Belgium.
Center for Gynecologic Oncology Amsterdam, Antoni van Leeuwenhoek-Netherlands Cancer Institute, the
Netherlands

#### **ABSTRACT TEXT**

A multidisciplinary discussion is necessary to tackle a complex and infrequent medical problem like cancer occurring during pregnancy. Pregnancy does not predispose to cancer but cancers occurring in women of reproductive age are encountered during pregnancy. Ultrasonography and magnetic resonance imaging are the preferred staging examinations, but also a sentinel node staging procedure is possible during pregnancy. Standard cancer treatment is aimed for. Operations can safely be done during pregnancy, but surgery of genital cancers can be challenging. The observation that chemotherapy administered during the second or third trimester of pregnancy, i.e. after the period of organogenesis, has little effect on the long term outcome of children adds to the therapeutic armamentarium during pregnancy. During the presentation we will give an overview of the recently published data.

Standard treatment should be aimed for in order not to jeopardize the maternal prognosis. Cancer treatment during pregnancy adds in the continuation of the pregnancy and the prevention of prematurity. It is accepted now that prematurity is worse when compared to antenatal exposure to chemotherapy. Apart from this, oncologists should discuss contraception in young cancer patients.



#### **ABSTRACT TITLE**

# Endometriosis as a precursor of ovarian carcinoma

#### ABSTRACT AUTHORS AND AFFILIATIONS

Ralf Bützow

#### **ABSTRACT TEXT**

Endometriosis is an estrogen dependent disease, which causes chronic inflammation and may lead to pelvic pain and infertility. Many epidemiological studies have shown that women with endometriosis have an increased (1,5 -2-fold) lifetime risk of ovarian carcinoma, particularly the endometrioid and clear cell subtypes of the disease. This association may partially be explained by shared genetic background of endometriosis and ovarian carcinoma. However, endometriosis and its atypical form are often found in the proximity of these carcinomas. Also, molecular changes similar to those in carcinoma have been detected in nearby endometriosis. This suggests that there is a direct link between these two diseases and endometriosis could be regarded as a precursor of cancer. The risk of cancer is associated with ovarian endometriosis, i.e. endometriomas and is increased by prolonged disease and/or older age at diagnosis and infertility. The progression of endometriosis to cancer is usually slow, possibly enabling diagnosis at an early stage of the disease. The risk is there, but it should not be exaggerated.



Maternal overweight and obesity during pregnancy and risks in offspring.

### ABSTRACT AUTHORS AND AFFILIATIONS

Sven Cnattingius, Clinical Epidemiology Unit Department of Medicine, Solna, Karolinska Institutet, SE-171 76 Stockholm, Sweden

#### **ABSTRACT TEXT**

Today more than 30% of women in Sweden and more than 50% of women in the USA are either overweight (BMI 25 to <30) or obese (BMI >30) in early pregnancy. Overweight/obesity is a global problem, and is presently more common that underweight in most low income countries. For mothers, risks of gestational diabetes and preeclampsia increase with increasing BMI, which explain that risks of medically indicated preterm delivery increase with maternal BMI. BMI is also associated with risk of spontaneous extremely (<27 weeks) preterm birth, possibly explained by factors related to systemic inflammation. Maternal obesity increases risks of asphyxia-related morbidities in term infants, including meconium aspiration, convulsions, and low Apgar scores. Maternal obesity is also associated with increased risk of congenital malformations in offspring. Offspring of overweight and obese women are at increased risks of stillbirth and infant mortality. The increased infant mortality risk is partly due to increased prevalence of preterm birth and partly due to increased infant mortality risks in term infants, due to asphyxia-related conditions and other neonatal morbidities. Weight gain between successive pregnancies is also associated with increased risks for a number of obesity-related pregnancy and neonatal complications, which is consistent with the hypothesis that change of exposure may influence risks.

Primary prevention of overweight and obesity is one of the main challenges in public health. Reducing maternal and offspring's risks in overweight and obese women will for a long time be one of the main challenges in antenatal, obstetrical, and neonatal care.



### ABSTRACT AUTHORS AND AFFILIATIONS

Sally Collins Oxford University Hospitals NHS Foundation Trust

**Massive Obstetric Haemorrhage** 

#### **ABSTRACT TEXT**

Haemorrhage remains the leading cause of maternal mortality, accounting for over one quarter (27 per cent) of deaths worldwide. Many of these are potentially avoidable. This will be an overview based on UK experience, which will include aspects of management in the event of massive bleeding as well as strategies to avoid it with particular reference to abnormally invasive placenta (accreta).



**ABSTRACT TITLE** 

The Zika virus epidemic in Brazil. Report of some cases assisted in the Fernandes Figueira Institute - Rio de Janeiro - Brasil.

### ABSTRACT AUTHORS AND AFFILIATIONS

Dias MAB & Pereira Junior JP
Fernandes Figueira Institute / Oswaldo Cruz Foundation - FIOCRUZ

#### **ABSTRACT TEXT**

In March 2015, Brazil notified the WHO of reports of an illness characterized by skin rash in northeastern states. From February 2015 to 29 April 2015, nearly 7000 cases of illness with skin rash were reported in this region. All cases are mild and there were not reported deaths. Of 425 blood samples taken for differential diagnosis, 13% were positive for dengue. Tests for chikungunya, measles, rubella, parvovirus B19, and enterovirus were negative. Zika was not suspected at this stage, and no tests for Zika virus were carried out.

In May 2015: Brazil's National Reference Laboratory confirms, by PCR, Zika virus circulation in the country. This is the first report of locally acquired Zika disease in the Americas. In the same month the Pan American Health Organization and WHO issue an epidemiological alert to Zika virus infection. In October 2015 Brazil reported an association between Zika virus infection and microcephaly. For neither event was a causal link proven. In February 2016, as infection moved rapidly through the areas occupied by Aedes mosquitos in the Americas, WHO declared that Zika infection associated with microcephaly and other neurological disorders constitutes a Public Health Emergency of International Concern (PHEIC). In the same month, local transmission of Zika infection had been reported from more than 20 countries and territories in the Americas.

In the end of 2015 the Department of Obstetrics of Fernandes Figueira Institute began to follow patients that reportes being infected with Zika virus. A protocol for prenatal consults and Fetal Ultrasound was established.

Fetal ultrasonography was performed in 42 ZIKV-positive women. Fetal abnormalities were detected by Doppler ultrasonography in 12 of the 42 ZIKV-positive women. Adverse findings included fetal deaths at 36 and 38 weeks of gestation (2 fetuses), in utero growth restriction with or without microcephaly (5 fetuses), ventricular calcifications or other central nervous system (CNS) lesions (7 fetuses), and abnormal amniotic fluid volume or cerebral or umbilical artery flow (7 fetuses). To date, 8 of the 42 women in whom fetal ultrasonography was performed have delivered their babies, and the ultrasonographic findings have been confirmed.



# Diagnosis of adenomyosis

### ABSTRACT AUTHORS AND AFFILIATIONS

Margit Dueholm Aarhus University Hospital

#### **ABSTRACT TEXT**

Adenomyosis is defined by the presence of ectopic endometrium in the myometrium. Traditionally, the diagnosis of adenomyosis is obtained from women in their fourth to fifth decade of life. However, imaging data suggest that adenomyosis may develop much sooner in life, particularly in women with endometriosis. Adenomyosis arise in the endo-myometrial junction and there are structural changes in the endo-myometrial junction both in adenomyosis and endometriosis, which has justified the introduction of an endo-myometrial dysfunction disease. This presentation will give a detailed and structured overview of the 2-Dimentionel and 3-Dimentionel Transvaginal Ultrasound and Magnetic Resonance Imaging features of adenomyosis demonstrated by pictograms and imaging and videos. An overview will be given on studies on diagnostic possibilities in adenomyosis, studies demonstrating structural changes in the junctional zone and the present classification of adenomyosis. Imaging guided minimally invasive treatment modalities in adenomyosis are demonstrated.



Vaginal vs. laparoscopic prolapse mesh? - Laparoscopic route

### ABSTRACT AUTHORS AND AFFILIATIONS

Jon Ivar Einarsson MD PhD MPH
Director of the Division of Minimally Invasive Gynecologic Surgery
Brigham and Women's Hospital
Associate Professor of Obstetrics and Gynecology
Harvard Medical School

#### **ABSTRACT TEXT**

The use of mesh for the treatment of pelvic organ prolapse has recently come under intense scrutiny, particularly when placed via the vaginal route. Laparoscopic sacrocolpopexy and sacrocervicopexy are associated with excellent long term clinical outcomes, limited morbidity and low mesh related complications. However, these procedures are technically demanding and some surgeons lack the necessary skills to be able to offer these treatment options to their patients. This lecture will describe our approach to apical pelvic organ prolapse with some clinical pearls that may facilitate the performance of these procedures.



# Fetal imprinting in obese pregnancies

### ABSTRACT AUTHORS AND AFFILIATIONS

Johan G Eriksson, University of Helsinki and Helsinki University Hospital, Folkhälsan Research Center, Helsinki, Finland

#### **ABSTRACT TEXT**

The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that several non-communicable diseases – including coronary heart disease and type 2 diabetes (T2D) - have their origins in prenatal life and in early childhood. The intrauterine milieu which is influenced by a large number of factors - including maternal characteristics - affects the developing fetus via a number of pathways resulting in the programming of future health outcomes.

Early life programming has mostly been studied in relation to long-term health outcomes in relation to being born with a small body size. Maternal obesity is associated with immediate adverse neonatal outcomes including an increased risk of congenital defects and miscarriage. However, recent studies have been reporting associations between maternal obesity and long-term health outcomes in the offspring. Maternal obesity in pregnancy has been associated with an increased risk of premature death in adult offspring. Further based upon findings from the Helsinki Birth Cohort Study it has been shown that higher maternal pregnancy BMI is associated with an increased risk of cancer, cardiovascular disease, and T2D among the adult offspring. The association with T2D is stronger in women, consistent with the transmission of T2D from the mother to her daughters being stronger than transmission to her sons.

One plausible explanation for the association between maternal adiposity during pregnancy and later offspring health is in utero programming. This may work through environmental, metabolic, genetic, and epigenetic mechanisms.



## Granulosa cell tumor – a unique ovarian cancer

### ABSTRACT AUTHORS AND AFFILIATIONS

Anniina Färkkilä University of Helsinki and Helsinki University Hospital

#### **ABSTRACT TEXT**

Adult-type granulosa cell tumor (AGCT) is a clinically and molecularly unique subtype of ovarian cancer. The incidence of AGCT is 0.6-0.8/100 000, and 20-30 new cases are diagnosed in Finland every year. The majority of AGCT patients are diagnosed at an early stage associated with excellent prognosis. The most common presenting symptom is abnormal vaginal bleeding, typically menstrual irregularities or postmenopausal bleeding. Surgery is the cornerstone in the treatment of both primary and relapsed AGCT, and chemotherapy is utilized only in advanced or surgically non-resectable cases. Tumor stage is the only factor consistently related to prognosis, however, every third of also the early stage patients relapse leading to death in 50% of these patients. AGCTs typically relapse after prolonged time periods, with median time to relapse being 4-7 years. The most accurate follow-up markers for AGCT are Anti-Müllerian Hormone and Inhibin B.

Molecularly, AGCTs is characterized by a unique somatic missense point mutation 402C->G (C134W) in a gene encoding for transcription factor FOXL2. FOXL2 402C->G mutation leads to increased proliferation and survival of granulosa cells, and promotes hormonal changes associated with AGCT. The histological diagnosis of AGCT can be challenging, and FOXL2 mutation has been shown to be crucial for differential diagnostics.

The major challenge in the management of AGCT patients is the identification and treatment of patients with high-risk or relapsed AGCT, and large international collaborations with molecularly defined AGCT cohorts are needed to improve and validate the treatment strategies for these patients.



# Prolapse surgery Vaginal vs. laparoscopic mesh? - Vaginal route

### ABSTRACT AUTHORS AND AFFILIATIONS

Christian Falconer

Department of Obstetrics and Gynecology, Danderyd Hospital, Danderyd and Karolinska Institutet, Stockholm, Sweden

#### **ABSTRACT TEXT**

Apical prolapse is defined as descent of the uterus and cervix, the cervix alone, or the posthysterectomy vaginal cuff down to the hymen, lower vagina, or past the introitus. An estimated 40.000 procedures are performed each year in the US to treat apical prolapse and its main symptoms: heaviness and bulging sensation. It is now recognized that women with advanced prolapse require adequate apical support to ensure the durability of a simultaneous anterior and/or posterior correction. Options for correcting apical prolapse can be broadly divided into trans-abdominal vs trans-vaginal procedures. Trans-vaginal treatments include sacrospinous ligament suspension with or without mesh, uterosacral ligament suspension, McCall´s culdoplasty and levator myorraphy.

Choosing between an intra-vs extra peritoneal approach is a common clinical dilemma; a recent review of apical prolapse suggests that the vaginal approach might be performed 80-90% of the time.

A recent Cochrane meta-analysis of level 1 data comparing abdominal sacral colpopexy (ASC) with sacrospinous ligament fixation (SSLF) showed that ASC was superior in terms of recurrent vault prolapse, post-operative stress urinary incontinence, and postoperative dyspareunia. However, the downsides of ASC include longer operating time, longer recovery time, and increased costs. Moreover, the analysis does not include SSLF using a special tool-kit (Uphold<sup>TM</sup>), designed for elevation and securing of the apex, which in recent studies shows the potential of improving the outcome of SSLF.

The main focus of this presentation is to inform about the tentative advantages in using the vaginal route, especially the Uphold™ procedure, as compared to abdominal sacral colpopexy in treatment of apical prolapse.



### **ABSTRACT TITLE**

## Strategies to reduce the risk of ovarian cancer

### ABSTRACT AUTHORS AND AFFILIATIONS

Henrik Falconer Karolinska University Hospital

#### **ABSTRACT TEXT**

In spite of recent advances in surgical and oncological treatment, ovarian cancer remains the most lethal gynecological cancer in developed countries. Attempts to develop screening programs have yet not demonstrated survival benefits in the general population. To date, risk-reducing salpingo-ophorectomy (RRSO) and oral contraceptives remain the most efficient measures to prevent ovarian cancer. The visual appearance of ovarian cancer has prompted the hypothesis that the disease arises within the ovarian epithelium and/or ovarian inclusion cysts. The presence of preinvasive lesions in the fallopian tubes of high-risk women (i.e. BRCA-mutation carriers) has led to new insights regarding the underlying pathology. The potential paradigm shift in the understanding of ovarian cancer may have effects on prevention in both high-risk groups and for the general population. To test the hypothesis that ovarian cancer primarily arises within the fallopian tubes, we recently conducted a population-based study based on nationwide health registers. All women with previous salpingectomy performed on benign indications (n=34433) were identified in a cohort exceeding 5.5 million Swedish women 1973-2010. Ovarian and tubal cancer was chosen as exposures and compared to controls, bilateral salpingectomy was associated with a HR of 0.35 (95% CI 0.17-0.73) to develop ovarian cancer later in life. We conclude that salpingectomy on benign indication was associated with a dramatic reduction of ovarian cancer. These data supports the hypothesis that ovarian cancer primarily originates from the fallopian tubes. Salpingectomy may be an effective method to prevent ovarian cancer in high-risk populations. Whether salpingectomy could prevent ovarian cancer in the general population is unclear. Further research is necessary to study the potential effect of salpingectomy on ovarian function.



PALM-COEIN: practical use of the FIGO classification of causes of AUB

### ABSTRACT AUTHORS AND AFFILIATIONS

lan S. Fraser AO, DSc, MD Conjoint Professor, School of Women's and Children's Health, Royal Hospital for Women, University of New South Wales, Sydney, Australia

#### **ABSTRACT TEXT**

Over the past 10 years, the FIGO Menstrual Disorders Committee has developed a whole series of new terminologies and definitions around abnormal uterine bleeding, and more recently has defined a new classification of the underlying causes of abnormal uterine bleeding (AUB) in women in the reproductive phase of life. This classification has become known by the mnemonic of PALM-COEIN, which highlights the different structural (ie. can be imaged) and non-structural (ie. molecular and cellular) causes of AUB. This classification has turned out to be very successful for day-to-day specialist clinical management in many different centres in different cultures, as well as being a useful training tool and a focus for standardisation of data recording for research and clinical trials. There are now well over 30 publications which address aspects of the FIGO AUB recommendations, including the PALM-COEIN classification, and these provide a very sound basis for understanding all aspects of pathogenesis, investigation and management of abnormal uterine bleeding. This presentation will offer an understanding of the causes of abnormal uterine bleeding and a practical focus for use of the PALM-COEIN classification in clinical practice.



## **Treatment of adenomyosis**

### ABSTRACT AUTHORS AND AFFILIATIONS

Axel Forman Aarhus University Hospital

#### **ABSTRACT TEXT**

Adenomyosis occurs in focal areas or as more diffuse infiltration of the uterine wall. Histology varies from solid forms to cystic lesions. The disease seems to cause bleeding disorders, pain and infertility but asymptomatic forms are frequent. Improved image diagnosis indicates that adenomyosis occurs also in younger women, sometimes as larger cysts. The levonorgestrel IUD offers an easy medical solution when applicable, and laparoscopic hysterectomy is effective in premenopausal woman. Conservative surgery is needed in infertility but the exact indications have not been defined. Surgical methods vary, the extent of excision needed to improve fertility is unknown and controlled studies on outcomes have not been performed. In small-sized focal adenomyosis close to the uterine cavity, hysteroscopic surgery seems feasible, but the different methods have not been compared and the risk of decreased future endometrial receptivity must be taken into account. For the diffuse forms, extensive surgery with opening of the uterine wall from the outside has been performed, with various methods for reconstruction of the uterine wall. Few data are available on the risk of uterine rupture in subsequent pregnancy. New techniques like radio frequency ablation and MRI-guided High Intensity Focused Ultrasound may represent a way forward but more studies are needed to assess the potential. The Scandinavian gynecological community has a special obligation to organize cooperating centers of excellence for systematic evaluation of indications for surgery, techniques and the effects on fertility and obstetrical outcomes in this complex disease.



## Obesity, diet and exercise in PCOS

### ABSTRACT AUTHORS AND AFFILIATIONS

Dorte Glintborg, Department of Endocrinology, Odense University Hospital, Odense, Denmark

#### **ABSTRACT TEXT**

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in premenopausal women affecting more than 10 %. Insulin resistance is present in more than 50% women with PCOS and the odds ratios for the metabolic syndrome and type 2 diabetes in PCOS are 2.9 and 4.4, respectively. Overweight and obesity result in a more severe phenotype of PCOS and life style intervention and weight loss are therefore considered the first line treatment.

Blunted ghrelin suppression during meals in women with PCOS could be associated with a decreased feeling of satiety, whereas the metabolic rate was unchanged in PCOS. It is currently debated whether certain diet types are superior regarding weight loss and metabolic risk factors in PCOS. Physical activity had no significant additive effect on weight loss.

Medical intervention with metformin and oral contraceptives could have important effects on body composition, but at present limited long term data are available.



Unplanned out-of-institution births in Norway 1999-2013.

### ABSTRACT AUTHORS AND AFFILIATIONS

Björn Gunnarsson, Norwegian Air Ambulance Foundation and NTNU, Norway; Sigurd Fasting, NTNU and Olavs Hospital, Norway; Eirik Skogvoll, NTNU and Olavs Hospital, Norway; Kjell Å Salvesen, NTNU and Olavs Hospital, Norway; Alexander Kr. Smárason, University of Akureyri and Akureyri Hospital, Iceland.

#### **ABSTRACT TEXT**

Perinatal mortality rate in Norway has continued to decline and was only 4.9 per 1000 births in 2013. This rate is so low that we can expect the decline to level off. However, audits form many countries have reported a high proportion of sub-optimal perinatal care and there likely exists opportunities to improve patient care and outcomes.

Unplanned out-of-institution births account for 7 out of 1000 births in Norway, which is a relatively high rate, and such births have been associated with increased perinatal mortality when compared to hospital births. These facts indicate plausible patient safety issues than need to be identified and acted upon. Patient safety is concerned primarily with the avoidance, prevention and amelioration of adverse outcomes or injuries stemming from health care itself. To date, activities to manage quality have not focused sufficiently on patient safety issues and very little is known about harm in pre-hospital care. We undertook studies of characteristics and outcome of unplanned out-of-institution births in Norway over a 15 year period and classified perinatal deaths according to cause and with focus on patient safety. The results will be presented at the meeting.



# The Genetic Background of Female Sexual Dysfunctions

## **ABSTRACT AUTHORS AND AFFILIATIONS**

Annika Gunst, M.A. (Psych), University of Turku

#### **ABSTRACT TEXT**

Female sexual dysfunctions (FSDs; low desire/arousal, orgasm problems and sex-related pain) are prevalent worldwide and commonly associated with decreased relationship quality and overall wellbeing. The etiology of FSDs is complex and the literature suggests a multifactorial background involving psychological, social, physiological and biological factors. Only recently have genetic studies tried to explore the genetic background of FSDs in order to identify genetic markers related to FSDs. To date, how much do we know about the genetic background of FSDs? What is the estimated heritability of FSDs? What challenges are there in the genetic study of FSDs?



# Sexual Assault - 10 years of experience from a center in Copenhagen

### ABSTRACT AUTHORS AND AFFILIATIONS

Malene Hilden. MD PHD, Center for Victims of Sexual Assault, Copenhagen University Hospital Rigshospitalet

#### **ABSTRACT TEXT**

Centers receiving victims of sexual assault has existed in Denmark since 2000, data from the center in Copenhagen are presented and discussed.

Who are exposed to sexual assault? What are the characteristics of the assault and the persons involved? How is the success of legal proceedings? What are the consequences of assault? How to prevent?



The challenges of treating sexological patients - advantages of a multidisciplinary approach

### ABSTRACT AUTHORS AND AFFILIATIONS

Astrid Højgaard, Head of Department, Sexological Centre, Aalborg University Hospital, Aalborg, Denmark. Sexological Research Centre, Aalborg University, Denmark

#### **ABSTRACT TEXT**

This presentation describes the patient flow in the second largest public sexological clinic in Denmark. We have 3000-3500 visits annually. The female diagnoses treated are anorgasmia, lubrication problems, hypoactive sexual desire, dyspareunia, vaginism, lichen sclerosis and vulvodynia. Furthermore, we treat rape victims and transgender persons. The number of visits allocated for each diagnosis is demonstrated. The diagnostic work up and staffing is presented. The patients are treated by specialists in gynecology, psychiatry, psychology and by nurses. Therapy is offered as individual, couple or group sessions. We have developed an online tool to collect patient data, which also enables us to ensure quality surveillance, which will be described. The impact of being funded by a somatic and a psychiatric hospital is discussed. Finally the challenges of being a public clinic with reimbursed treatments is discussed.



# What's new in ectopic pregnancy?

### ABSTRACT AUTHORS AND AFFILIATIONS

Professor Andrew Horne

University of Edinburgh UNITED KINGDOM

#### **ABSTRACT TEXT**

Ectopic pregnancies are a serious gynaecological emergency that can be fatal. As such, prompt diagnosis and safe timely treatment is essential. There have bee recent preclinical studies describing new molecularly targeted therapeutic approaches for ectopic pregnancy. Notably, bench-to-bedside studies have examined the use of combination gefitinib (orally available epidermal growth factor receptor inhibitor) and methotrexate. Preclinical studies suggest that combination gefitinib and methotrexate is highly effective in inducing placental cell death, and is significantly more effective than methotrexate alone. In early human trials, encouraging preliminary efficacy data have shown that combination gefitinib and methotrexate can rapidly resolve tubal ectopic pregnancies, and large extra-tubal ectopic pregnancies. If a large clinical randomized controlled trial confirms these findings, combination gefitinib and methotrexate could become a new medical treatment option for ectopic pregnancy.



# Outpatient surgical management of bleeding disturbances

# ABSTRACT AUTHORS AND AFFILIATIONS

Ritva Hurskainen, MD, associate professor/Hyvinkää Hospital, Finland

### **ABSTRACT TEXT**

Outpatient surgery has grown in popularity during recent years and about 65% of all surgical procedures are done on an outpatient basis. All gynaecology units should provide a dedicated outpatient service to women with abnormal uterine bleeding. There are clinical and economic benefits associated with this type of service and recent innovations have improved the technology very applicable. With shorter procedure times and easiness outpatient treatments are preferred by patients but also limit the feasibility, safety, accuracy and effectiveness of the procedure. Good information about procedures is obligatory and the experience of pain is necessary to take in account.

Ambulatory hysteroscopy is a safe, feasible, and accurate procedure for diagnosing intrauterine pathology. Common procedures include endometrial polypectomy, removal of small submucous fibroids, endometrial adhesions, removal of residua after pregnancy, removal of lost intrauterine devices and biobsies for glandular cervical cytology.

Manual vacuum aspiration (MVA) is a quick procedure (5–10 minutes) and can performed in office, clinic or emergency room. It is performed with the use of a handheld syringe as a source of suction for removing uterine contents. It can be used with cervical dilatation under painkillers or/and paracervical block. Complications are rare and especially the incidence of uterine adhesions much lower than with curettage. The price is significantly cheaper than D&C, the equipment costs less than a curette set and there are savings in the operation room time.



**ABSTRACT TITLE** 

Preterm birth: an update

# ABSTRACT AUTHORS AND AFFILIATIONS

Bo Jacobsson MD, PhD Professor, Sahlgrenska Academy, Gothenburg University, Gothenburg; Sweden.

#### **ABSTRACT TEXT**

Preterm delivery (PTD) is a serious global health problem and one of the leading causes of child death worldwide. PTD includes both spontaneous and iatrogenic PTD. Spontaneous PTD stands for 70% of all cases and constitutes of preterm labor (PTL) and preterm prelabor rupture of membranes (PPROM). PTD is strongly related to increased perinatal mortality and short and long term morbidity. The economic costs of PTD are huge.

The heritability of gestational age is estimated to be >30%, however, only a very small fraction of variability in gestational age could be explained by currently known PTD-risk-increasing genetic polymorphisms. There still are no genome-wide association studies (GWAS) published for the phenotypes "PTD" or "gestational age" (as compared to approx. 100 for "diabetes"). However, positive development approaches.

The etiology behind spontaneous PTD is complex but many studies have indicated that inflammation/infection is important. Microbes are believed to ascend from the lower genital tract and invade the decidua, chorioamniotic membranes, amniotic fluid and, in some cases, also the fetus. Inflammation could trigger myometrial contractions, rupture of the membranes and cervical maturation leading to PTD. Recently, also sterile intrauterine inflammation has been described. Although bacteria have been suggested to be important in the etiology of spontaneous PTD, antibiotics have not been proven to make neither the outcome better and have even been associated with worse perinatal outcome.

The dogma of the "sterile womb" has been challenged in a groundbreaking study published in Science in late May 2014, where Kjersti Aagaard et al. suggested that placenta is not sterile and has a flora more similar to the oral cavity than to the vagina. During the last couple of years my research group published in high-ranked journals several observational studies: we found that women who delivered at term had more often consumed oral probiotic products than women who had PTD and preeclampsia. This supports the hypothesis that oral consumption of potentially immune-modulating bacteria can, via unknown mechanisms, effect the gestation. Interestingly, in a study by Yeganegi et al., the supernatant of the probiotic organism Lactobacillus rhamnosus was found to reduce the lipopolysaccharide (LPS) inflammatory response in placental trophoblast cells. In another study the same group showed that supernatant from Lactobacillus rhamnosus culture could reduce the rate of LPS-induced PTD in mice.

The "Intergrowth study" has indicated that in a set of low risk pregnant women the preterm birth frequency is around 4.5%. To be able to reduce the Nordic countries' figures to that level, several different methods needs to be used in a systematic approach. No single method will be likely to have an impact on a large group of high-risk women. Such approach needs to be based on determined clinical subset of clinical and biological risk factors. Such an approach will be very difficult to achieve but is a highly prioritized research project.



# Pregnancy after bariatric surgery

# ABSTRACT AUTHORS AND AFFILIATIONS

Kari Johansson (PhD), Department of Medicine, Solna, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden

### **ABSTRACT TEXT**

Background: There is a growing number of pregnancies occurring after bariatric surgery, but the effects of bariatric surgery on reproductive outcomes are unclear as large-scale studies are lacking.

Method: Using Swedish nationwide health registers and the Scandinavian Obesity Surgery Register (SOReg), we identified women who had undergone bariatric surgery prior to pregnancy. Between 2006 and 2011, 627,693 singleton pregnancies were identified in the Swedish Medical Birth Register of which 670 occurred after bariatric surgery in women for whom pre-surgery weight was documented. For each pregnancy after bariatric surgery, up to 5 control pregnancies were matched by pre-surgery BMI, age, parity, smoking, education, and delivery year. We assessed risks for gestational diabetes, large-for-gestational-age (LGA), small-for-gestational-age (SGA), preterm birth, stillbirth, neonatal death, and major congenital malformations.

Results: Compared to control pregnancies, pregnancies in women with prior bariatric surgery were associated with lower risks for gestational diabetes (1.9% vs. 6.8%; P<0.001), and LGA birth (8.6% vs. 22.4%; P<0.001). In contrast, higher risk was observed for SGA birth (15.6% vs. 7.6%; P<0.001). Post-surgery pregnancies had shorter length of gestation (273.0 vs. 277.5 days; P<0.001) and a borderline increased risk for the combined outcome stillbirth and neonatal death (1.7% vs. 0.7%; P=0.056). No statistically significant association could be detected between bariatric surgery and congenital malformations.

Conclusion: Bariatric surgery is associated with both positive and negative pregnancy and perinatal outcomes.

Reference: N Engl J Med 2015;372:814-24



# **ABSTRACT TITLE**

# **Prediction and Future Treatment of Preeclampsia**

# ABSTRACT AUTHORS AND AFFILIATIONS

S. Ananth Karumanchi, MD, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

### **ABSTRACT TEXT**

Imbalance of angiogenic growth factors in the maternal circulation contributes to the pathogenesis of preeclampsia. Soluble fms-like tyrosine kinase 1 (sFlt1), an endogenous anti-angiogenic protein that antagonizes vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) appears to be a central player in this paradigm. Overexpression of sFlt1 in pregnant rats produced hypertension, proteinuria and glomerular endotheliosis, the classical pathological renal lesion of preeclampsia. High serum sFlt1 and low serum free PIGF have been observed in preeclampsia. Abnormalities in these circulating angiogenic proteins are not only present during clinical preeclampsia, but also antedate clinical symptoms by several weeks. Another potential soluble factor secreted by the placenta that is elevated in women with preeclampsia is soluble endoglin (sEng). Endoglin (Eng) is an angiogenic receptor expressed mainly on the surface of endothelial cells, but also by placental syncytiotrophoblast. Eng acts as a co-receptor for transforming growth factor-beta, a potent pro-angiogenic molecule) signaling in endothelial cells. Eng mRNA is up-regulated in the preeclamptic placenta. In addition, the extra-cellular region of endoglin referred to as sEng, is released in excess quantities into the circulation of preeclamptic patients. Furthermore, sEng appeared to exacerbate the vascular damage mediated by sFlt1 in pregnant rats resulting in severe preeclampsia-like illness including the development of thrombocytopenia and fetal growth restriction. In this presentation, I will focus on clinical studies demonstrating the utility of angiogenic markers in the serum/plasma for the diagnosis and prediction of preterm preeclampsia. I will also discuss novel methods that target sFlt1 and/or sEng as potential therapeutic options for patients with severe preterm preeclampsia.



# Prevention of pre-eclampsia

# ABSTRACT AUTHORS AND AFFILIATIONS

Hannele Laivuori, Medical and Clinical Genetics and Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital and Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland

# **ABSTRACT TEXT**

Pre-eclampsia is a heterogeneous placenta-mediated vascular pregnancy complication with diverse clinical presentations. Placenta is a prerequisite for the disease process and delivery of the placenta is the only cure.

Various methods has been tested to prevent pre-eclampsia including low-salt diet, diuretics, antihypertensive drugs, nutritional supplementation and antithrombotic agents as well as physical exercise. Many preventive measures have been successful in small studies but failed in larger trials. Calcium supplementation in women with low calcium diets has shown moderate reductions in the incidence of pre-eclampsia in high-risk women. Meta-analyses of small to medium size randomized controlled trials demonstrate a 10-17% relative risk reduction for pre-eclampsia with low-dose aspirin started before 16 weeks of gestation. However, recent data from meta-analysis of three larger randomized trials with lower doses of aspirin were contradictory. Low molecular weight heparin emerges as a promising therapy for recurrent pre-eclampsia and other placenta-mediated pregnancy complications. Statins have been used in animal models of pre-eclampsia to revert the angiogenic imbalance. Low-dose pravastatin use was associated with a more favorable pregnancy angiogenic profile in a pilot study of women at high risk for pre-eclampsia. Preliminary safety and pharmacokinetic data justify using pravastatin in larger clinical trials.

Despite advances in the understanding of the pathophysiology and clinical course of pre-eclampsia, we have not been able to prevent this disorder. Currently our understanding of disease subtypes is limited. Pre-eclampsia is not a single disorder and we need more knowledge of distinct pathophysiologies to develop more specific preventive measures.



The NOSS project - from epidemiology to audit, education and international collaboration.

# ABSTRACT AUTHORS AND AFFILIATIONS

Lotte B Colmorn1, Jens Langhoff-Roos1, Maija Jakobsson2, Anna-Maija Tapper3,4, Mika Gissler5,6, Pelle G Lindqvist7, Karin Källen8,9, Karin Gottvall8, Kari Klungsøyr10,11, Per E Børdahl12, Ragnheiður I. Bjarnadóttir13, Lone Krebs14

- 1. Department of Obstetrics, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark.
- 2. Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Helsinki, Finland.
- Department of Gynecology and Pediatrics, Helsinki University Central Hospital, Helsinki, Finland.

### **ABSTRACT TEXT**

The NOSS project - from epidemiology to audit, education and international collaboration.

Serious rare complications in pregnancy are important but under-researched - which calls for international collaboration. At a Nordic workshop in September 2008 funded by NFOG and NOMBIR (the Nordic Medical Birth Registries) we designed a common project to describe and analyze rare serious pregnancy complications that occur more often in women with a previous caesarean section.

In 2009 - 2012, Nordic obstetricians in collaboration with the Nordic Birth Registries collected case-based information on all cases of peripartum hysterectomy, uterine rupture, placenta accreta and severe postpartum haemorrhage, and used information from the medical birth registries to describe the background population and identify risk factors.

Based on UKOSS and NOSS, colleagues at Oxford Perinatal Epidemiology Unit initiated an international collaboration (INOSS) for joint collection of information on several other serious conditions such as eclampsia, amniotic fluid embolism, cardiac arrest, SHIP (sudden hemoperitoneum in pregnancy), sepsis and anaphylaxis

Currently, the definitions are being concensed by a Delphy process, and a recommendation of specific variables associated with the conditions that should be collected (the CROWN initiative) is coming up.

Cases and results of analyses of the NOSS project have been discussed at Nordic workshops in 2012 - 2014 for obstetricians and PhD students. In collaboration with the NFOG maternal mortality group we have compared the severe complications as near-misses with maternal deaths.

Even though information on rates and risk factors are valuable, audit and narratives based on the train of events leading to the severe complications are of utmost importance. We should avoid blame and guilt in the process of audit. But a realistic description of the rate, risk factors and suboptimal care is needed. We all want to prioritize proactive management and prevent potentially avoidable severe complications in obstetrics.



Health benefits vs risks of hormonal contraception- the big picture.

# ABSTRACT AUTHORS AND AFFILIATIONS

Øjvind Lidegaard, professor, Department of Gynaecology, Rigshospitalet, University of Copenhagen

### **ABSTRACT TEXT**

Many benefits from hormonal contraception explain their widespread and increasing worldwide use. Few, but not trivial concerns should also be considered, however.

#### Benefits

First an effective reversible protection against pregnancy. Less menstrual complain and bleeding, and improvement of acne and hirsutism. Relief in women with endometriosis and PCOS. A substantial reduction in ovarian and endometrial cancer, and a modest decrease in colo-rectal cancer.

#### Risks.

Venous thrombosis is increased six fold in users of combined hormonal contraception with 3rd and 4th generation progestogens, patch and with vaginal ring, and three fold with 1st and 2nd generation progestogens. Progestogen only pills and LNG-IUS do not increase the risk. Arterial thrombosis is increased about 50% in users of combined products, progestogen only contraception risk free.

With ten per cent of women of reproductive age on antidepressant medicine, a 50% increase in use of antidepressants and of a depression diagnosis a year after starting use of hormonal contraception is not a trivial finding. The relative risk among users of hormonal contraception is highest in adolescence, and vanishes with increasing age. Both combined and progestogen only products increase the risk, and no consistent risk difference was found according to progestogen type.

Current users of combined pills have modest increase in cervical- and breast cancer. Little is known about the influence of progestogen only products and about combined products with newer progestogens.

#### Balance.

For a majority of women, benefits outweigh risks, but careful clinical counselling should ensure the right choice of type of hormonal contraception.



**ABSTRACT TITLE** 

Endometrial polyps. Should they stay or should they go? In Gynecological Symposium: Up-to-date on bleeding disturbances.

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Marit Lieng, Oslo University Hospital and the University of Oslo.

#### **ABSTRACT TEXT**

Endometrial polyps. Should they stay or should they go?

The incidence of endometrial is relatively high in women suffering from abnormal uterine bleeding. Endometrial polyps are also frequently diagnosed by transvaginal ultrasound in asymptomatic women. Endometrial polyps may be malignant; they may give symptoms such as abnormal uterine bleeding, and may also have a negative impact on fertility.

In this presentation, the clinical implications, the risk of malignancy and the evidence for diagnosis and management of endometrial polyps will be described. The effect of treatment of endometrial polyps will be emphasized, and evidence based guidelines for treatment of endometrial polyps in asymptomatic and symptomatic women will be provided.



# Menopause, Hormones and Memory

# ABSTRACT AUTHORS AND AFFILIATIONS

Pauline M. Maki University of Illinois at Chicago

### **ABSTRACT TEXT**

Prospective cohort studies demonstrate that complaints of forgetfulness and errors on memory tests increase as women transition through the menopause even after controlling for advancing age. Recent studies in midlife women indicate that vasomotor symptoms, the primary symptoms of menopause, are related to memory difficulties as well as alterations in brain structure and function. These relationships are evident only when vasomotor symptoms are measured using ambulatory skin conductance monitors and not when symptoms are measured by self-report. The "critical window hypothesis" states that use of hormone therapy during the perimenopausal or early postmenopausal period confers favorable cognitive effects whereas later use confers negative effects. For cognitive endpoints, there is some support for this hypothesis for estrogen alone but less support for combined hormone therapy. Specifically, small randomized clinical trials in younger postmenopausal women show that estrogen therapy improves verbal memory, particularly among surgically menopausal women. Clinical trials in older postmenopausal women show neutral effects of estrogen therapy on verbal memory. Recent randomized clinical trials of combined hormone therapy in younger postmenopausal women show neutral cognitive effects. Notably, those trials were not conducted in women with bothersome vasomotor symptoms, so it is unclear whether hormone therapy improves cognition in symptomatic women. The specific formulation of oral conjugated equine estrogen and medroxyprogesterone acetate appears to have adverse effects on memory in both younger and older postmenopausal women and increase risk of all-cause dementia. Whether hormone therapy alters the risk for Alzheimer's disease is a critical public health question because the prevalence of Alzheimer's is increasing, more women than men will die of the disease, and there is no cure. A randomized clinical trial of the critical window hypothesis is not feasible. Impressively, three of three observational studies to date support the critical window hypothesis for Alzheimer's disease endpoints. Unfortunately, it will not be feasible to test the hypothesis in a randomized clinical trial.



# **ABSTRACT TITLE**

# Can we predict and prevent pelvic organ prolapse and other forms of pelvic floor dysfunction?

# ABSTRACT AUTHORS AND AFFILIATIONS

Ian Milsom & Maria Gyhagen, Department of Obstetrics & Gynaecology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden

### **ABSTRACT TEXT**

Pelvic floor dysfunction (PFD = Pelvic organ prolapse; urinary incontinence; and faecal incontinence) is a common problem (prevalence  $\approx$  46%), affecting millions of women throughout the world (1). It has a negative influence on quality of life and its global costs are high. The aetiology of PFD is known to be multifactorial but obstetric trauma during childbirth is considered to be the most important risk factor. Annually, millions of women throughout the world undergo reparatory surgery for pelvic organ prolapse and urinary incontinence (2).

A major barrier to preventing pelvic floor disorders (PFDs) has been the inability to accurately identify women at risk. Challenges include the long time between obstetric events and the onset of PFDs. Up until now it has been difficult to counsel women on risk factors for subsequent PFD as there has been little good quality long term data available. Robust long-term epidemiological data at 12- 20 years after delivery (3,4) and objective pathophysiological data (pudendal nerve trauma and levator avulsion)(5) are now available. Prediction models capable of predicting the development of PFDs 12-20 years after delivery based on available data from two large independent population studies (3,4) have been constructed and validated. These prediction models provide valid individualized estimates of risk of developing PFDs 12-20 years after delivery. They significantly advance our ability to counsel women before and after delivery and identify women for future prevention studies.

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# Pathomechanisms of Adenomyosis uteri (AM)

# ABSTRACT AUTHORS AND AFFILIATIONS

Mechsner S

Endometriosis Centre Charité, Department of Gynecology, Charité Medical University Berlin, Berlin, Germany

#### **ABSTRACT TEXT**

Adenomyosis means the occurrence of endometrial cells within the myometrium. It could be present as a diffuse superficial form or with deeper infiltration. There are also focal forms, which are able to affect the adjacent organs such as the bladder. Over the years the real prevalence of adenomyosis uteri has been underestimated. However, the ongoing better quality of ultrasound and the possibility of MRI demonstrated a high prevalence of adenomyosis in patients with endometriosis (EM), especially in patients with infertility and ranked the prevalence between 80-91 % of endometriosis patients. The high prevalence may direct the attention on a possible involvement of adenomyosis on the pathogenesis of AM and EM-associated infertility. Furthermore, some new data suggest that this could be an impact on miscarriages. The patients suffer from severe dysmenorrhea, high menstrual bleeding, pelvic pain and dyspareunia.

The pathogenesis of Adenomyosis still remains to be unclear. There is the idea of an peristaltic-dependent induction of microscopic tissue injury at the EMJZ, which in turn leads to the translocation of the basal endometrium into the myometrium with consecutive development of adenomyotic lesions. This tissue injury might stimulate a process of tissue repair in which estrogen is locally produced, which in turn stimulates angiogenesis, proliferation and a local OT synthesis. The local OT activated oxytocin receptors on the myometrial smooth muscle fibers cause more hyperperistalsis. Subsequently, more tissue injury occurs and a vicious circle is established. Microscopic findings underlay this theory. Furthermore ultrastructural analysis of the junctional zone identifies stem-cell like cells, which might be involved in the pathogenesis of this disease. The adenomyotic-associated myometrial cells show an over expression of the oxytocin receptor as well as changes in their architecture. Both might lead to dysperistalsis of the myometrial cells and the reduced uterine blood flow causes ischemic pain. The myometrial innervation seems to be disturbed, a deletion of sympathetic nerve fibers might be an further factor in the functional changes of the myometrium.



# Update on metformin in PCOS - Metformin and treatment of infertility

# ABSTRACT AUTHORS AND AFFILIATIONS

Laure Morin-Papunen, Phd, MD

Department of Obstetrics & Gynecology , Oulu University Hospital and Medical Research Centre and PEDEGO

Research Unit, Oulu University, Oulu, Finland

### **ABSTRACT TEXT**

The intrinsic role played by insulin resistance and hyperinsulinemia in the pathogenesis of PCOS has led to the use of insulin-lowering drugs for the treatment of the syndrome. Numerous studies have indicated that metformin improves hyperinsulinemia and insulin resistance, decreases androgen levels and improves menstrual cyclicity in PCOS. Previous reports and meta-analyses suggest that metformin may improve ovulation induction 1.5 to 4 times compared to placebo alone. Later, these results could not be confirmed in two large randomized studies, where metformin was significantly less effective than clomiphene, and the combination of the two drugs did not bring any advantages. In the most recent Cochrane meta-analysis the addition of metformin to an ovulation-induction agent significantly improved clinical pregnancy rates (PRs), but not live birth rates (LBRs). Two recent RCTs conducted in Nordic countries, however, showed that a pretreatment of 3 months with metformin improved the PRs and LBRs by 15% after its combination with IVF/ICSI in non-obese and with standard infertility treatment in obese women. The last recommendation of the American Association of Clinical Endocrinologists, American College of Endocrinology and AE-PCOS Society is that metformin may be useful as an adjuvant agent in certain groups of women with PCOS, such as obese women.

The efficacy of metformin in addition to gonadotropin stimulation or laparoscopic drilling remains to be defined. Recent RCTs could not show any beneficial effect of .metformin on early spontaneous miscarriage rates. However, metformin has been shown to decrease significantly the risk of ovary hyperstimulation syndrome during assisted reproductive technology.



ABSTRACT TITLE	
ABSTRACT AUTHORS AND AFFILIATIONS	
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ABSTRACT TEXT	



# **Evolving treatment of missed abortion**

# ABSTRACT AUTHORS AND AFFILIATIONS

Dr. Kevin Sunde Oppegaard, Dept. of Gynaecology, Helse Finnmark, Klinikk Hammerfest, Norway

#### **ABSTRACT TEXT**

Spontaneous abortion or "miscarriage" happens in approximately one out of six pregnancies. Approximately one in four women will have an early pregnancy failure during her lifetime. Among unselected patients seeking help from a gynaecological emergency room, a high proportion are diagnosed and/or treated for miscarriage. If no embryo has developed within the gestation sac, the pregnancy is termed 'anembryonic' (formerly called 'blighted ovum'). If an embryo or fetus is present, but without cardiac activity and the patient has experienced no symptoms, the pregnancy is termed 'silent', 'missed' or 'delayed abortion'. Previously, the standard treatment of missed abortion before 13 weeks' gestation has been vacuum aspiration. However, after the introduction of effective methods of medical abortion more than 25 years ago, similar medical methods to treat early pregnancy loss have been introduced. This presentation will present an overview of the available research and recommendations for management.



#### **ABSTRACT TITLE**

# Use of magnesium sulphate in very preterm birth

# ABSTRACT AUTHORS AND AFFILIATIONS

Hanne Trap Wolf

Hvidovre Hospital, Copenhagen, Denmark

#### **ABSTRACT TEXT**

Magnesium sulphate (MgSO4) has been used in obstetrics for decades, but the actual use of MgSO4 is unknown.

I will present the background for using MgSO4 in obstetrics and give an overview of the current knowledge of possible mechanisms of action of MgSO4. Also, I will present results from the EPICE (European Perinatal Intensive Care in Europe) cohort, which is a population-based, prospective cohort of infants born at 22+0 weeks to 31+6 weeks of gestation in one of 19 regions in 11 member states of the European Union including Sweden and Denmark. I will show surprisingly low rates of use of MgSO4 for severe preeclampsia, eclampsia and HELLP, a very low use of MgSO4 as neuroprotection and an almost non-existing use of MgSO4 as a tocolytic.

Currently, it is heavily debated whether MgSO4 can be used to protect the fetal and neonatal brain. Meta-analyses have indicated that MgSO4 administered prior to preterm birth may decrease the risk of cerebral palsy in the infant. However, this has been questioned in a trial sequential analysis, which showed that additional data would be needed before accepting MgSO4 as an evidence-based therapy for neuroprotection. I will present the study protocol and thoughts behind an ongoing randomised, controlled trial including 500 women in Denmark in giving birth before 32 weeks of gestation.



# Big Brother is Killing you and other aspects of Recurrent Pregnancy Loss

# ABSTRACT AUTHORS AND AFFILIATIONS

Henriette Svarre Nielsen Fertility Clinic and Recurrent Pregnancy Loss Unit Rigshospitalet Copenhagen University Hospital Denmark

### **ABSTRACT TEXT**

Pregnancy loss is the most common complication in early pregnancy with a frequency of 15-20% with the majority due to chromosomal abnormalities that are not compatible with life. These pregnancy losses can be considered an "internal quality assurance". In contrast to these acceptable losses are the losses of chromosomal normal fetuses. Chromosomally normal pregnancy losses increase with increasing number of consecutive pregnancy losses. A subgroup of approximately 1-3% of all women experience recurrent pregnancy loss (RPL) defined as three or more consecutive pregnancy losses. The frequency of RPL is comparable to that of other serious problems in pregnancy such as gestational diabetes and preeclampsia. RPL greatly impact the women's lives as major depression is highly prevalent among women with RPL. If an ongoing pregnancy is achieved obstetric complications are significantly increased. Women suffering RPL have a significantly increased risk of later cardiovascular disease.

Approximately half of the RPL cases remain unexplained after standard clinical investigations but immunology most likely play an important role. An example is the accumulating evidence that immune reactions against male-specific antigens are responsible for a subpopulation of women with secondary RPL after the birth of a boy (Big brother is killing you). There are limited treatment options available outside clinical trials.

This presentation will give an overview of RPL with focus on immediate and long-term consequences, clinical evaluation and handling. The field of RPL research will be introduced.



**ABSTRACT TITLE** 

# Prevention of cervical cancer-the big picture

# ABSTRACT AUTHORS AND AFFILIATIONS

Jorma Paavonen, MD, Department of Obstetrics and Gynecology University Hospital, Helsinki Finland

### **ABSTRACT TEXT**

not fiction.

The disease burden caused by human papillomavirus (HPV) is enormous. Cervical cancer is one of the leading causes of premature death in women. HPV also causes large proportion of other ano-genital and oropharyngeal cancers. Secondary prevention of cervical cancer by cytology (Pap) screening programs has turned out to be highly effective in cancer prevention in countries with orga-nized screening programs. However, most cancer cases occur in countries without such screening programs or in low income countries. Secondary prevention has multiple steps in the detection of cervical precancer, and plays no role in eradication of HPV. Most women with cervical precancer are young. The management, such as loop conization, is a surgical procedure which increases the risk for preterm delivery in subsequent pregnancies. Thus, over-treatment is a problem in many cases, not just undertreatment. Adverse pregnancy outcome increases the overall HPV disease burden. Women with abnormal pap smear findings need prolonged surveillance with repeat pap smears, colposcopies and colposcopy biopsies. These procedures cause anxiety, pain, bleeding, and other complications, and in general decrease the quality of life.

Primary prevention of HPV disease burden by vaccination is a great opportunity. End-of-study anal-yses of global efficacy trials of prophylactic HPV vaccines in young women have already been com-pleted. The current vaccines (Gardasil, a quadrivalent HPV 6/11/18 vaccine; Cervarix, a bivalent HPV 16/18 vaccine) have demonstrated extremely high performance in the prevention of HPV infec-tion and HPV disease caused by the vaccine HPV types and other closely related high risk HPV types. Both vaccines show excellent safety and immunogenicity profile. High grade cervical intraepi-thelial neoplasia (CIN3) has been used as a surrogate marker for cervical cancer in the clinical trials. HPV vaccines also protect against genital warts and vulvar and vaginal precancer as well as anal precancer in men. An extended spectrum 9-valent HPV-vaccine has proven highly effective against persistent infection and disease caused by the five non-HPV 16/18 high risk HPV types. The current vaccines are not therapeutic, thus the efficacy rates are high in young individuals not already ex-posed to HPV (HPV-naive individuals). These vaccines have already been implemented in many countries with variable vaccination coverage rates. Highest coverage rates have been obtained in countries with school-based vaccination programs. In countries were HPV vaccination programs have been implemented several years ago, real-life health benefits have already been demonstrat-ed, such as almost disappearance of genital warts or decreasing rates of abnormal pap smear find-ings in young women and decreasing need for colposcopies and colposcopy biopsies. Emerging data based on cancer registry linkages suggest that the efficacy against CIN3 translates into real-life efficacy against cervical cancer. Also, no safety signals suggesting link between HPV vaccines and autoimmune diseases have been demonstrated. HPV vaccines are the first vaccines mandated only for one gender. Yet men have equally high HPV rates and are as likely to transmit HPV to their partners. Lack of gender equity is also an ethical problem. Thus, male HPV vaccination is ethically sound and would promote equality and social re-sponsibility as well as sexual health in both genders. Australia is a model country leading the way on HPV vaccination in boys. HVP vaccination for males is well accepted by young men as well as par-ents and healthcare providers. The strikingly low HPV vaccination coverage rates in some countries are a cause of major concern, and depend on many factors. This missed opportunity of HPV vaccination must be addressed. Con-tinued evalua-

tion of vaccination promoting processes is needed so that adolescents will be ultimate-ly protected against HPV related disease burden. GAVI is already leading the way to make HPV vaccines available in low income countries. In conclusion, eradication of HPV is a true opportunity in the future, and this goal is based on facts,



# Nordic abortion collaborative study

# ABSTRACT AUTHORS AND AFFILIATIONS

Kevin Sunde Oppegaard, MD Dept. of Gynaecology, Helse Finnmark, Klinikk Hammerfest, Norway Prof Erik Qvigstad, MD Faculty of Medicine, University of Oslo and Dept. of Gynaecology, Women and Children's Division, Ullevål University Hospital, Norway Christian Fiala, MD GynMed Clinic, Vienna, Austria Prof Oskari Heikinheimo, MD Dept. Obstetrics and Gynaecology, University of Helsinki and Kätilöopisto Hospital/Helsinki University Central Hospital, Helsinki, Finland

# **ABSTRACT TEXT**

A short tale of a trial and tribulations in the frozen north. The insider story of how the first	
NFOG-funded collaborative project lurched from conception to completion. A one-off, or a recipe to	for
success?	



**Conartas:** Committee on nordic ART and safety

# ABSTRACT AUTHORS AND AFFILIATIONS

Anja Pinborg, MD, DMSc, professor Department of Obstertrics and Gynaecology, Hvidovre Hospital, University of Copenhagen Kettegaard Allé 30, DK-2650 Hvidove, Denmark anja.bisgaard.pinborg@regionh.dk

### **ABSTRACT TEXT**

The Committee of Nordic ART and Safety (CoNARTaS) is a collaboration of four Nordic countries (Sweden, Norway, Finland, Denmark) who has the responsibility of a cohort of all children conceived after assisted reproductive technologies (ART) and their mothers from 1982 to 2007. The Steering Committee comprises two representatives from each of the four Nordic countries. The cohort comprises 92.000 ART children and their mothers with information on conception method (IVF, ICSI and frozen embryo transfer (FET)) and with four parity and year of delivery-matched controls per ART child

Currently eight scientific papers have been published; one describing the methodology behind the CoNARTaS and seven papers on different short and long term outcomes such as perinatal death, children conceived by FET, cancer, trends-over-time in perinatal outcomes, older-age mothers in ART and finally four papers on preeclampsia and malformations are in preparation. More than 17 abstracts have been accepted for poster or oral presentations at international congresses.

This presentation will entail a short description on how to build up an international cooperative network and how to maintain it including standardization and pooling of data and legal aspects. Further I will give a short summary on the major scientific goals in the CoNARTaS cohort and finally the new cohort extended with the birth cohorts from 2008-2014 will be described with perspectives and future scientific aims. The CoNARTaS cohort provides a unique possibility to assess long term morbidity and mortality in children conceived after ART herein cardiovascular disease, diabetes and malignancies.



# Up-to-date on non-invasive Rh diagnostics and prophylaxis

# ABSTRACT AUTHORS AND AFFILIATIONS

Susanna Sainio FRC Red Cross Blood Service

### **ABSTRACT TEXT**

Despite receiving an anti-D injection after delivery up to 2 % of RhD-negative mothers become immunized. The majority of immunizations (55-80%) are presumed to result from spontaneous occult fetomaternal hemorrhage occurring in the third trimester. To prevent these residual cases of immunization, routine antenatal anti-D prophylaxis (RAADP) has been offered to all RhD-negative women in North America, Australia and many European countries since mid-1990s. Several studies have confirmed that RAADP is a cost-effeccient method of reducing the immunization risk by additional 50-66 %. However, until 2010s, the standard care in the Nordic countries comprised postnatal anti-D prophylaxis and antenatal prophylaxis, given only in connection with potentially sensitising events during pregnancy, such as spontaneous miscarriages, terminations of pregnancy and invasive fetal diagnostic procedures.

As a result of the discovery of cell-free fetal DNA in maternal plasma, detection of the RHD gene offers now a tool for non-invasive prenatal prediction of the fetal RhD type. Thus it is possible to target RAADP only to the RhD negative women who are carrying RhD positive fetus, helping to avoid unnecessary treatment in approximately 40% of women. Although backed up by evidence-based medicine and economics, the appropriate clinical use of anti-D prophylaxis in pregnancy is also a question of ethics and the availability and of anti-D immunoglobulin.

In Scandinavia, national RAADP programs including fetal RHD screening were implemented first in Denmark in 2010 and in Finland in2014. In Sweden, initial studies were conducted in the Stockholm region already in 2009-2011, followed by national implementation in 2015. Here, I present a review of the implementation process of a targeted RAADP program in Finland and the most exiting recent studies from Denmark and Sweden, along with current recommendations and guidelines in other Nordic countries.



#### **ABSTRACT TITLE**

# Women's reproductive rights - a global challenge

# ABSTRACT AUTHORS AND AFFILIATIONS

Prof Lesley Regan Royal College of Obstetricians & Gynaecologists

### **ABSTRACT TEXT**

"Saving the lives of women and enhancing their well- being is less a function of technology and sophisticated medical skills than of changes in the way that women are offered access to, and benefit from, high standards of care."

The Human Rights Workshop is a framework for the FIGO Human Rights/Women's Health Project. It is based upon the United Nations Declaration of Human Rights.

In essence, the approach seeks to have clinicians and professional health educators consider how human rights and healthcare outcomes are related to their own health, in the care of their patients and in the care of all citizens of their communities and states.

During this interactive session you will be invited to join a table of congress delegates and meet your workshop facilitator. Together you will be shown how to perform an integrated human rights checklist of your last personal health care encounter. At the end of this section you will be able to demonstrate how many human rights you took for granted during this health care encounter.

Your group will then move on to explore a health care scenario using a human rights based approach. You will be given a clinical case study and a list of reproductive health care competencies that will describe how to apply the principles of human rights to the daily practice of women's health care. A checklist for quality care integrating Human Rights and Health will also be provided along with 5 essential questions to be discussed for each case study. Www.Glowm.com

Learning objectives. During this session you will be given the training required to:-

- a) Describe standards of quality care as competencies that apply principles of human rights to the daily practice of women's health care
- b) Identify the Human Rights posed by the case scenario
- c) Identify and discuss the responses of each of the health care providers and how they respect or threaten the rights of the woman applicable to the scenario.
- d) Identify and discuss whether the health care system protected or infringed the rights of the woman in this particular encounter.

At the end of the workshop you will be invited to participate in a debriefing session during which your comments, criticisms and suggestions for improving the workshop will be welcomed. Your feedback is essential to help us progress this important FIGO educational project. www.Glowm.com



How are rape victims taken care of in the Nordic countries?

# ABSTRACT AUTHORS AND AFFILIATIONS

Berit Schei, St. Olavs Hospital, Trondheim University Hospital, Norwegian University of Science and Technology (NTNU), Norway

#### **ABSTRACT TEXT**

Victims of rape need emergency health care services including treatment of injuries, prevention of sexual transmitted infections and pregnancies. Also, victims need close follow up in order to reduce the harmful psychological affects and long term disability. In order to optimize the legal process following the event, collection of biological trace evidence during the examination is needed as well as the systematic documentation of injuries. The development in the Nordic countries of specialized Sexual Assault Care Centers has been aimed at bridging the health care needs with the needs of the legal system. There are huge variations between the Nordic Countries as to how the services for victims of rape have been organized. In some of the Nordic countries, there is a formal specialization in forensic medicine. Hence forensic services have traditionally cared for the victims of rape. Since this type of service was mainly adapted to the needs of victims who already had reported to the police; the acknowledgment of lack of services for victims not reporting to the police, sparked a discussion on how to organize the services. In countries as Norway, without a specialization in forensic medicine, the lack of forensic knowledge and skills among clinicians became the base for discussion. Still, after several decades of discussions; models of care vary between the Nordic countries, as well as within the country. In spite of organizational differences between the Nordic countries, gynecological skills and knowledge are crucial in order to optimize services.



# Fetal and Perinatal Postmortem Imaging and Minimally Invasive Autopsy

# ABSTRACT AUTHORS AND AFFILIATIONS

NJ Sebire Great Ormond Street Hospital and UCL London UK

### **ABSTRACT TEXT**

Fetal and perinatal autopsy examination provides additional information regarding the underlying diagnosis or mechanism of death in around 10-50% of cases depending upon clinical circumstances. Nevertheless, in the United Kingdom, the majority of parents no longer consent to standard traditional autopsy examination. The reasons for this are complex but appear related to feelings that the infant has 'suffered enough' and an unwillingness to allow large incisions to be made.

For these reasons, and in order to offer something which may be acceptable to do his parents for whom standard autopsy examination is not acceptable, the use of a range of cross-sectional post-mortem imaging approaches has been evaluated. The largest study to date suggests that in the fetal population the final diagnosis or cause of death has a 95% concordance based on post-mortem imaging and noninvasive assessment compared to traditional autopsy examination. Studies are ongoing at present to determine the additional diagnostic yield of limited image guided or endoscopic tissue sampling.

In addition, a range of potentially novel imaging approaches are being developed for use in the post-mortem setting which are not applicable in clinical circumstances in life, but may provide unique information regarding the three-dimensional pathogenesis of a range of diseases. This presentation provides an overview of the current state of post-mortem imaging and less invasive autopsy in fetuses and infants including future likely directions.



# Preterm delivery in women of migrant origin

# ABSTRACT AUTHORS AND AFFILIATIONS

Ingvil Krarup Sørbye, Norwegian Advisory Unit for Women's Health, Department of Obstetrics, Oslo University Hospital, Norway.

### **ABSTRACT TEXT**

Preterm delivery is an important cause of neonatal death and disability; however, the etiology is poorly understood. Preterm delivery rates vary substantially between countries and regions, with a consistently higher risk among some ethnic groups. Rates in high-income settings also vary according to the mother's country of origin; however, to which degree differences are influenced by physiological or pathological factors remains contested.

Using data from Norway, preterm delivery rates in the main migrant groups are presented, as well as by subcategories of spontaneous and iatrogenic preterm delivery and by gestational age groups. Preterm delivery rates in Norway after migration are compared to the corresponding rates in the country of origin, demonstrating the lower risk in most groups after migration. The impact of migrants' length of residence post-migration is also explored.

Potential mechanisms for disparities in preterm delivery rates between population groups are discussed, such as misclassification bias, disparities in average gestational length and the prevalence and detection of fetal and maternal morbidity.

When assessing preterm delivery rates across ethnic and migrant groups, the use of standardized, ultrasound-based pregnancy dating method is crucial. Current evidence does not justify the provision of a different clinical care approach to minority or migrant women solely based on their country of origin; however, these labels may serve as flags for further inquiry on individual risk factors and a detailed obstetric history.



#### Intraamniotic infection – state of art

# ABSTRACT AUTHORS AND AFFILIATIONS

Vedran Stefanovic, A/Professor, Fetomaternal Medical Center, Department of Obstetrics and Gynecology, Helsinki University Hospital, Finland

### **ABSTRACT TEXT**

Preterm labour (PTL) is a syndrome, but there is enough evidence that the major cause is intra-amniotic infection (IAI) and/or inflammation . Clinical chorioamnionitis occurs in only less than 20% of pregnancies complicated by IAI and/or inflammation. Consequently, substantial proportion of fetuses of women with preterm premature rupture of membranes (PPROM) and PTL with intact membranes remaining in utero are exposed to the persistent or developing inflammatory process with possible development of fetal inflammatory response syndrome (FIRS) which leads to the short and long-term adverse outcome. Subclinical IAI in patients with either PTL or PPROM is proposed as the strongest predictor of adverse outcome, even in the absence of demonstrable microbial invasion of the amniotic cavity (MIAC). According to the current literature, amniocentesis for determination of intraamniotic inflammation and IAI has been established as a part of routine care in women with high risk of PTL (cervical shortening and/or bulging membranes with intraamnionic sludge), in those with threatening preterm labour with intact membranes and women with PPROM. Modern techniques of molecular microbiology should be used concomitantly with the culture methods and antibiotic treatment should be covering the anaerobic microbes, as well. Waiting for classical chorioamnionitis signs and symptoms to occur should be abandoned in the modern obstetrical management of such patients. Despite of the presence of three small observational studies that showed improved neonatal outcome when amniocentesis was used as a part of clinical protocol, randomized trials are needed to determine the best timing of delivery.



#### **ABSTRACT TITLE**

# Symptoms of anxiety in women with PCOS

# ABSTRACT AUTHORS AND AFFILIATIONS

Elisabet Stener-Victorin I PhD, Associate Professor Karolinska Institutet Dept of Physiology and Pharmacology I Reproductive Endocrinology and Metabolism

#### **ABSTRACT TEXT**

A woman with polycystic ovary syndrome (PCOS) display an impaired emotional well-being and reduced health related quality of life and increasing evidence demonstrate that a large proportion of these women present clinical relevant psychiatric ill-health. Symptoms of anxiety and depression, without a diagnosis, may significantly impact a person's emotional well-being and may have clinical implications.

Although higher prevalence of symptoms of anxiety in women with PCOS, there is no direct explanation for the cause of this association. Sub-group analyses in earlier, smaller studies demonstrate that hirsutism, infertility and obesity, all common clinically features of PCOS, does not explain the association between PCOS and emotional distress. In recent larger population based study, hirsutism was shown to be a strong contributor indicating that androgen excess may drive psychiatric ill-health. Although circulating testosterone has not been found to be significantly related to effect size variations in meta-regression analyses, it may be due to small sample size and that methods used to determine sex steroids have low sensitivity and specificity.

In experimental setting, maternal androgen exposure cause an anxiety-like behavior in female and male rats at adult age. The anxiety-like behavior was accompanied by disordered androgen receptor function in amygdala, together with changes in estrogen receptor-alpha, serotonergic and GABAergic genes in amygdala and hippocampus. These findings may be critical in the understanding of how maternal androgen excess has the potential to increase the risk of developing anxiety disorders in daughters and sons of PCOS mothers.

The current clinical and experimental knowledge will be presented.

#### References

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# **ABSTRACT TITLE**

# Placental pathology in intra-uterine fetal demise.

#### ABSTRACT AUTHORS AND AFFILIATIONS

Thora S Steffensen, M.D. Tampa General Hospital Tampa, FL 33606 USA

### **ABSTRACT TEXT**

Stillbirth (intra-uterine fetal demise) is an adverse pregnancy outcome that up until a few years ago did not receive much attention. Epidemiologic studies have reported association between placental disorders and stillbirth. Between 11 and 65% of stillbirths have been attributed to a placental cause depending on study. Classification systems with increased emphasis on placental findings, when used, will reduce the proportion of unexplained stillbirths, which emphasizes the importance of histopathologic examination of the placenta in cases of stillbirth.

Lack of standardized definitions of placental abnormalities has impaired assessment of the significance of individual placental abnormalities, but recent consensus criteria (Amsterdam Placental Workshop Group 2014 meeting) for placental diagnosis may facilitate further progress in this area. Based on the 2014 Amsterdam Placental Workshop Group criteria on placental classification, 216 singleton stillbirths (gestational age > 22 weeks) over a 9 year period (2007-2015) examined with a full autopsy at a large teaching hospital were reviewed. The main findings will be reviewed, with emphasis on the group of fetuses that were of appropriate weight for gestational age, and clinically significant placental pathology demonstrated with images. Issues related to communicating the autopsy findings to the obstetrician will also be discussed.



# Contraception – is sexuality in jeopardy?

# ABSTRACT AUTHORS AND AFFILIATIONS

Inger Sundström Poromaa1, Kristina Gemzell Danielsson2, Marie Bixo3, Lena Marions2, Cecilia Lundin1, Jan Brynhildsen4, Agota Malmborg4, Ingela Lindh5, Hanna Bengtsdotter 6, Izabella Jawad6.

1Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden 2Department of Women's and Children's Health, Karolinska Institute, Sweden 3Department of Clinical Health, Obstetrics and Gynecology, Umeå University, Umeå, Sweden

### **ABSTRACT TEXT**

Objective: Female sexuality is influenced by cultural, socioeconomic and biological factors, and among the latter, hormonal status is thought to play a role. Hormonal contraception may positively influence sexuality by improving dysmenorrhea, acne and hirsutism, but may also have negative effects in the form of reduced lubrication and dyspareunia. In young women, approximately 15% of hormonal contraceptive users report sexual side effects, and 8% of women who had discontinued hormonal contraceptive stated that the reason was sexual side effects. However, results are inconsistent and placebo-controlled trials are lacking. The only contraceptive method thus far with reportedly neutral, or even positive effects, is the hormonal intrauterine device.

Methods: We report on an investigator-initiated, multi-center, randomized, double-blinded, placebo-controlled study of 202 healthy women in need of contraception. Women were randomized to a COC (1.5 mg estradiol and 2.5 mg nomegestrolacetate) or placebo for three treatment cycles. Main outcome measure was the McCoy Female Sexuality Questionnaire which was filled out prior to randomization, during the final treatment cycle, and one month after the end of the trial.

Results: Prior to randomization, no difference in sexual function was noted between women randomized to placebo or active treatment. Combined oral contraceptive use was associated with small, but significantly lowered scores for vaginal lubrication, sexual interest, and satisfaction with sexual activity. Orgasm, satisfaction with sex partner, and sexual attractiveness scores did not differ between groups.

Conclusions: Combined oral contraceptives use is associated with reduced functioning in several aspects of sexual function. Further analyses on contributing factors to these results are ongoing.



# Consequences of rape

# ABSTRACT AUTHORS AND AFFILIATIONS

Anna Tiihonen Möller, MD, PhD Stockholm South Hospital Sweden

### **ABSTRACT TEXT**

Each year, approximately 3-4% of the Swedish female population experiences being raped. A rape is one of the most traumatic experiences a person can be exposed to and is associated with the highest risks of developing severe mental health problems such as for example posttraumatic stress disorder and depression.

Victim resistance during rape is often critical issues in handling of and recovery from a sexual assault. Active resistance is by many still looked upon as the "normal reaction" during rape. However, studies have indicated that just as animals, humans exposed to extreme threat can react with a state of Tonic Immobility (TI) characterized by an involuntary, temporary state of motor inhibition, analgesia, and suppression of vocalization. Our results show that as much as 70% of the women in our clinic report a significant immobility reaction during the rape. Prior trauma history and psychiatric treatment history is found being associated with this reaction and TI is also associated with the development of PTSD. This information is useful not only for the legal system but also for our patients. As self-blame and feelings of guilt is common after sexual assaults, especially if not having made any resistance, this knowledge should be used in psycho educational treatment post assault.



# The choice of suture material in vaginal prolapse surgery

# ABSTRACT AUTHORS AND AFFILIATIONS

Ida Bergman, MD/Department of Clinical Science and Education at Södersjukhuset, Karolinska Institutet and the Division of Obstetrics and Gynecology at Södersjukhuset, Stockholm Sweden; Marie Westergren Söderberg, MD, PhD/Department of Clinical Science and Education at Södersjukhuset, Karolinska Institutet and the Division of Obstetrics and Gynecology at Södersjukhuset, Stockholm Sweden; Anders Kjaeldgaard, MD, PhD/ Department of Clinical Sciences, Karolinska Institutet, Stockholm, Sweden; Marion Ek, MD, PhD/Department of Clinical Science and Education at Södersjukhuset, Karolinska Institutet and the Division of Obstetrics and Gynecology at

### **ABSTRACT TEXT**

Introduction: The optimal suture material in traditional prolapse surgery is still an open question. Our aim was to investigate if there is a difference in symptomatic recurrence after anterior and posterior colporraphy comparing the use of rapidly (RA) versus slowly absorbable (SA) sutures.

Method: A population-based longitudinal cohort study with data from the Swedish National Quality Register for Gynecological Surgery. A total of 1107 women who underwent anterior colporraphy and 557 women who underwent posterior colporraphy between Sept 2012-2013 were included. Two groups in each cohort were created based on which suture material was used. Pre- and postoperative prolapse related symptoms and patient satisfaction were assessed. In-between group comparisons were performed using univariate and multivariate logistic regression.

Results: We found a significantly lower rate of symptomatic recurrence one year after anterior colporraphy in the SA suture group compared with in the RA suture group, 50/230 (22%) vs 152/501 (30%), odds ratio 1.6 (CI 1.1-2.3), (p = 0.01). The SA group had also a significantly higher patient satisfaction rate, 83 % vs 75 %, oddsratio 1.6 (CI 1.04-2.4), (p = 0.03). In the posterior colporraphy cohort there was no significant difference between the suture materials, neither in symptomatic recurrence rates nor in patient reported satisfaction rates.

Conclusions: Use of slowly absorbable sutures decreases the odds for having a symptomatic recurrence after an anterior colporraphy compared to the use of rapidly absorbable sutures. In posterior colporraphy the choice of suture material does not affect the rate of symptomatic recurrence.



Breech presentation: a risk factor for cerebral palsy?

# ABSTRACT AUTHORS AND AFFILIATIONS

Solveig Bjellmo, Møre and Romsdal Hospital Trust, Dept. of Obstetrics and Gynecology, Ålesund, NTNU; Marit Martinussen, Dept. of Laboratory Medicine, Children's and Women's Health (LBK), Trondheim, NTNU; Pål Richard Romundstad, Department of Public Health, Trondheim, NTNU; Guro Andersen, Vestfold Hospital Trust, Cerebral palsy Register of Norway; Tønsberg Runa Heimstad, St Olavs hospital, Trondheim University Hospital, LBK. Sissel Hjelle, Møre and Romsdal Hospital Trust, Dept. of Obstetrics and Gynecology, Ålesund; Torstein Vik, LBK, Trondheim, Norwegian University of Science and Technology (NTNU).

### **ABSTRACT TEXT**

Aim: To study whether breech vaginal delivery is a risk factor for cerebral palsy (CP).

Material: Perinatal data on 15 205 singletons in breech presentation among 479 648 singletons born at term without congenital anomalies during 1999-2008 were abstracted from the Medical Birth Registry of Norway and was merged with clinical data from the Cerebral Palsy Register of Norway. Mode of delivery was recorded as planned cesarean section (CS), emergency CS and vaginal delivery. Odd ratios (OR) with 95% confidence intervals (CI) were calculated as estimates of the risk for CP as well as for early neonatal mortality (ENM) and neonatal mortality (NNM) among children delivered in breech vaginally or with planned CS, using cephalic presentation as the reference.

Results: Among the children born in breech 17 had CP (1.1 per 1 000). Compared with cephalic presentation (0.98 per 1 000), the overall risk for CP in breech deliveries was not increased (OR 1.1; CI: 0.7-1.8), and this finding was independent of mode of delivery (vaginal delivery: OR: 1.1; CI: 0.5-2.8). However, breech vaginal delivery was associated with a nearly four-fold relative risk for NNM (OR: 3.7; CI: 1.6 -8.3), and nearly five-fold for ENM (OR: 4.7; CI: 1.9 – 11.5).

Conclusion: Breech delivery is not a risk for CP in this study. However, the higher risks for ENM and NNM following vaginal deliveries are of concern. Further studies are needed to explore if the latter findings are caused by a higher proportion of lethal anomalies/complications among fetuses in breech position.